Faculty of MedicineMasaryk UniversityBrnoCzech RepublicDepartment of Functional Diagnostics and Rehabilitation

PROCEEDINGS SYMPOSIUM

NONINVASIVE METHODS IN CARDIOLOGY

Edited by: F. Halberg, T. Kenner, B. Fišer, J. Siegelová

2007

The Symposium takes place under the auspices of

Prof. PhDr. Petr Fiala, Ph.D., Rector of Masaryk University Brno

Prof. MUDr. Jan Žaloudík, CSc., Dean of Faculty of Medicine Masaryk University Brno

SPONSORS:

Kardio-Line Pliva – Lachema Medicom International s.r.o. PRO.MED.CS Praha a.s.

ISBN 978-80-7013-463-4

CONTENS

MINIMAL REQUIREMENTS FOR DIAGNOSTIC BLOOD PRESSURE RECORDING <i>Kenner T</i>	5
GLOBAL CHALLENGES OF MONITORING VASCULAR VARIABILITY AND SPACE WEATHER <i>Halberg F</i> .	10
CHRONOMICS OF SOLAR ACTIVITY AND PERINATAL EVENTS Cornélisen, G.	
1-DAY VERSUS 7-DAY CHAT: INDICATORS OF PHYSIOLOGICAL VERSUS PUTATIVELY PATHOLOGICAL BLOOD PRESSURE DYNAMICS Schwarzkopff O	
GEOGRAPHICALLY PROXIMAL VERSUS GLOBAL GEOMAGNETIC REFERENCE VALUES FOR BIOLOGICAL STUDIES Cornélisen G	
CUGINI'S MINIMAL CHANGE HYPERTENSIVE RETINOPATHY, RESOLVED CHRONOBIOLOGICALLY WHILE DIPPING FAILS, SUPPORT THE CONCEPT OF "PRE-HYPERTENZION" Cornélisen G	
CONFIDENCE INTERVALS ASSESS THE CONGRUENCE OF PERIODS CHARACTERIZING MANY NEONATAL TRANSDISCIPLINARY NIKITYUK CYCLES <i>Malkova I</i> .	62
RENAL FAILURE AND LONG-TERM EXERCISE TRAINING - A REVIEW <i>Kohzuki M</i>	65
NON-INVASIVE IMAGING TECHNIQUES IN CASES OF CARDIAC FAILURE <i>Wolf, J-E</i>	68
EFFECT OF LOW VOLTAGE ELECTRICAL STIMULATION ON ANGIOGENESIS IN RAT SKELETAL MUSCLE Nagasaka M.	
CIRCADIAN BLOOD PRESSURE VARIATION ANALYZED FROM 7-DAY MONITORING Siegelová J.	75
ANALYSIS OF BAROREFLEX FUNCTION BY MEANS OF MATHEMATICAL MODEL <i>Fišer B</i>	
FUNCTIONAL IMPAIRMENT AND QUALITY OF LIFE IN PATIENTS AFTER ACUTE STROKE <i>Tarasová M</i>	
WATER IMMERSION AND PHYSIOTHERAPY IN PATIENTS WITH PARKINSON DISEASE <i>Pospíšil P.</i>	
PHYSIOTHERAPY AND CIRCADIAN BLOOD PRESSURE VARIABILITY Havelková A.	
FITNESS IN MULTIPLE SCLEROSIS Konečný L.	
PHYSIOTHERAPY LASTING THREE MONTHS IN PATIENTS AFTER STROKE <i>Bártlová B.</i>	131
EXERCISE TRAINING IN OBESE PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE Pochmonová J.	139
EXERCISE TRAINING IN MEN AFTER CORONARY ARTERY BYPASS SURGERY Chludilová V.	
FUNCTIONAL EVALUATION IN CHILDREN WITH CEREBRAL PALSY AFTER 6-MONTHS THERAPY <i>Drlíková L</i> .	

MINIMAL REQUIREMENTS FOR DIAGNOSTIC BLOOD PRESSURE RECORDING

Thomas Kenner Physiologisches Institut, Graz

Some historical considerations

The first device which has been successfully used in clinical practice for indirect blood pressure measurement was a tonometer invented 1880 by Samuel von Basch in Vienna. A tonometer "imitates" the palpating finger which is feeling the pulse.

One hundred and eleven years ago, in 1896, Scipione Riva Rocci, an Italian pediatrician, published his invention, the most widely used cuff technique for blood pressure measurement in a local Italian clinical journal.

One problem in the application of both cuff or tonometer has to do with the criterion for the reading of pressure values. The most interesting to be mentioned are: feeling the pulsations, hyperemia and reddening of the finger, Korotkow sounds (1905), and the oscillatoric criterion (von Recklinghausen, 1906).

An important problem concerning all techniques of indirect blood pressure measurement is the possible influence on the result of the dimension and of the tissue properties of the location of the measurement.

A marked step towards the non-invasive recording of pulsatile arterial pressure was a technique, which was developed and described by the physiologist Richard Wagner in the 1940-th. His technique of arterial unloading was a predecessor of the finger-cuff technique by Penaz in 1969 (5).

The distension of arteries, in particular the volume pulse, can be used as an indicator of blood pressure. As an example I have reported in 1959 an attempt to calculate the value of the peripheral resistance and thus the pressure in the pulmonary artery from X-ray recordings with the socalled electrokymographic technique (2). In this case it was necessary to use a mathematical model for the interpretation of the results. As described by Wetterer and Kenner (1968) transmission line models can be applied to determine the frequency dependence of the pressure transformation including the so called peripheral amplification which is due to pulse wave reflections (7). Recently O'Rourke (1996) used

the application of a transfer function to determine the aortic root pressure from tonometric measurements of the radial pressure pulse (4).

One further important group of techniques for the indirect measurement of blood pressure is based on the relation between arterial pressure and pulse wave velocity. From a statistical viewpoint the pulse wave velocity is a function of age and blood pressure, as was nicely shown by Schimmler already in 1965 (7). Since the relation between pulse wave velocity and pressure is unique in each individual, a special calibration has to be made. Phenomena like hysteresis have to be taken into account, which means that the result of the measurement depends on the trend of the blood pressure variation.

The influence of gravity on the static pressure in all arteries should be mentioned when blood pressure recording is discussed. The difference between the arterial pressure values at the level of the head and of the kidney in an upright and a reclined position is remarkable and may amount to about 45 mm Hg. The first observations concerning the effect of gravity on the pulse contour have been published by J. von Kries in 1891 (6). Raising and lowering of the arm may lead to a variation of the local pressure in the radial artery of about 50 to 70 mmHg, depending on the length of the arm.

Conditions concerning the application of different techniques

The availability and application of non-invasive monitoring of blood pressure and the development of specific technical devices leads to an important and interesting discussion. This discussion has to include the answer to the following questions:

1) What are the necessary limits of precision and/or of accuracy of the measurement of single pulses?

2) What are the constraints with respect to the limits of the duration of periods of application of continuous recording?

The cuff technique of Riva Rocci (3)

The problem of sufficient and/or necessary accuracy and precision is a matter of discussion related to all non-invasive techniques. The Riva-Rocci-Korotkow technique can be considered reasonably accurate but not highly precise (3). The same is true for the oscillometric measurement with a cuff device, which is mostly used for blood pressure measurement by automatic devices.

The "classical" techniques to record systolic and diastolic blood pressure values by application of a brachial cuff has a low precision. However, the long term application is nearly unlimited in that the duration depends on the tolerance of the measured person. For the purpose of every day control and also for long duration measurement the described properties are highly sufficient.

The tonometric technique propagated by O'Rourke (4)

It turns out that the technique developed and described by O'Rourke and coworkers which is now available under the name Sphygmocor® is designed to attain high precision in representing the calculated contour of the central aortic pressure pulse (4). The arterial pulses are recorded by a hand-held tonometer at the radial artery. The central aortic pressure contour and the corresponding pressure values are then calculated by application of a transfer function. The high precision is important in order to permit to estimate particular indices e.g. the amplification index. This index is assumed to be of importance for the diagnostic purposes. With respect to an application of extended time, the pulse recording at the radial artery by a tonometric technique limits the duration of the measuring.

The questions concerning the reliability and the diagnostic value of the calculated pressure contour and of the new indices appear to me to be quite a bit subjective. As discussed extensively in the book by Wetterer and Kenner (7), there exist techniques for the quite precise estimation of pulse transmission and reflection, which seem tome more reliable than the new indices.

The arterial unloading technique invented by Penaz (5)

The application of the finger cuff as invented by Penaz was technically modified by several authors and companies, and was recently improved by the company CNSystems® for continuous pulsatile pressure recording in a device "Task force monitor"®. The main use of this device is the recording of reactions to orthostatic load by tilt table test. However, from a more general aspect, any device which is based on the Penaz-technique is capable to be applied for long term experiments.

The limits and demands of duration

Since there exists a well-known circadian variability of blood pressure (1) – and of course many other biological variables e.g. like heart rate – it seems absurd to try a reliable diagnostic observation from just one or a few pressure measurements taken within the period of a physicians visit.

Normal and pathological variations of the circadian variation of blood pressure may be important for the diagnosis of cardiovascular diseases. Therefore, a 24 hour recording of the blood pressure appears to be the minimum demand for diagnostic purposes. Halberg (1) demands even longer periods of recording, since some effects can only be understood if e.g. circaseptan or even longer periods can be included in the time of observation.

In general, a compromise between the diagnostic necessity and the tolerance of the patient must be agreed upon.

The consequence of such necessities is the fact, that the classical Riva Rocci method as well as the improved arterial unloading techniques are superior to modern techniques of tonometric recording and estimation of indices.

Abstract

The condition for a minimal diagnostic requirement for blood pressure recording, is the possibility to continuously observe blood pressure during at least 24 hours.

An analysis of available non-invasive techniques for blood pressure recording shows, that the "classical" Riva Rocci method is still superior to more modern techniques, which restrict the time of "high accuracy recording" to less than a few minutes. Also, an improved arterial unloading technique, as invented by Penaz, can under the given condition also be recommended for diagnostic purposes.

Supported by MSM0021622402

Literature

 Cornelissen G, Halberg F (1994): Introduction to Chronobiology. Medtronic, University of Minnesota

(2) Kenner T (1959): Über die elektrokymographische Pulskurve der Arteria pulmonalis.

Arch Kreislaufforschung 29: 268 - 290

(3) Kenner T, Gauer OH (1962): Untersuchungen zur Theorie der auskultatorischen Blutdruckmessung.

Pflügers Archiv 275: 23 - 45

(4) O'Rourke MF (1996): Radical assessment of arterial pressure.Z. Kardiol 85: Suppl 3: 134 – 135

(5) Penaz J (1969): Czech Patent 133205, Prague

(6) Von Kries J (1892): Studien zur Pulslehre.Akademische Verlagsbuchhandlung von J.C.B. Mohr, Freiburg

(7) Wetterer E, Kenner T (1968): Dynamik des Arterienpulses.Springer Verlag, Berlin-Heidelberg-New York

GLOBAL CHALLENGES OF MONITORING VASCULAR VARIABILITY AND SPACE WEATHER

Franz Halberg¹, Germaine Cornélissen¹, Robert B. Sothern¹, Dewayne Hillman¹, George S.

Katinas¹, Ellis S. Nolley², Larry A. Beaty², Kuniaki Otsuka³, Jarmila Siegelova⁴, Frank

Greenway⁵, Alok Gupta⁵, Miguel Revilla⁶, Anatoly Masalov⁷, Elena V. Syutkina⁸, Inna Malkova⁸, Sergei M. Chibisov⁹, Othild Schwartzkopff¹ and Earl E. Bakken¹⁰

¹University of Minnesota, Minneapolis, MN, USA

²Phoenix Group, Institute of Electrical and Electronics Engineers, Minneapolis, MN, USA (<u>http://www.phoenix.tc-ieee.org;</u> cf. <u>http://www.sphygmochron.org/</u>)

³Tokyo Women's Medical University, Medical Center East, Tokyo, Japan ⁴Masaryk University, Brno, Czech Republic

⁵Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA, USA ⁶University of Valladolid, Spain

⁷Lebedev Physical Institute, Moscow, Russia

⁸Scientific Center for Children's Health, Academy of Medical Sciences, Moscow, Russia

⁹People's Friendship University of Russia, Moscow, Russia

¹⁰North Hawaii Community Hospital Inc., Kamuela, HI, USA

Objective

In keeping with Walter Kofler's extended view of health and ecology (1), focus on time structures, i.e., chronomes extends into (and assesses) the everyday variability of the biosphere and into its complementary cosmos by

1. the current provision of computer-aided analyses (in exchange for the data), initially mainly of blood pressures (BP) and heart rates (HR), not only for clinics and care providers, but above all for the public, for self-helpers in individualized vascular health care;

2. by a service of transdisciplinary comparative analyses of a vast array of physiological and archival time series, and by

3. using the accumulating information base for a cartography leading to an atlas with reference standards as a requisite for diagnoses already being delivered of otherwise silent vascular variability disorders (VVD) that may coexist as a vascular variability syndrome (VVS);

4. seeking further improvements of individuals' as well as populations' health and well-being, by

a. obtaining improved gender, age and ethnicity-qualified reference values for BP and HR now in the light of decades-long (2, 3) and eventually for lifelong outcomes, and

b. obtaining refined harbingers of hard events;

c. mapping social time structures including religious proselytism (4), crime (5), terrorism (6) and other aggression (7), all possibly related to unseen, not consciously felt magnetic and other nonphotic as well as photic influences,

d. analyzing any triggering (as Chizhevsky put it), and/or any more consistent roles played by the cosmos, such as pulling, driving or amplifying built-in frequencies (8) in important events among human affairs related to the ills of society;

5. and eventually for developing countermeasures for the undesirable consequences of unseen magnetics and other nonphotics, just as we heat and air condition against seen and felt photic and thermal effects.



Status quo

An international BIOCOS project (on The BIOsphere and the COSmos) currently provides a multilingual, transdisciplinarily educative and analytical worldwide service. Thereby, BIOCOS renders a diagnosis relating to high BP more reliable (a below) and/or detects other different forms of vascular variability disorders (VVD), including



a. MESOR-hypertension (MHT), as a diagnosis of consistently high BP based on an account of variability (vs. "hypertension" that may lack such a safeguard) and

b. CHAT, short for circadian hyper-amplitude-tension. Both MHT and CHAT are diagnosed on the basis of a comparison with reference standards from gender- and age-matched peers;

c. an excessive above-threshold (of 60 mm Hg) pulse pressure (EPP);

d. a deficient heart rate variability, DHRV, and

e. ecphasia, an odd timing of the circadian rhythm of BP but not of that of HR. Irrespective of kind of VVD, Figures 1 and 2 show how often the first 4 (a-d) VVDs coexist, and that as yet all 5 conditions have not been found to coexist in the same person in a population of 1171 people.





Figure 2.





Figure 3 illustrates, for two populations, the N of cases in each category and Figure 4 shows a high risk of severe vascular disease, notably when these VVDs, other than a high BP (MHT), coexist. Coexistence then constitutes a vascular variability syndrome (VVS) with 2 or more (up to 4) components without or usually with end organ damage. A VVD or a VVS is silent to the conventional care provider as well as the care receiver. In the absence of MHT, VVDs can characterize prehypertension, Figure 5 (9), and prediabetes, i.e., individuals with a fasting hyperglycemia and an impaired morning oral glucose tolerance test (10), Figure 6a-d (11). VVDs

can further constitute complications for patients with MHT who are being treated for it. It is important for "hypertensives" and validated patients with MHT alike to ascertain that the treatment, albeit reducing or eliminating, e.g., a high BP does not do so at the cost of inducing another VVD in BP and/or HR with a still higher risk of hard events.

If these services, offered by BIOCOS in exchange for the data analyzed, can be extended on an appropriate scale, the accumulating transverse data could also help track biological effects of solar variability analyzed by time-structural chronomics and may complement the lessons learned thus far longitudinally. The discovery of transyears is a case in point, prompting a "remove and replace" approach in physiology, Figure 7, where surgery is replaced by solar variability. We document a. the driving by the solar wind of a spectral component (transyear with a period of \sim 1.3 years) in BP (by finding its partial loss when the same component is no longer detected in the solar wind), and b. the built-in nature insofar as part of it persists, albeit with some damping, when





*Results from 6-year prospective study on 297 (adding all Ns) patients classified by 3 risks (8 circles), supported by findings on total of 2,807 subjects for total of over 160,769 sets of blood pressure and heart rate measurements. Data from K Otsuka.

Figure 4.

Figure 4. CHAT is one of several conditions related to the variability in blood pressure (BP) and/or heart rate (HR) that is associated with an increase in vascular disease risk. The circadian (or preferably circaseptan profile) with too large a pulse pressure (the difference between systolic [S] BP and diastolic [D] BP, i.e., between the heart's contraction or relaxation, or the extent of change in pressure during a cardiac cycle) and a decreased HR variability (gauged by the standard deviation of HR) in relation to a threshold, preferably eventually all in gender- and age-matched peers are two other risk conditions (as is an abnormal circadian timing of BP but not of HR, not shown). Vascular disease risk is elevated in the presence of any one of these risk factors, and is elevated further when more than a single risk factor is present, suggesting that these abnormalities in variability of BP and HR are mostly independent and additive. Abnormalities in the variability of blood pressure and heart rate, impossible to find in a conventional office visit (the latter aiming at the fiction of a "true" blood pressure), can raise cardiovascular disease risk (gauged by the occurrence of a morbid event like a stroke in the next six years) from 4% to 100%. By comparison to subjects with acceptable blood pressure and heart rate variability, the relative cardiovascular disease risk associated with a decreased heart rate variability (DHRV), an elevated pulse pressure (EPP) and/or circadian hyper-amplitude-tension (CHAT) is greatly and statistically significantly increased. These risks, silent to the person involved and to the care provider, notably the risk of CHAT, can usually be reversed by chronobiologic self-help, also with a non-pharmacologic approach in the absence of MESOR-hypertension.





* Comparison of "Truly Normotensive Subjects" (TNS) and "Putatively Normotensive Subjects" (PNS) with Incipient Signs of Hypertensive Retinopathy. Data from P Cugini et al. (International Ophthalmology 1999; 22: 145-149). Minimal retinal alterations, presumably reflecting an increased vascular disease risk, are NOT associated with abnormal DNR, but rather with the chronobiologically predicted elevation in circadian BP amplitude (middle, right).

Figure 5

Figure 5: Subjects with minimal change retinopathy have daytime mean values of systolic blood pressure (SBP) higher than those without retinopathy (top left); a dipping classification not only fails to resolve prehypertension, but misleads, being normal in the presence of a minimal-change retinopathy, yet abnormal in the absence of minimal change retinopathy (bottom). Chronobiology shows an increase in circadian amplitude as well as MESOR, in the presence (PNS) versus the absence (TNS) of minimal retinopathy, top right. \mathbb{C} Halberg.

the solar wind loses that component. Transyears gain in applied importance, when in some geographic locations they replace a calendar-year component in the spectrum of sudden cardiac death (12) and suicides (13), yet overall in all available data as a whole, the photic, thermic and social calendar dominates worldwide. Transyears again gain even more in importance when, in the biggest MIPT Terrorism Knowledge Base (1968-2005), they dominate the spectrum in the absence



Altered Blood Pressure and Heart Rate Variability in "Prediabetes" but not in Normoglycemia

Incidence of Altered Blood Pressure Dipping* Similar in "Prediabetes" and in Normoglycemia



Figure 6a. Several vascular variability disorders characterizing prediabetes (right half) may be part of a premetabolic syndrome. Note that they are missing in the (small sample of) six control subjects, with normoglycemia and an acceptable glucose tolerance test (left half) (11). See also Figures 6c and d. Data of A. Gupta. © Halberg.

Figure 6b. A dipping classification fails to separate prediabetes from normoglycemia (when a chronobiologic approach does so, Figure 6a) (11). Dipping also fails in other situations (and misled in the case of Cugini's prehypertension [Fig. 5]). Data of A. Gupta. © Halberg. of a calendar-year component (6), as they do in mental function of a human adult (14). This figurative telescopy and microscopy in time now rests mainly on longitudinal (decades-long) data from a few test pilots and decades-, and in a few cases centuries-long archived data from the biosphere and its cosmos, but a stream of hybrid (linked cross-sectional) worldwide data could constitute a major service of monitoring solar variability. The physiological data could be aligned and analyzed for associations and interrelations with the cosmos, with which they likely resonate at built-in frequencies. Results thus far already pertain to individual (12, 13) and societal, biological and economic health. The accumulating information base on time-varying behavior of cycles with congruent transdisciplinary periods constitutes indispensable information for health and ecology (1-3) to be collected systematically by a website, Figure 8 (14).



Figure 6c. Vascular variability disorders. *irrespective of kind, separate* 2 groups of subjects in 7-day records but not in 24-hour records. Large diamonds *indicate that a vascular* variability disorder also characterized the record as a whole when a twocomponent model consisting of cosine curves with periods of 24 and 12 hours was fitted by least squares to all data, thereby washing out any occasional transient abnormality. Ordinate indicates the percentage of days when at least one parameter deviated from 90% prediction limits describing clinically healthy peers matched by gender and age (100% is the total number of days in each individual record, varying from 3 (N=1), 4 (N=1) and 6 (N=2) to otherwise 7 days) (11). Data of A. Gupta. © Halberg.

This international multilingual website (managed with pertinent educative endeavors) sooner or later will require permanent national and international governmental centers in their own right to serve for:

1) education of the public in self-help for health care, preferably in late primary and earliest secondary education (15), including adult individuals interested in learning about preventive health care and wishing to be informed about the status of their BP and HR at any given time (not flying blind) (16) notably when being treated by care providers;

2) education of the care provider upstream in medical and other health related schools and downstream in postgraduate courses in interpreting sphygmochrons, the extended cosinor and broader chronomic analyses;

3) thus replacing the homeostatic misconception of a "true" BP value (even though it was historically most useful by leading many millions of people to effective treatment) by the dynamics in the form of generally understandable parametric and nonparametric indices of BP and HR (a true BP has been untenable since 1880 [17] and 1904 [18; cf. 19]). Guidelines based on reference values for physiological variability and available background literature with minimal standards for data collection and analysis are to be offered (2, 3, 19-22);



Incidence (% days/subject) of Certain Vascular Variability Disorders Investigated

Figure 6d. Separate breakdown by four different variability disorders documenting the merits of an initial 7-day record vs. one based on fewer days (11). Data of A. Gupta. © *Halberg.*

4) providing information about and standards for commercially available tools for manual or automatic measurement, some ambulatorily usable monitors being available through BIOCOS in exchange for the data to be collected, with an 80% reduction in cost by contacting corne001@umn.edu;

5) lead up to international agreement on minimal sampling and, given appropriate time series, minimal analysis requirements, as standards, recommended by institutions such as the IEEE and the International Union of Physiological Sciences consulting and reporting to professional societies of care givers;

6) making chronobiologic procedures for diagnosis (as a sphygmochron [20-23]) and therapeutics (as a sequential test [24] and parameter comparison [25]) (preferably automatically) available on an appropriate scale for the worldwide public, with some computer-savvy individuals, saving care providers' time, as long as no abnormality is found and informing and educating the care provider as need be (see 2 above). BIOCOS services have already documented the ubiquity of a VVD (26). Although the incidence of VVDs is relatively low, the associated risk is high. Their assessment concerns all of those now diagnosed and treated for high BP worldwide (since VVDs can silently complicate this condition), i.e., hundreds of millions of people worldwide; incapacitation after a



Figure 7. Time courses of the frequency structures of the speed of the solar wind (SWS) (top) and of an elderly man's (FH) systolic and diastolic blood pressure and heart rate, SBP, DBP and HR (rows 2-4, respectively), examined by gliding spectral windows. Human systolic (S) blood pressure (BP) selectively resonates with solar wind speed (SWS) (top 2 sections). No obvious resonance, only minor coincident change in diastolic BP (DBP) or heart rate (HR) is seen (bottom 2 sections). Aeolian Rhythms* in gliding spectra of SWS and SBP change in frequency (smoothly [A] or abruptly [B,C,D], bifurcating [D,F] and rejoining [G], they also change in amplitude (B) (up to disappearing [C,E] and reappearing). During a nearly 16- year span there are no consistent components with a period averaging precisely 1 year in the 3 physiologic variables, probably an effect of advancing age. While post hoc ergo propter hoc reasoning can never be ruled out, an abrupt change on top in SWS is followed in the second row in SBP by the disappearance of some components, suggesting that as a first demonstration, some of FH's cis- and transyear components were driven by the SW [since they disappeared with a lag of about a transyear following the disappearance (subtraction) of the same components from the SWS spectrum]. The persistence of other spectral features in turn suggests endogenicity, i.e., an evolutionary acquisition of solar transyear oscillations that may reflect solar dynamics for the past billions of years. Blood pressure and heart rate data are from a man 70 years of age at start of around-the-clock monitoring, mostly at 30-min intervals, with interruptions for nearly 16 years.

*FH, man, 70 years (y) of age at start of automatic half-hourly around the clock measurements for ~ 16 y (N=2418 daily averages, total ~ 55000). Gliding spectra computed with interval = 8 y, resolution low in time but high in frequency, increment = 1 month, trial periods from 2.5 to 0.4 y, with harmonic increment = 0.05. Darker shading corresponds to larger amplitude. When several of these broad bands disappear in the

SWS, at E, parts of the bands in SBP also disappear, with a lag (delay) at E', while other parts persist. These components are presumably built into organisms over billions of years, as persistence without corresponding components in SWS shows, but can be driven in part by the solar wind, as their disappearence after loss of corresponding components in SWS suggests. "Aeolian", derived from Aeolus, Greek god of winds, who packed the winds up, then let them loose and had them change, conceivably a proper choice for the solar wind's pervasive role in human affairs. \bigcirc Halberg.



Preventive (left) and curative (lower right) health care can yield the dividend of biomedical monitoring of space weather (top right) by time-structural analyses of ambulatory blood pressure and heart rate series¹

Figure 8. The Phoenix Project of volunteering members of the Twin Cities chapter of the Institute of Electrical and Electronics Engineers (<u>http://www.phoenix.tc-ieee.org</u>) is planning on developing an inexpensive, cuffless automatic monitor of blood pressure and on implementing the concept of a website (<u>www.sphygmochron.org</u>) for a service in exchange for the data that in turn are to be used for refining methods and for monitoring psychophysiological effects of their variability in space weather. © Halberg.

massive stroke can also match any other insult. The costs are great. There is an urgent need for prehabilitation by education, Figure 9. The same vascular and broader transdisciplinary surveillance resolves new spectra of magnetic signatures, Figure 10, and may help clarify the effect of solar variability upon human affairs as an endeavor complementing the monitoring in physics introduced by Humboldt, Gauss and Sabine. Tangible current challenges and future applications lead to the roots of social disease, to crime (5) and violence (6, 7), as well as to sudden cardiac death (12) and suicide (13), to even broader global health and ecology.





Figure 9. Pre-habilitation, preferably before as well as with or after rehabilitation (for further vascular disease prevention and more generally). By the early detection of disease risk syndromes in the individual subject, countermeasures for primary prevention can be instituted. Such pre-habilitation in health can also complement rehabilitation in disease and can be a major goal of health care. Pre-habilitation would complement an across-the-board reduction of risk factors, the latter implemented by changes in lifestyle. The three entangled structures under Chronomics stand for trends (left), chaos (right) and transdisciplinary cycles (above) that constitute the reproducible element of the many matching time structures resolved in both the biosphere and its cosmos in the last decade, extending the view of health and ecology (1). \bigcirc Halberg.



Supported by MSM0021622402

Figure 10. Signatures of the societal and photic-thermic vear (photoperiodism) and of nonphotic (magnetic) environmental cycles are resolved by gliding spectra. Therein, along an abscissa of time and an ordinate of trial periods, shading reveals the wobbly nature and time course of a statistically significant spectral component in consecutive sections (intervals) of the analvzed. Phototime series and magnetoperiodisms coexist and compete in the same clinically healthy man (RBS) during adulthood (from 21-60 years of age, between 1967 and 2007). Gliding spectra computed all on daily averages with interval = 10 vears, increment = 4 months, harmonic increment = 0.05; ordering Ptest of zero-amplitude value from assumption at lightest shading is <0.01, darker shading corresponds to larger *amplitude*.

In *a*, in RBS's circulation, the yearly component dominates (most for diastolic [D] blood pressure [BP], consistently also for systolic [S] BP, and somewhat fading with time for heart rate [HR]). In **b**, a yearly component is mostly albeit intermittently also present in self-rated vigor (V), mood (M) and core temperature (T), but in c only to a lesser extent in 1-minute estimation (1MTE), in the speed of the solar wind (SWS) or the geomagnetic index (aa). The same individual's time structure shows wobbly aeolian (after Aeolus, ruler of winds in ancient Greek mythology) cycles, waxing and waning to the point of disappearing and reappearing in amplitude, drifting, splitting, bifurcating and rejoining in frequency, resonating with different environmental (seen and unseen) schedules.

Like photoperiodisms, magnetoperiodisms have their signatures in circadian patterns of disease. In some geographic locations, photoand magnetoperiodism coexist, and in others, magnetoperiodisms replace photoperiodisms, e.g., in sudden cardiac death, suicide, crime and terrorism. © Halberg.

References

- 1. Kofler WW. The need on a "critical extended evolution related view" of reality as a basis for an "extended view" of health. Science without Borders, Transactions of the International Academy of Science H&E, 2003/2004; 1: 27-54.
- 2. Müller-Bohn T, Cornélissen G, Halhuber M, Schwartzkopff O, Halberg F. CHAT und Schlaganfall. Deutsche Apotheker Zeitung 2002; 142: 366-370 (January 24).
- Halberg F, Schwartzkopff O, Cornélissen G, Hardeland R, Müller-Bohn T, Katinas G, Revilla MA, Beaty L, Otsuka K, Jozsa R, Zeman M, Csernus V, Hoogerwerf WA, Nagy G, Stebelova K, Olah A, Singh RB, Singh RK, Siegelova J, Dusek J, Fiser B, Czaplicki J, Kumagai Y, Chibisov SM, Frolov VA. Vaskuläres Variabilitäts-Syndrom (VVS) und andere Chronomik 2005-2007. Sitzungsberichte der Leibniz-Sozietät, in press.
- 4. Starbuck S, Cornélissen G, Halberg F. Is motivation influenced by geomagnetic activity? Biomedicine & Pharmacotherapy 2002; 56 (Suppl 2): 289s-297s.
- 5. Halberg F, Otsuka K, Katinas G, Sonkowsky R, Regal P, Schwartzkopff O, Jozsa R, Olah A, Zeman M, Bakken EE, Cornélissen G. A chronomic tree of life: ontogenetic and phylogenetic 'memories' of primordial cycles keys to ethics. Biomedicine & Pharmacotherapy 2004; 58 (Suppl 1): S1-S11.
- 6. Grigoryev PYe, Vladimirskii BM. The cosmic weather affects the terrorist activity. Reports of Taurida University, in press.
- Halberg F, Cornélissen G, Schack B, Wendt HW, Minne H, Sothern RB, Watanabe Y, Katinas G, Otsuka K, Bakken EE. Blood pressure self-surveillance for health also reflects 1.3-year Richardson solar wind variation: spin-off from chronomics. Biomedicine & Pharmacotherapy 2003; 57 (Suppl 1): 58s-76s.
- 8. Halberg F, Cornélissen G, Sothern RB, Hillman D, Schwartzkopff O, Beaty LA, Nolley ES, Otsuka K, Watanabe Y, Siegelova J, Fiser B, Homolka P, Singh RB. Re: Global Health and Ecology: Individualized inferential statistical blood pressure assessment for health care and large-scale space weather monitoring. Invited presentation for Natural cataclysms and global problems of modern civilization, Baku, Azerbaijan, September 24-28, 2007, in press.
- 9. Cugini P, Cruciani F, Turri M, Regine F, Gherardi F, Petrangeli CM, Gabrieli CB. 'Minimalchange hypertensive retinopathy' and 'arterial pre-hypertension', illustrated via ambulatory blood-pressure monitoring in putatively normotensive subjects. International Ophthalmology 1999; 22(3): 145-149.
- Sanchez de la Pena S, Gonzalez C, Cornélissen G, Halberg F. Blood pressure (BP), heart rate (HR) and non-insulin-dependent diabetes mellitus (NIDDM) chronobiology. S8-06, 3rd Int Congress on Cardiovascular Disease, Taipei, Taiwan, 26-28 Nov 2004. Int J Cardiol 2004; 97 (Suppl 2): S14.
- 11. Gupta AK, Greenway FL, Cornélissen G, Halberg F. Vascular variability disorders in Louisiana, in prediabetes and in healthy women taking sex hormones. In preparation.
- 12. Halberg F, Cornélissen G, Katinas G, Tvildiani L, Gigolashvili M, Janashia K, Toba T, Revilla M, Regal P, Sothern RB, Wendt HW, Wang ZR, Zeman M, Jozsa R, Singh RB, Mitsutake G, Chibisov SM, Lee J, Holley D, Holte JE, Sonkowsky RP, Schwartzkopff O,

Delmore P, Otsuka K, Bakken EE, Czaplicki J, International BIOCOS Group. Chronobiology's progress: season's appreciations 2004-2005. Time-, frequency-, phase-, variable-, individual-, age- and site-specific chronomics. J Applied Biomedicine 2006; 4: 1-38. <u>http://www.zsf.jcu.cz/vyzkum/jab/4 1/halberg.pdf</u>

- 13. Cornélissen G, Halberg F. Chronomics of suicides and the solar wind. Br J Psychiatry 2006; 189: 567-568.
- 14. Sothern RB, Katinas GS, Cornélissen G, Czaplicki J, Halberg F. Differential congruence of periods in helio- and/or geomagnetics and in human psychophysiology. 2nd World Congress of Chronobiology, Tokyo, November 4-6, 2007, in press.
- 15. Halberg F. Challenges from "60 years of [not yet] translational chronobiology". (Lecture opening a symposium at Experimental Biology 2007, Washington DC, April 29, 2007, on "Circadian rhythms: from animals to humans".) Reports of Taurida University, in press.
- 16. Halberg F, Smith HN, Cornélissen G, Delmore P, Schwartzkopff O, International BIOCOS Group. Hurdles to asepsis, universal literacy, and chronobiology—all to be overcome. Neuroendocrinol Lett 2000; 21: 145-160.
- Fossel M. Editor's Note [to Halberg F, Cornélissen G, Halberg J, Fink H, Chen C-H, Otsuka K, Watanabe Y, Kumagai Y, Syutkina EV, Kawasaki T, Uezono K, Zhao ZY, Schwartzkopff O. Circadian Hyper-Amplitude-Tension, CHAT: a disease risk syndrome of anti-aging medicine. J Anti-Aging Med 1998; 1: 239-259]. J Anti-Aging Med 1998; 1: 239.
- 18. Zadek I. Die Messung des Blutdrucks am Menschen mittelst des Basch'chen Apparates. Berlin, med. F., Diss., 25. Nov 1880. Berlin: Schumacher; 1880. 48 p.
- 19. Janeway TC. The clinical study of blood pressure. New York: D. Appleton & Co.; 1904. 300 pp.
- Cornélissen G, Halberg F, Bakken EE, Singh RB, Otsuka K, Tomlinson B, Delcourt A, Toussaint G, Bathina S, Schwartzkopff O, Wang ZR, Tarquini R, Perfetto F, Pantaleoni GC, Jozsa R, Delmore PA, Nolley E. 100 or 30 years after Janeway or Bartter, Healthwatch helps avoid "flying blind". Biomedicine & Pharmacotherapy 2004; 58 (Suppl 1): S69-S86.
- 21. Halberg F, Cornélissen G, Wall D, Otsuka K, Halberg J, Katinas G, Watanabe Y, Halhuber M, Müller-Bohn T, Delmore P, Siegelova J, Homolka P, Fiser B, Dusek J, Sanchez de la Peña S, Maggioni C, Delyukov A, Gorgo Y, Gubin D, Carandente F, Schaffer E, Rhodus N, Borer K, Sonkowsky RP, Schwartzkopff O. Engineering and governmental challenge: 7-day/24-hour chronobiologic blood pressure and heart rate screening. Biomedical Instrumentation & Technology 2002: Part I, 36: 89-122; Part II, 36: 183-197.
- 22. Halberg F, Cornélissen G, Halberg J, Schwartzkopff O. Pre-hypertensive and other variabilities also await treatment. Am J Medicine 2007; 120: e19-e20. doi:10.1016/j.amjmed.2006.02.045.
- 23. Cornélissen G, Halberg F, Otsuka K, Singh RB, Chen CH. Chronobiology predicts actual and proxy outcomes when dipping fails. Hypertension 2007; 49: 237-239. doi:10.1161/01.HYP.0000250392.51418.64.
- 24. Cornélissen G, Halberg F, Hawkins D, Otsuka K, Henke W. Individual assessment of antihypertensive response by self-starting cumulative sums. J Medical Engineering & Technology 1997; 21: 111-120.

- 25. Bingham C, Arbogast B, Cornélissen Guillaume G, Lee JK, Halberg F. Inferential statistical methods for estimating and comparing cosinor parameters. Chronobiologia 1982; 9: 397-439.
- 26. Cornélissen G, Delcourt A, Toussaint G, Otsuka K, Watanabe Y, Siegelova J, Fiser B, Dusek J, Homolka P, Singh RB, Kumar A, Singh RK, Sanchez S, Gonzalez C, Holley D, Sundaram B, Zhao Z, Tomlinson B, Fok B, Zeman M, Dulkova K, Halberg F. Opportunity of detecting pre-hypertension: worldwide data on blood pressure overswinging. Biomedicine & Pharmacotherapy 2005; 59 (Suppl 1): S152-S157.

CHRONOMICS OF SOLAR ACTIVITY AND PERINATAL EVENTS

Germaine Cornélissen¹, Dana Johnson¹, Inna Malkova², Elena V. Syutkina², Anatoly Masalov³, Jarmila Siegelova⁴, Bohumil Fiser⁴, Franz Halberg¹

¹University of Minnesota, Minneapolis, Minnesota, USA ²Scientific Center for Children's Health, Academy of Medical Sciences, Moscow, Russia ³Lebedev Physical Institute, Moscow, Russia ⁴Masaryk University, Brno, Czech Republic

Introduction

Newborns are sensitive to their environments near and far, revealing cyclic signatures of their cosmos in their morphology, physiology and pathology. Analyses thus far, notably when the periods resolved are congruent in many geographic locations, suggest that there is a need to apply a remove-and-replace approach whenever it occurs naturally, to much longer and equidistant time series, so that the mechanisms underlying associations can be analyzed and countermeasures can be developed for newborns' care.

Method

Chronomics, the inferential statistical approach to transdisciplinary cycles and broader time structures - chronomes - in the biosphere and its cosmos, was applied to perinatal data against the background of earlier studies (1, 2) with methods described elsewhere (3, 4). The database consisted of monthly values of 18 perinatal variables, including rates of incidence of several complications in pediatric care and anthropometric measures at birth: toxicosis, miscarriage, anemia, respiratory infection, pyelonephritis, gestosis, premature labor, premature membrane rupture, APGAR-1, APGAR-5, birth weight, birth height, head circumference at birth, chest circumference at birth, small-for-gestational age (SGA), perinatal brain damage, jaundice, and excessive weight loss.

Data obtained by consulting medical records were summarized as monthly rates or monthly averages for an about 21-year span from the beginning of 1985 to the end of 2005. There were interruptions in the recording. Data were not collected in 1987-1989 (3 years), 1992-1993 (2 years), 1996-1998 (3 years), and 2001-2002 (2 years), prompting procedures to overcome the grave problem of artifacts from gaps (5, 6). Each section was first analyzed separately to assess any circannual variation by the least squares fit of a 1-year cosine curve to the data, yielding estimates of the MESOR (midline-estimating statistic of rhythms, a rhythm-adjusted mean), the double amplitude (a measure of the predictable extent of change within a year), and the acrophase (a measure of the timing of overall high values recurring each year). For each variable, the circannual rhythm characteristics of each section were further summarized by population-mean cosinor to check on the reproducibility of the circannual characteristics from one section to another.

Least squares spectra were also obtained covering the frequency range from one cycle in 21 years to about 4 cycles per year, using a 0.2-harmonic increment. Model building was done by nonlinear least squares, according to the following procedure: Based on earlier work, components with periods of about 21 and 10.5 years were anticipated. Spectral peaks suggested components with periods of about 10.5 and/or about 5 years. Plots of the data as a function of time suggested the presence of trends for some of the variables. Accordingly, the following models were fitted: 1. A single about 10.5-year cycle; 2. An about 10.5-year cycle and a second-order polynomial trend; 3. An about 5-year cycle and a second-order polynomial trend; 4. An about 10.5-year cycle with a second harmonic term; 5. An about 21-year cycle with a second harmonic term; 8. An about 21-year cycle with a second harmonic term; 8. An about 21-year cycle with a second harmonic term; 8. An about 21-year cycle with a second harmonic term; 9. An about 21-year cycles. A comparison of results from the different trial models helped determine the extent of consistency of a given component. The model selected for fitting to the data was that associated with the smaller residual variance that included components also identified as spectral peaks. Models consisting of components with estimated periods exceeding

the duration of the observation span by more than 10% were discarded. When none of the trial models reached statistical significance, a linear or quadratic trend was fitted to the data.

Analyses were designed to also focus on the presence of any transyears, components with periods between 1 and 2 years, with a 95% confidence interval not overlapping these limits. While spectra included peaks in the transyear region, their validity was questioned since spurious transyears could stem from the large gaps occurring at almost cyclic intervals in the perinatal data series. In order to check on this possibility and in view of the presence of circadecadal cycles in many of the perinatal variables, monthly Wolf numbers for the span from Jan 1985 to Dec 2005 were analyzed in the same fashion as the perinatal data, either using all data or only data for months when perinatal data were available. Large spurious peaks are present not only in the transyear range but also at frequencies as low as one cycle per 4 years. Much larger amplitudes were seen at frequencies higher than one cycle in about 4 years for the series with gaps than for the original equidistant series without missing values. Model building for the perinatal variables is here limited to components with periods longer than 4 years, although new procedures were developed to validate transyears that for several variables were more prominent than any (not always present) yearly component.

Results

By population-mean cosinor, a circannual component was detected with statistical significance only for gestosis (P=0.029), borderline statistical significance being reached also for respiratory infection (P=0.078). When the circannual amplitude is expressed as a percentage of the MESOR (to accommodate changes in overall mean associated with low-frequency components such as the Hale and/or Schwabe cycles), or when it is equated to one (to test only for a clustering of acrophases, irrespective of the amplitude), a circannual rhythm is detected with statistical significance for both variables, Table 1. As seen in Table 2, many of the variables are highly intercorrelated. Many variables share similar trends.

Least squares spectra indicate the presence of low-frequency trends for most variables. Nonlinearly, results were consistent for four of the variables. An about 11-year cycle is found to characterize respiratory infections and APGAR-1 and APGAR-5 scores, whereas premature labor seems to follow an about 15-year cycle, possibly related to a global solar cycle (7). Premature brain damage also seems to be primarily characterized by a Schwabe cycle. A Hale or Schwabe cycle could not be validated nonlinearly for four other variables. A linear trend best describes miscarriage, gestosis, and SGA, whereas a second-order polynomial is found to characterize jaundice. Based on a trial model consisting of an about 10.5-year cycle and its second harmonic, the Schwabe cycle is validated nonlinearly for 6 of the 54 variables, with estimated periods varying between 10.23 and 11.59 years. An about 9.3-year component is also found for premature membrane rupture using a model consisting only of the Schwabe cycle. Table 3 illustrates the main positive nonlinear results for some of the variables and shows the great uncertainties involved.

Some results are in keeping with earlier work. About 10- and 20-year cycles also characterized neonatal anthropometric measures in data from Nikityuk in Moscow and in Kazakstan, and in data from Denmark and from Minnesota, as reported elsewhere (2).

References

- 1. Nikityuk BA, Alpatov AM. Secular trend in human growth and development, and solar activity cycles. Studies in Human Ecology 1984; 5: 51-70.
- Halberg F, Cornélissen G, Otsuka K, Syutkina EV, Masalov A, Breus T, Viduetsky A, Grafe A, Schwartzkopff O. Chronoastrobiology: neonatal numerical counterparts to Schwabe's 10.5 and Hale's 21-year sunspot cycles. In memoriam Boris A. Nikityuk. Int J Prenat Perinat Psychol Med 2001; 13: 257-280.
- 3. Cornélissen G, Halberg F. Chronomedicine. In: Armitage P, Colton T, editors. Encyclopedia of Biostatistics, 2nd ed. Chichester, UK: John Wiley & Sons Ltd; 2005. p. 796-812.
- Refinetti R, Cornélissen G, Halberg F. Procedures for numerical analysis of circadian rhythms. Biological Rhythm Research 2007; 38 (4): 275-325. http://dx.doi.org/10.1080/09291010600903692
- 5. Halberg F, Cornélissen G, Katinas G, Tvildiani L, Gigolashvili M, Janashia K, Toba T, Revilla M, Regal P, Sothern RB, Wendt HW, Wang ZR, Zeman M, Jozsa R, Singh RB,

Mitsutake G, Chibisov SM, Lee J, Holley D, Holte JE, Sonkowsky RP, Schwartzkopff O, Delmore P, Otsuka K, Bakken EE, Czaplicki J, International BIOCOS Group. Chronobiology's progress: season's appreciations 2004-2005. Time-, frequency-, phase-, variable-, individual-, age- and site-specific chronomics. J Applied Biomedicine 2006; 4: 1-38. <u>http://www.zsf.jcu.cz/vyzkum/jab/4_1/halberg.pdf</u>

- 6. Halberg F, Cornélissen G, Katinas G, Tvildiani L, Gigolashvili M, Janashia K, Toba T, Revilla M, Regal P, Sothern RB, Wendt HW, Wang ZR, Zeman M, Jozsa R, Singh RB, Mitsutake G, Chibisov SM, Lee J, Holley D, Holte JE, Sonkowsky RP, Schwartzkopff O, Delmore P, Otsuka K, Bakken EE, Czaplicki J, International BIOCOS Group. Chronobiology's progress: Part II, chronomics for an immediately applicable biomedicine. J Applied Biomedicine 2006; 4: 73-86. <u>http://www.zsf.jcu.cz/vyzkum/jab/4 2/halberg2.pdf</u>
- Markov VI, Sivaraman KR. New results concerning the global solar cycle. Solar Phys 1989; 123: 367-380.

Supported by MSM0021622402

	P.R.	P	MESOR	+ C.I.	Amplitude	(95% C.I.)	Acrophase	<i>(95</i> %	C.I.)
Amplitude: Orig	inal u	nits							
1 Toxicosis	16.8	0.153	0.328	0.099	0.044 (,)	-236 ()
2 Miscarriage	9.8	0.320	0.296	0.149	0.028 (,)	-203 ()
3 Anemia	17.0	0.827	0.279		0.013 (,)	-343 ()
4 RespInfectio	28.6	0.078	0.191	0.073	0.043 (,)	-154 ())
5 Pyelonephrit	12.2	0.700			0.009 (,)	-15 (ý
6 Gestosis	14.8	0.029	0.199			0.009, 0.047)	-68 (-	354,	-110)
7 PrematureLab	9.2	0.830	0.239		0.006 (,)	-93 ()
8 PremMRupt	6.2	0.946	0.493	0.084	0.002 (,)	-197 (,)
9 APGAR-1	6.0	0.857	7.324	0.219	0.028 (,)	-83 (,)
10 APGAR-5	8.8	0.910	8.280	0.322	0.007 (,)	-208 (,)
11 BW	12.6	0.230	3402.8	46.27	20.88 (,)	-251 (,)
12 Ht	9.4	0.593	51.06	0.693	0.105 (,)	-239 (,)
13 HC	10.4	0.307	34.75	1.013	0.056 (,)	-82 (,)
14 CC	8.2	0.670	34.19	0.625	0.039 (,)	-66 (,)
15 SGA	7.6	0.574			0.007 (,)	-136 ()
16 PerinBrnDama		0.772	0.372		0.013 (,)	-150 ()
17 Jaundice		0.334			0.041 (,)	-355 (,)
18 ExcessWtLoss	19.2	0.246	0.149	0.026	0.043 (,)	-204 (,)
Amplitude: Perc	entage	of ME	SOR						
19 Toxicosis	-	0.136	0.328	0.099	14.010 (,)	-231 (,)
20 Miscarriage	9.8	0.262	0.296	0.149	8.969 (,)	-215 ()
21 Anemia		0.436	0.279		11.241 (,)	-346 (,	ý
22 RespInfectio		0.045	0.191			9.581,32.118)	-168 (-		-232)
23 Pyelonephrit	12.2	0.911	0.093		5.806 (,)	-10 (,)
24 Gestosis		0.028	0.199			7.529,19.983)	-59 (-	356	-116)
25 PrematureLab	9.2	0.796	0.239		3.619 (,)	-63 (,)
26 PremMRupt	6.2	0.984	0.493		0.286 (,)	-180 (ý
27 APGAR-1		0.850	7.324		0.393 (,)	-84 (,	ý
28 APGAR-5	8.8	0.891	8.280	0.322	0.087 (,)	-208 (,)
29 BW	12.6	0.232	3402.8	46.27	0.614 (,)	-251 (,)
30 Ht	9.4	0.591	51.06	0.693	0.207 (,)	-240 (,)
31 HC	10.4	0.308	34.75	1.013	0.164 (,)	-81 (,)
32 CC	8.2	0.667	34.19	0.625	0.117 (,)	-68 (,)
33 SGA	7.6	0.708			3.740 (,)	-116 ()
34 PerinBrnDama	16.0	0.875	0.372		2.296 (,)	-152 ()
35 Jaundice	17.8	0.343			7.800 (,)	-358 (ý
36 ExcessWtLoss	19.2	0.228	0.149	0.026	29.136 (,)	-208 (,)
Amplitude: Equa	1 +0 0	ne							
37 Toxicosis		0.564	0.328	0.099	0.519 (,)	-222 (_)
88 Miscarriage		0.401	0.296	0.149	0.468 (,)	-196 ()
39 Anemia	17.0	0.549	0.279		0.466 (,)	-354 ()
10 RespInfectio	28.6	0.037	0.191			0.276, 1.179)	-157 (-	115.	-224)
11 Pyelonephrit	12.2	0.862	0.093	0.037			-46 ()
12 Gestosis	14.8	0.002	0.199	0.048	0.792 (()	-68 (-11.	
43 PrematureLab	9.2	0.818	0.239	0.054	0.314 (,)	-51 (± ± /)
14 PremMRupt			0.493		0.137 (, ,	-131 ()
45 APGAR-1		0.921	7.324	0.219	0.185 (-50 (,)
46 APGAR-5	8.8	0.837	8.280	0.322	0.274 (,)	-263 (,)
47 BW	12.6		3402.8	46.27	0.259 (`	-257 ()
48 Ht	9.4	0.807	51.06	0.693	0.247 (,)	-258 (,)
49 HC	10.4	0.359	34.75	1.013	0.352 (-64 ()
50 CC	8.2	0.876	34.19	0.625	0.212 (/ /	-21 (,)
50 CC 51 SGA	7.6	0.999	0.138	0.023	0.019 (<i>,</i>)	-38 (,)
51 SGA 52 PerinBrnDama	16.0	0.799	0.372	0.157	0.277 (,)	-110 (')
53 Jaundice	17.8	0.521	0.461	0.159	0.534 (,)	0 (')
54 ExcessWtLoss	19.2	0.057	0.149	0.026	0.702 (,)	-212 (')
51 LACC55WCL055	± J• Z	0.057	0.149	0.020	0.702 (,)	212 ('	,

Table 1: Circannual variation of several perinatal variables*

*Note failure to detect circannual variations in most variables examined, in keeping with the lack of a prominent peak at the trial period of a calendar year and the presence of often larger amplitudes at prior periods corresponding to transyears.

0.11741 -0.02630	Jaundice 0.34031 0.40436 0.	atBrainDa 0.44091 0.35982 0.	SGA 0.16709 0.37090 0.	ChestC -0.52258 -0.52610 -0.	HeadC -0.61191 -0.70091 -0.	Ht 0.41219 0.36932 0.	BW -0.05104 -0.13425 -0.1	APGAR-5 0.22774 0.39882 0.	APGAR-1 -0.37150 -0.15137 -0.	mMembR 0.22299 0.28129 0.1	PremLabo 0.03960 -0.12223 0.0	Gestosis -0.26682 -0.33680 -0.	yelonephrit 0.33539 0.25105 0.	respInfect 0.25822 0.36427 0.	Anemia 0.61430 0.56507 1.	Miscarriage 0.48133 1.00000	Toxicosis 1.00000
	0.60545 0.29922	0.54399 0.11603	0.29657 0.13321	-0.64161 -0.34209	-0.76825 -0.40195	0.45210 0.47440	-0.12939 0.08441	0.33589 0.57623	-0.28420 0.23473	0.13393 0.02094	0.04803 0.21050	-0.22493 -0.23946	0.40275 0.09704	0.40515 1.00000	1.00000		
-0.13914	0.31778	3 0.22490 -0.05377	0.09031	-0.40483	-0.37114	0.35414	-0.06795	0.22222	-0.11436	-0.00825	0.02056	-0.03581	4 1.00000	0			
	-0.10209		-0.19926 -	0.29032	0.37484	-0.29922	0.04341	-0.35589	-0.12239	-0.29885 -	-0.10561	1.00000					
	0.00654	-0.14332	-0.10768 -	0.00412 -	0.06094 -	0.18614	0.06695	0.15973	0.06586 -	-0.06664	1.00000						
	0.15248 -	0.19893	-0.07463 -	-0.06832	-0.23473	0.13012	0.06155	0.04274	-0.19947	1.00000							
	-0.01692	-0.56896	-0.06979	0.08348	0.16967	0.14997	0.18019	0.61791	1.00000								
	0.45602	-0.10302	0.21489	-0.51145	-0.54873	0.60971	0.06871	1.00000									
0.00851	-0.12174	-0.10539	-0.65246	0.50995	0.36326	0.54388	1.00000										
-0.18697	0.43280	0.20384	-0.14441	-0.31104	-0.43405	1.00000											
0.18697 0.10444	-0.66002	-0.48757	-0.51185	5 -0.31104 0.89198 1.00000	1.00000												
0.15512 -0.01688	-0.63359	-0.27084	-0.53057	1.00000													
0168	0.3241).1777.	1.0000														
0.07796 -0.26453	0.19750	4 1.00000															
	1.00000																
1.00000																	

Table 2: Correlation matrix*

Pearson product-moment correlations coefficients for paired variables. Bold indicates statistically significant correlation (P<0.05).

Table 3: Nonlinear results with different models show Schwabe or Hale cycles putative signatures by CIs (95% confidence intervals) overlapping the about 10.5, 15 and 21-years*

Variable	Pe	riod (95% (plitude (95%	6 CI)	A-Harm 2 (95% CI)				
Trial Model: Period = 21.0 years											
Toxicosis	26.126	17.732	34.520	0.10	0.06	0.14					
Miscarriage	37.100	11.026	63.174	0.14	0.09	0.19					
Anemia	23.500	21.490	25.510	0.25	0.21	0.29					
Pyelonephritis	27.233	7.345	47.122	0.04	0.01	0.07					
Gestosis	30.534	0.867	60.202	0.05	0.01	0.08					
Premature Labor	15.112	11.003	19.221	0.05	0.00	0.09					
Premature Membrane	21.817	13.460	30.173	0.08	0.03	0.12					
Rupture											
APGAR-1	10.174	9.687	10.661	0.40	0.26	0.54					
Head Circumference	29.397	25.286	33.509	0.96	84.00	1.07					
Chest Circumference	29.415	20.127	38.703	0.59	0.44	0.75					
SGA	31.231	1.097	61.365	0.04	0.01	0.07					
Perinatal Brain Damage	20.277	17.577	22.976	0.17	0.11	0.23					
Jaundice	38.126	8.682	67.569	0.19	0.06	0.32					
	Trial Mo	odel: Perio	od = 21.0 ye	ears and ?	1st-order P	olynomial					
Toxicosis	11.470	7.248	15.692	0.05	0.00	0.12					
Pyelonephritis	18.614	5.197	32.031	0.03	0.00	0.06					
Premature Labor	15.375	10.158	20.592	0.05	0.00	0.09					
Premature Membrane	14.798	11.622	17.974	0.08	0.03	0.14					
Rupture											
APGAR-1	10.556	9.847	11.266	0.39	0.26	0.53					
APGAR-5	10.442	9.835	11.049	0.29	0.19	0.38					
Birth Weight	12.951	9.625	16.277	51.66	0.97	102.36					
Head Circumference	15.230	9.306	21.155	0.32	0.18	0.46					
Chest Circumference	14.251	11.684	16.817	0.32	0.12	0.53					
Perinatal Brain Damage	10.841	9.649	12.034	0.18	0.09	0.27					
			od = 21.0 y		2nd Hamo	nic Term					
APGAR-1	19.920	18.877	20.964	0.15	0.05	0.24	0.40	0.25	0.55		
APGAR-5	22.724	21.203	24.245	0.19	0.13	0.24	0.33	0.24	0.43		
Chest Circumference	22.352	19.150	25.553	0.66	0.47	0.86	0.32	0.05	0.60		
Perinatal Brain Damage	16.289	14.618	17.960	0.22	0.13	0.31	0.18	0.11	0.26		
Trial Mo	del: Period	= 21.0 yea	rs and 2nd	Hamoni	c Term and	l 1st-order					
Toxicosis	11.357	10.235	12.480	0.08	0.02	0.15	0.08	0.00	0.16		
APGAR-1	16.828	15.209	18.446	0.41	0.26	0.56	0.39	0.24	0.54		
APGAR-5	17.938	15.625	20.251	0.22	0.07	0.37	0.27	0.16	0.38		
Perinatal Brain Damage	15.825	13.780	17.871	0.22	0.13	0.30	0.16	0.06	0.27		
Excess Weight Loss	13.973	12.513	15.433	0.06	0.00	0.12	0.06	-0.01	0.12		

*Overlap indicates no more than great uncertainties and need for more data.

Results not shown when model did not fit data:

- for period = 21.0 years, respiratory infection, APGAR-5, birth weight and height at birth, and excess weight loss;

- for period = 21.0 years and first-order polynomial, miscarriage, anemia, respiratory infection, gestosis, height at birth, SGA, jaundice and excess weight loss;

- for period = 21.0 years and 2nd harmonic term, toxicosis, miscarriage, anemia, respiratory infection, pyelonephritis, gestosis, premature labor, premature membrane rupture, birth weight, height at birth, head circumference, SGA, jaundice and excess weight loss;

- for period = 21.0 years, 2nd harmonic term and 1st-order polynomial: miscarriage, anemia, respiratory infection, pyelonephritis, gestosis, premature labor, premature membrane rupture, birth weight, height at birth, head and chest circumference, SGA and jaundice

1-DAY VERSUS 7-DAY CHAT: INDICATORS OF PHYSIOLOGICAL VERSUS PUTATIVELY PATHOLOGICAL BLOOD PRESSURE DYNAMICS

Othild Schwartzkopff•, Kuniaki Otsuka*, Shirley Stinson‡, Germaine Cornélissen•, Jarmila Siegelova§, Inna Malkova¶, Elena V. Syutkina¶, Anatoly Masalov∆, Bohumil Fiser§, Franz Halberg•

•University of Minnesota, Minneapolis, MN, USA
*Tokyo Women's Medical University, Medical Center East, Tokyo, Japan
‡University of Alberta, Edmonton, AB, Canada
§Masaryk University, Brno, Czech Republic

Scientific Center for Children's Health, Academy of Medical Sciences, Moscow, Russia ΔLebedev Physical Institute, Moscow, Russia

Objective

To document further beyond earlier studies (1, 2) the need for a minimal 7-day record, if abnormalities indicating a risk of stroke and other severe illness greater than that of hypertension (3, 4) are to be picked up and reliably diagnosed in order to be treated if they are consistent upon further monitoring.

Method

The linear-nonlinear extended cosinor (5-7) had demonstrated on several hundred series that the vast majority of invariably complete 7-day-long blood pressure (BP) records, the circadian periods had a 95% confidence interval that overlapped the precise 24-hour length.

Results

Sets of hundreds of 7-day series from several continents showed great day-to-day variability. Table 1 summarizes 3-hourly manual BP and HR measurements around the clock for 7 days. The average for a week of 136 mm Hg can vary as daily averages between 130 and 143 mm Hg SBP.
The day-night ratio for DBP can indicate a dipper on 4 days, reverse dipping on 3 days and thus nondipping as the overall result. Table 2 also reveals week-to-week variability by chronobiologically interpreted ambulatory blood pressure measurements (C-ABPM). Figure 1 shows analyses of a record from an elderly woman (OS) who had monitored herself for years and had no MESOR elevations, but had occasional 1-day CHAT (in 24-hour spans of course); the CHAT was eliminated from all 7-day records when these were analyzed as a whole, Figure 2. The contribution of outlying days' records was washed out by the fit of a fixed 2-component model (of 24-hour and 12-hour cosine curves) to the entire series, the purpose of the procedure. Thus, when in Figure 3 all data are summarized for this MESOR-normotensive elderly woman on a daily basis, there is 7% 1-day-CHAT, while on a weekly analysis, there is 0% 7-day CHAT in Figure 4: one more reason to insist on a minimal 7-day record, so that no false diagnosis is likely to be given to those who have only transient CHAT while an individual who has frequent CHAT is recognized, further investigated and treated if necessary.

The difference between 1-day and 7-day CHAT is further apparent when a batch of 15 series was picked to compare the daily incidence of CHAT with the weekly incidence, when the weekly summary was again computed by the fit by cosinor of a 2-component model of a 24- and a 12-hour cosine curve. When the 7-day record was analyzed on a daily basis, Figure 5 shows that of the 15 elderly individuals, only 3 had no day without CHAT and none had CHAT on each day. Twelve persons (80%) had one or more days with CHAT, which is a physiologically encountered condition. One of them had 5 single-day analyses documenting 1-day CHAT, but no overall excessive circadian amplitude, no 7-day CHAT. Only 3 of the 15 elderly subjects, 20% rather than 80%, had a diagnosis of 7-day CHAT. A diagnosis of 7-day CHAT or of less frequent CHAT should prompt further monitoring. The lack of 1-day as well as 7-day CHAT, while reassuring in the absence of other variability disorders, does not dispense with further monitoring, e.g., at yearly intervals, until unobtrusive, generally affordable instrumentation becomes available so that nobody ever flies blind (8), keeping the week-to-week variability in mind.

Supported by MSM0021622402

References

- Schaffer E, Cornélissen G, Rhodus N, Halhuber M, Watanabe Y, Halberg F. Outcomes of chronobiologically normotensive dental patients: a 7-year follow-up. JADA 2001; 132: 891-899.
- 2. Halberg F, Cornélissen G, Sothern RB, Hillman D, Schwartzkopff O, Beaty LA, Nolley ES, Otsuka K, Watanabe Y, Siegelova J, Homolka P, Fiser B, Singh RB. Re: Global Health and Ecology: Individualized inferential statistical blood pressure assessment for health care and large-scale space weather monitoring. Invited presentation for Natural cataclysms and global problems of modern civilization, Baku, Azerbaijan, September 24-28, 2007, in press.
- 3. Otsuka K, Cornélissen G, Halberg F. Predictive value of blood pressure dipping and swinging with regard to vascular disease risk. Clinical Drug Investigation 1996; 11: 20-31.
- 4. Halberg F, Cornélissen G, International Womb-to-Tomb Chronome Initiative Group: Resolution from a meeting of the International Society for Research on Civilization Diseases and the Environment (New SIRMCE Confederation), Brussels, Belgium, March 17-18, 1995: Fairy tale or reality ? Medtronic Chronobiology Seminar #8, April 1995, 12 pp. text, 18 figures. URL http://www.msi.umn.edu/~halberg/
- 5. Halberg F. Chronobiology: methodological problems. Acta med rom 1980; 18: 399-440.
- 6. Cornélissen G, Halberg F. Chronomedicine. In: Armitage P, Colton T, editors. Encyclopedia of Biostatistics, 2nd ed. Chichester, UK: John Wiley & Sons Ltd; 2005. p. 796-812.
- Refinetti R, Cornélissen G, Halberg F. Procedures for numerical analysis of circadian rhythms. Biological Rhythm Research 2007; 38 (4): 275-325. http://dx.doi.org/10.1080/09291010600903692.
- Fossel M. Editor's Note [to Halberg F, Cornélissen G, Halberg J, Fink H, Chen C-H, Otsuka K, Watanabe Y, Kumagai Y, Syutkina EV, Kawasaki T, Uezono K, Zhao ZY, Schwartzkopff O. Circadian Hyper-Amplitude-Tension, CHAT: a disease risk syndrome of anti-aging medicine. J Anti-Aging Med 1998; 1: 239-259]. J Anti-Aging Med 1998; 1: 239.

diastolic (D) blood pressure (BP) and heart rate (HR)(C-MBPM) reveals day-to-day variability: SS, F, 72 y Table 1: Chronobiologically interpreted, systematic manual 7-day/24-h monitoring of systolic (S) and

	Φ	15:13	DNR	16.66%	12.26	19.51	18.10	19.70	10.27	19.83	15.39	
HR	2A	17.69	SD	9.19	11.14	9.10	7.44	10.54	6.92	8.13	10.45	
	Σ		mean	79.60	81.35	81.00	74.57	78.67	82.75	79.67	81.20	
	φ	14:10	DNR	7.22%	-7.72	14.15	14.50	-13.20	14.33	-0.25	12.33	
DBP	2A	7.99	SD	7.21	5.42	7.79	8.24	8.11	6.67	6.34	6.22	
	Σ	76.1	Mean	76.56	77.73	75.64	74.14	79.56	76.75	79.75	73.00	
	φ	15:36	DNR	1.72%	-2.91	5.33	7.19	-10.86	4.42	-0.92	-0.19	
SBP	2A	2.49	SD	9.68	8.53	9.85	9.47	10.07	8.01	6.22	10.35	
	Σ	134.6	Mean	136.32	137.27	135.18	132.14	142.78	135.88	142.00	130.10	
Date	Jun 07				22-23 Fri/Sat	23-24 Sat/Sun	24-25 Sun/Mon	25-26 Mon/Tue	26-27 Tue/Wed	27-28 Wed/Thu	28-29 Thu/Fri	

*C: chronobiologically collected and interpreted BP and HR measurement; MBPM: manual blood pressure measurement

(about every 3 hours around the clock for 7 days)

M: MESOR (midline-estimating statistic of rhythm), a rhythm-adjusted mean, that may differ slightly from arithmetic mean listed below 2A: double circadian amplitude: extent of predictable change within a day

or circadian acrophase: a measure of timing of overall high values occurring each day, expressed in hr:min
or circadian acrophase and the second s

SD: standard deviation; DNR: day-night ratio

Underlining indicates abnormality in DNR of SBP and DBP

Table 2: Day-to-day variability can differ from week to week (I vs. I	-to-day va	ariability o	can differ	from we	ek to wee		I): FH, M, 88 y	88 y	
Date Series May 2007	Systolic b M ± SE	Systolic blood pressure (mm Hg) : SE A ± SE φ ± t	nm Hg) φ ± SE	Diastolic b M ± SE	Diastolic blood pressure (mm Hg) ± SE A ± SE φ ± \$	nm Hg) φ ± SE	Hear M ± SE	Heart rate (beats/min) A ± SE	φ ± SE
I D7 Mon	1337+36	8 18 + 5 18	-219 + 35	729+22	934 + 3 18	-234 + 19	+ 9 1	3 39 + 2 87	-294 + 52
08 Tue	123.4 ± 3.5	16.70 ± 5.06	I I	70.5 ± 2.5	12.59 ± 3.57	-216 ± 16	56.9 ± 1.7	4.63 ± 2.45	-19 ± 29
09 Wed	139.3 ± 3.1	29.01 ± 4.49	-233 ± 9	78.5 ± 1.8	18.85 ± 2.60	-234 ± 8	+ 2.5	3.81 ± 3.49	-159 ± 52
10 Thu	117.4 ± 3.2	6.45 ± 4.64	-197 ± 40	65.5 ± 1.9	5.85 ± 2.79	-205 ± 26	± 1.2	6.25 ± 1.65	-8 ± 15
11 Fri	125.6 ± 3.1	13.30 ± 4.47	-257 ± 19	68.4 ± 2.4	13.21 ± 3.50	-238 ± 14	± 1.2	6.65 ± 1.77	-27 ± 15
12 Sat	123.3 ± 3.4	7.74 ± 4.44	-273 ± 37	63.9 ± 2.3	10.85 ± 2.93	-309 ± 19	н 1.5	7.32 ± 2.26	-10 ± 15
<u>13 Sun</u>	116.9 ± 2.7	8.62 ± 4.01	-244 ± 25	66.8 ± 2.1	6.79 ± 3.06	-252 ± 24	⊨ 1.1	5.20 ± 1.55	-348 ± 18
Range of variability	116.9 – 139.3	6.45 – 29.01	-197 – -273	63.9 – 78.5	5.85 – 18.85	-205 – -309		3.39 – 7.32	-294 – -27 (& "-159")
II 22 Tue	123.7 ± 2.6	11.23 ± 3.70	-266 ± 19	72.1 ± 2.1	9.29 ± 2.99	-273 ± 18		10.55 ± 1.99	-42 ± 10
23 Wed	124.9 ± 3.5	17.69 ± 4.99	-190 ± 16	67.9 ± 2.5	10.91 ± 3.56	-181 ± 18		3.35 ± 2.83	-12 ± 47
24 Thu	131.5 ± 2.9	12.20 ± 4.14	-235 ± 19	72.4 ± 2.2	9.84 ± 3.17	-226 ± 18	62.3 ± 2.2	12.90 ± 3.07	-45 ± 14
25 Fri	128.3 ± 3.6	18.55 ± 5.10	-219 ± 15	71.7 ± 2.4	16.27 ± 3.48	-220 ± 12		6.05 ± 1.23	-32 ± 12
26 Sat	126.9 ± 2.3	15.98 ± 3.22	-255 ± 11	70.2 ± 2.3	13.37 ± 3.24	-247 ± 14		4.37 ± 1.78	-15 ± 23
<u>27 Sun</u>	124.0 ± 2.2	13.02 ± 3.10	-197 ± 14	67.6 ± 1.8	8.40 ± 2.55	-199 ± 17		6.16 ± 2.36	-5 ± 22
28 Mon	126.1 ± 2.9	13.81 ± 4.15	-220 ± 17	71.0 ± 2.6	10.41 ± 3.63	-225 ± 20		7.46 ± 1.68	-15 ± 13
Range of variability	123.7 – 131.5	11.23 – 18.55	-190 – -266	67.6 - 72.4	8.40 – 16.27	-181 – -273		3.35 - 12.90	-5 – -45
M: MESOR (midline-estimating statistic of rhythm), a rhythm-adjusted mean, that may differ slightly from arithmetic mean A: circadian amplitude: half the extent of predictable change within a day	estimating statisti e: half the extent	ic of rhythm), a r of predictable cl	hythm-adjusted hange within a c	mean, that ma day	y differ slightly fr	om arithmetic n	nean		
-			- -					· · ·	0

Daily spans cover midnight to midnight

of SYSTOLIC BLOOD PRESSURE (SBP) DURING ~2 YEARS ALTERNATE BETWEEN MOSTLY ACCEPTABLE and RARELY UNACCEPTABLE* CONSECUTIVE AVERAGES (above) and CIRCADIAN SWINGS (below)



Results from non-overlapping 24-h intervals in serial sections on half-hourly around the clock data; OS (F, 81-82 y) on atenolol treatment. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude Tension.





* Results from non-overlapping 7-day intervals in serial sections on half-hourly around the clock data; OS Tension. When 1-day intervals are used, occasional unacceptable results occur. (F, 81-82 y) on atenolol treatment. ** MH = MESOR-Hypertension, CHAT = Circadian Hyper-Amplitude

Figure 2



SBP-MESOR (mm Hg)

* OS (F, 81-82 y in 2005-2006) on (25 mg/day, on awakening) atenolol treatment.

Results from non-overlapping (fractionated) serial sections over daily intervals on half-hourly around-the-clock measurements. Daily records with fewer than 36 values discarded.

Figure 3

168h-BASED CHAT/MESOR-HYPERTENSION INDEX 0.0/0.0 MESOR (M) and DOUBLE AMPLITUDE (2A) OF SYSTOLIC BLOOD PRESSURE (SBP)*



* OS (F, 81-82 y in 2005-2006) on (25 mg/day, on awakening) atenolol treatment.

Results from non-overlapping (fractionated) serial sections over weekly intervals on half-hourly around-the-clock measurements analyzed. Weekly records with fewer than 224 values discarded.

Figure 4





GEOGRAPHICALLY PROXIMAL VERSUS GLOBAL GEOMAGNETIC REFERENCE VALUES FOR BIOLOGICAL STUDIES

Germaine Cornélissen¹, Waldemar Ulmer², Inna Malkova³, Elena V. Syutkina³, Anatoly Masalov⁴, Rüdiger Hardeland⁵, Hans-Joachim Linthe⁶, Armin Grafe⁶, Kuniaki Otsuka⁷, Jarmila Siegelova⁸, Bohumil Fiser⁸, Franz Halberg¹

¹Halberg Chronobiology Center, University of Minnesota, Minneapolis, Minnesota, USA ²VARIAN International, Zug, Switzerland

³Scientific Center for Children's Health, Academy of Medical Sciences, Moscow, Russia ⁴Lebedev Physical Institute, Moscow, Russia ⁵University of Göttingen, Germany

⁶GeoForschungsZentrum Potsdam, Niemegk, Germany

⁷Tokyo Women's Medical University, Medical Center East, Tokyo, Japan ⁸Masaryk University, Brno, Czech Republic

Background

Geomagnetic activity during spans matching two experiments (actually surveys) in Göttingen on tumor cell growth is here analyzed. The spectrum of the planetary geomagnetic disturbance index Kp is compared with that of the local geomagnetic disturbance index K from Niemegk (the closest recording station identified). One protocol specified cells cultured at pH 6.9 over 44 days in 1997, another followed a few days later at pH 7.3 also over 44 days (1). During each span, four kinds of mammalian tumor cells were grown (B14, C3H, G9L and L1210). After detrending the growth curve, two major components were identified with periods of 7 days and 24 hours, both synchronized to the social week and day, respectively. The circaseptan amplitude was much larger than the circadian amplitude for each culture at each pH. A third spectral component with a period slightly longer than a month was also found. Of primary interest were the findings (on cells kept mostly in continuous darkness) that the circaseptan component not only had an amplitude much larger than that of a circadian rhythm but also that the rhythms were 1-week and 24-hour synchronized. It seemed reasonable to seek similar precise components in the environment, notably since near-weekly but not precisely 1-week-long cycles had been found earlier in the polarity of the interplanetary magnetic field (2) and in geomagnetic activity (3-5).

Materials and Methods

In order to explore whether the tumor cell cultures could have been synchronized by magnetoperiodisms, both the planetary index Kp of geomagnetic activity and the index from Niemegk (NGK) were analyzed during the same two 44-day spans as the two surveys on tumor cell cultures' growth. Analyses consisted of linear-nonlinear rhythmometry by the extended cosinor (6).

Results

As seen in Figure 1a, Kp and NGK follow a similar time course. The two indices are highly correlated (r>0.85, P<0.001), Figure 1b. The major expected difference between the two indices is apparent from the least squares spectra of Kp in Figures 2a-b vs. NGK in Figures 3a-b: whereas the circadian component is not statistically significant for Kp (which is an average index from several stations worldwide), it clearly corresponds to a major spectral peak for the local index NGK during both study spans.

The nonlinear results are shown in Table 1. For Kp, only the circaseptan component could be validated with statistical significance. During the first survey, the period of Kp does not differ from 7 days as the 95% confidence interval for the period covers 7 days. During the second survey, the circaseptan is slightly longer than 7 days. In the case of NGK, the circaseptan period does not differ from 7 days during either survey. In addition, the circadian component is detected with statistical significance, its period not differing from 24 hours. Whereas the circadian amplitude is larger than the circaseptan one during the first survey, it is slightly smaller during the second survey.

As compared to results on tumor cell growth, results on Kp or NGK differ in several respects. First, the circaseptan-to-circadian amplitude ratios are quite different, with the circaseptan considerably and invariably more prominent than the circadian in the cell cultures but not in geomagnetic activity. Second, the slight tendency of Kp to assume a period somewhat longer than 7 days during the second survey contrasts with the 7-day synchronized component characterizing all four tumor cell cultures at both pH values investigated. As seen in the least squares spectra, the 7-day component (corresponding to the vertical line at 1 cycle/week) by no means corresponds to the tallest spectral peak in the case of Kp or NGK. Several other peaks are observed to bracket the circaseptan component of Kp or NGK. A possible modulation of the circaseptan component by the very prominent about 27-day variation corresponding to the solar rotation period around its axis must be kept in mind.

Discussion

Effects of geomagnetic activity or magnetic storms are inferentially documented, acting directly on cell division (7) and indirectly on cancer therapy (8, 9), on cardiac function (10-12) and the endocrines (13). Associations at the population level with terrorism are also reported (14).

Conclusion

It seems possible that geomagnetics, gauged by a local index (NGK), but not on the basis of data for the planetary index Kp, contributed to the synchronization of the tumor cell cultures at both the circadian and circaseptan frequency. The circaseptan-to-circadian amplitude ratios in Kp and NGK differ, however, from those found in the cell cultures investigated. We cannot suggest that any spectral component characterizing geomagnetics was responsible for what appears to be an unknown precise 7-day and 24-hour (societal or equipment-derived) synchronizer. Almost certainly, however, in any biospheric study, the nearest geomagnetic disturbance index, rather than only any planetary index, should be considered, even when, in the absence of records from a nearby station, important results are sometimes found at the planetary level (7, 14).

Supported by MSM0021622402

REFERENCES

- Ulmer W, Cornélissen G, Revilla M, Siegelova J, Dusek J, Halberg F. Circadian and circaseptan dependence of the beta-ATP peak of four different cancer cell cultures: implications for chronoradiotherapy. Scripta medica (Brno) 2001; 74: 87-92.
- Gonzalez ALC, Gonzalez WD. Periodicities in the interplanetary magnetic field polarity. J Geophys Res 1987; 92: 4357-4375.
- Halberg F, Breus TK, Cornélissen G, Bingham C, Hillman DC, Rigatuso J, Delmore P, Bakken E, International Womb-to-Tomb Chronome Initiative Group: Chronobiology in space. Keynote, 37th Ann. Mtg. Japan Soc. for Aerospace and Environmental Medicine, Nagoya, Japan, November 8-9, 1991. University of Minnesota/Medtronic Chronobiology Seminar Series, #1, December 1991, 21 pp. of text, 70 figures.
- 4. Roederer JG. Are magnetic storms hazardous to your health? Eos, Transactions, American Geophysical Union 1995; 76: 441, 444-445.
- 5. Vladimirskii BM, Narmanskii VYa, Temuriantz NA. Global rhythmics of the solar system in the terrestrial habitat. Biophysics 1995; 40: 731-736.
- 6. Halberg F. Chronobiology: methodological problems. Acta med rom 1980; 18: 399-440.
- Halberg F, Cornélissen G, Schwartzkopff O, Katinas GS, Chibisov SM, Khalitskaya EV, Mitsutake G, Otsuka K, Scheving LA, Bakken EE. Chronometaanalysis: magnetic storm associated with a reduction in circadian amplitude of rhythm in corneal cell division. Proceedings, International Conference on the Frontiers of Biomedical Science: Chronobiology, Chengdu, China, September 24-26, 2006, p. 40-42.
- 8. Blank MA, Cornélissen G, Halberg F. Circasemiseptan (about half-weekly) and/or circaseptan (about-weekly) pattern in human mitotic activity? In vivo 1995; 9: 391-394.

- Blank MA, Gushchin VA, Halberg F, Portela A, Cornélissen G. X-irradiation chronosensitivity and circadian rhythmic proliferation in healthy and sarcoma-carrying rats' bone marrow. In vivo 1995; 9: 395-400.
- Otsuka K, Cornélissen G, Weydahl A, Holmeslet B, Hansen TL, Shinagawa M, Kubo Y, Nishimura Y, Omori K, Yano S, Halberg F. Geomagnetic disturbance associated with decrease in heart rate variability in a subarctic area. Biomedicine & Pharmacotherapy 2001; 55 (Suppl 1): 51s-56s.
- Chibisov SM, Cornélissen G, Halberg F. Magnetic storm effect on the circulation of rabbits. Biomedicine & Pharmacotherapy 2004; 58 (Suppl 1): S15-S19.
- Cornélissen G, Halberg F, Breus T, Syutkina EV, Baevsky R, Weydahl A, Watanabe Y, Otsuka K, Siegelova J, Fiser B, Bakken EE. Non-photic solar associations of heart rate variability and myocardial infarction. J Atmos Solar-Terr Phys 2002; 64: 707-720.
- 13. Jozsa R, Halberg F, Cornélissen G, Zeman M, Kazsaki J, Csernus V, Katinas GS, Wendt HW, Schwartzkopff O, Stebelova K, Dulkova K, Chibisov SM, Engebretson M, Pan W, Bubenik GA, Nagy G, Herold M, Hardeland R, Hüther G, Pöggeler B, Tarquini R, Perfetto F, Salti R, Olah A, Csokas N, Delmore P, Otsuka K, Bakken EE, Allen J, Amory-Mazaudier C. Chronomics, neuroendocrine feedsidewards and the recording and consulting of nowcasts -- forecasts of geomagnetics. Biomedicine & Pharmacotherapy 2005; 59 (Suppl 1): S24-S30.
- Grigoryev PYe, Vladimirskii BM. The cosmic weather affects the terrorist activity. Conference, Scientific Notes of Taurida University, in press.

Figure 1: Geomagnetic Activity Index Kp and Local Niemegk K Index During Spans Matching Two Surveys on Tumor Cell Growth

a. Similar time course of the two indices:



Experiments #1&2: pH = 6.9&7.3

b. High correlation between the two indices:



Figure 2. Spectra of Kp:







	Circaseptan						Circadian						
	Period (h)	(95%	CI)	Amplitude (au)	(95%	CI)	Period (h)	(95%	CI)	Amplitude (au)	(95%	CI)	
						ĸ	(p						
Exp #1	169.32	159.02	179.63	0.43	0.12	0.73							
Exp #2	176.56	168.52	184.60	0.64	0.33	0.96							
	Niemegk K												
Exp #1	169.44	155.13	183.76	0.37	0.01	0.72	24.04	23.81	24.27	0.47	0.12	0.82	
Exp#2	177.15	166.09	188.20	0.56	0.18	0.93	24.01	23.80	24.22	0.53	0.16	0.90	

Table 1. Nonlinear results in surveys investigated

CUGINI'S MINIMAL CHANGE HYPERTENSIVE RETINOPATHY, RESOLVED CHRONOBIOLOGICALLY WHILE DIPPING FAILS, SUPPORTS THE CONCEPT OF 'PRE-HYPERTENSION'

Germaine Cornélissen¹, Pietro Cugini², Jarmila Siegelova³, Bohumil Fiser³, Franz Halberg¹

¹University of Minnesota, Minneapolis, Minnesota, USA ²University "La Sapienza", Rome, Italy ³Masaryk University, Brno, Czech Republic

"Prehypertension" is a term with many meanings considered from at least two perspectives, one homeostatic (1-8), the other chronobiologic (9-18). The homeostatic view bases the diagnosis of the condition on the repeated measurement of the blood pressure (BP), starting with no more than one or a few measurements at a few office visits and managing the patient on this basis. (The Austrian guidelines deserve credit for requiring a minimum of 30 measurements, without, however, specifying their timing and thus not prescribing sampling that would allow an assessment of periodic variations [7]). Prehypertension, homeostatically, can be, e.g., a systolic (S) blood pressure (BP) between 120 and 139 mmHg and/or diastolic (D) BP between 80 and 89 mmHg (3). Only in special cases does the homeostatic physician offer the opportunity of a 24-hour profile as the (false) gold standard and still usually interprets the results by 24-hour, if not spotcheck-derived, 24-hour means, daytime and nighttime means, according to several national and international guidelines, also recommending fixed, time-invariant target BPs for human adults of any gender, age (above 18 years) and ethnicity. By contrast, in his 1880 thesis for his medical degree, Ignaz Zadek explicitly did not wish to evaluate "the" BP of a given patient, but rather the variability (13, 14), and Theodore C. Janeway in 1904 argued for the collection of enough data to evaluate periodic variations before seeing a patient (15).

Pietro Cugini, former Professor of Internal Medicine at the University of Rome 'La Sapienza', went an important step further by formulating what, according to his co-authors (GC and FH), may be called "Cugini's minimal-change hypertensive retinopathy", based on elevations of both the circadian rhythm-adjusted BP mean (MESOR), M, and amplitude, A, as compared to control subjects without retinopathy. Cugini used chronobiologic methodology but applied it to only 24-hour records and interpreted the results in the light of conventional guidelines. From a methodological viewpoint, his studies are valuable since he shows an inferentially-validated statistically significant difference in M and a difference in circadian A in patients with Cugini's minimal-change hypertensive retinopathy. Several inferences can be drawn from his study:

1. By the time of a minimal retinopathy, there can be not only an elevated BP-M, but also an increased circadian A as compared to controls, and it will be important to see in longitudinal studies whether the rise in circadian A precedes that in MESOR as suggested by other evidence (16-18).

2. As Cugini himself notes, the number of subjects (and, we add, the duration of each record) are to be extended with a hybrid (linked cross-sectional) design for additional, more reliable 7-day-based cases as well as for reference values, and further for starting longitudinal surveillance of BP not only in adults but also in primary and secondary education; under-diagnosis of hypertension has been reported for children and adolescents (19).

3. The elevation in circadian amplitude of BP is relatively modest and on the average remains below available thresholds derived from clinically healthy gender-, age- and ethnicity-matched peers (20, 21). The elevation in circadian A does not involve an increased risk of hard events until a threshold is reached (20), i.e., until there is an overswinging (CHAT, short for circadian hyper-amplitude-tension). Cugini's pre-hypertension is hence an optimal stage when the individual should be treated to reverse the path toward a high risk of ischemic stroke, myocardial infarction, kidney disease and blindness, since CHAT can be treated (9, 22; cf. 23).

4. Methodologically, Figure 1 shows that from the viewpoint of a classification based on the nocturnal fall in BP in terms of averages (original data were not available to GC and FH), the

subjects with retinopathy are dippers while those without retinal involvement are non-dippers. In this analysis, a classification based on the day-night ratio (dipping) actually misleads while earlier it only failed to work in predicting hard events, when a chronobiologic approach worked (24-26).





* Comparison of "Truly Normotensive Subjects" (TNS) and "Putatively Normotensive Subjects" (PNS) with Incipient Signs of Hypertensive Retinopathy. Data from P Cugini et al. (International Ophthalmology 1999; 22: 145-149). Minimal retinal alterations, presumably reflecting an increased vascular disease risk, are NOT associated with abnormal DNR, but rather with the chronobiologically predicted elevation in circadian BP amplitude (middle, right).

Figure 1: Subjects with minimal change retinopathy have daytime mean values of systolic blood pressure (SBP) higher than those without retinopathy (top left); a dipping classification not only fails to resolve prehypertension, being normal in the presence of a minimal-change retinopathy, yet abnormal in the absence of minimal change retinopathy (bottom). Chronobiology shows an increase in circadian amplitude as well as MESOR, in the presence (PNS) versus the absence (TNS) of minimal retinopathy, top right. © Halberg.

Conclusion. Cugini's prehypertension should stimulate ophthalmologists to recommend 7day/24-hour chronobiologically interpreted ABPM, in order to detect and treat variability disorders of children and adolescents, as well as adults, and vice versa to recommend an ophthalmological examination whenever a BP variability disorder is found.

Supported by MSM0021622402

REFERENCES

- O'Brien E, Staessen J. Normotension and hypertension defined by 24-hour ambulatory blood pressure monitoring. Blood Pressure 1995; 4: 266-282.
- Japanese Society of Hypertension Guidelines Subcommittee for the Management of Hypertension. Guidelines for the management of hypertension for general practitioners. Hypertension Res 2001; 24: 613-634.
- 3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289 (19): 2560-2672.
- Guidelines Committee, 2003 European Society of Hypertension. European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003; 21: 1011-1053.
- 5. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, Verdecchia P, European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertension 2003; 21(5): 821-848.

- 6. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in humans and experimental animals. Part I: Blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation 2005; 111: 697-716.
- 7. Magometschnigg D. Definition und Klassifikation der Hyperton 2004; 8 (1): 12-13.
- 8. Deutsche Hochdruckliga e.V. (DHL) und Deutsche Hypertoniegesellschaft (DHL/DHG). Leitlinien zur Hypertonie. <u>www.paritaet.org/RR-Liga Guidelines.htm</u> 2006.
- 9. Halberg F, Cornélissen G, International Womb-to-Tomb Chronome Initiative Group: Resolution from a meeting of the International Society for Research on Civilization Diseases and the Environment (New SIRMCE Confederation), Brussels, Belgium, March 17-18, 1995: Fairy tale or reality? Medtronic Chronobiology Seminar #8, April 1995, 12 pp. text, 18 figures. <u>http://www.msi.umn.edu/~halberg/</u>
- Cugini P, Petrangeli CM, Capodaglio FP, Chiera A, Cruciani F, Turri M, Gherardi F, Santino G. 'Retinopatia tensiva a lesioni minime' e pre-ipertensione arteriosa: evidenze dal monitoraggio della pressione arteriosa in soggetti reputati normotesi a 'rischio zero'. Rec Progr Med 1997; 88: 11-16.
- Cugini P, Fontana S, Pellegrino AM, Lucia P, Stirati G, Cruciani F, Scibilia G, Pachi A. Il concetto di "pre-ipertensione arteriosa" alla luce del monitoraggio ambulatorio non-invasivo della pressione arteriosa. Rec Prog Med 1998; 89: 559-568.
- 12. Cugini P, Cruciani F, Turri M, Regine F, Gherardi F, Petrangeli CM, Gabrieli CB. 'Minimalchange hypertensive retinopathy' and 'arterial pre-hypertension', illustrated via ambulatory blood-pressure monitoring in putatively normotensive subjects. International Ophthalmology 1999; 22(3): 145-149.
- Zadek I. Die Messung des Blutdrucks am Menschen mittelst des Basch'chen Apparates. Berlin, med. F., Diss., 25. Nov 1880. Berlin: Schumacher; 1880. 48 p.

- Zadek I. Die Messung des Blutdrucks am Menschen mittelst des Basch'chen Apparates. Z klin Med 1881; 2: 509-551.
- Janeway TC. The clinical study of blood pressure. New York: D. Appleton & Co.; 1904. 300 pp.
- Halberg J, Halberg E, Hayes DK, Smith RD, Halberg F, Delea CS, Danielson RS, Bartter FC. Schedule shifts, life quality and quantity modeled by murine blood pressure elevation and arthropod lifespan. Int J Chronobiol 1980; 7: 17-64.
- Kumagai Y, Shiga T, Sunaga K, Cornélissen G, Ebihara A, Halberg F. Usefulness of circadian amplitude of blood pressure in predicting hypertensive cardiac involvement. Chronobiologia 1992; 19: 43-58.
- Watanabe Y, Cornélissen G, Halberg F, Bingham C, Siegelova J, Otsuka K, Kikuchi T. Incidence pattern and treatment of a clinical entity, overswinging or circadian hyperamplitudetension (CHAT). Scripta medica (Brno) 1997; 70: 245-261.
- Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. JAMA 2007; 298: 874-879.
- Cornélissen G, Halberg F, Schwartzkopff O, Delmore P, Katinas G, Hunter D, Tarquini B, Tarquini R, Perfetto F, Watanabe Y, Otsuka K. Chronomes, time structures, for chronobioengineering for "a full life". Biomed Instrum Technol 1999; 33: 152-187.
- Hillman DC, Cornélissen G, Scarpelli PT, Otsuka K, Tamura K, Delmore P, Bakken E, Shinoda M, Halberg F, International Womb-to-Tomb Chronome Initiative Group. Chronome maps of blood pressure and heart rate. University of Minnesota/Medtronic Chronobiology Seminar Series, #2, December 1991, 3 pp. of text, 38 figures.
- Shinagawa M, Kubo Y, Otsuka K, Ohkawa S, Cornélissen G, Halberg F. Impact of circadian amplitude and chronotherapy: relevance to prevention and treatment of stroke. Biomedicine & Pharmacotherapy 2001; 55 (Suppl 1): 125s-132s.
- Halberg F, Cornélissen G, Halberg J, Schwartzkopff O. Pre-hypertensive and other variabilities also await treatment. Am J Medicine 2007; 120: e19-e20. doi:10.1016/j.amjmed.2006.02.045.

- 24. Otsuka K, Cornélissen G, Halberg F. Predictive value of blood pressure dipping and swinging with regard to vascular disease risk. Clinical Drug Investigation 1996; 11: 20-31.
- 25. Bingham C, Cornélissen G, Chen C-H, Halberg F. Chronobiology works when day-night ratios fail in assessing cardiovascular disease risk from blood pressure profiles. Abstract, III International Conference, Civilization diseases in the spirit of V.I. Vernadsky, People's Friendship University of Russia, Moscow, Oct. 10-12, 2005, p. 111-113.
- Cornélissen G, Halberg F, Otsuka K, Singh RB, Chen CH. Chronobiology predicts actual and proxy outcomes when dipping fails. Hypertension 2007; 49: 237-239. doi:10.1161/01.HYP.0000250392.51418.64.

CONFIDENCE INTERVALS ASSESS THE CONGRUENCE OF PERIODS CHARACTERIZING MANY NEONATAL TRANSDISCIPLINARY NIKITYUK CYCLES

Inna Malkova¹, Elena V. Syutkina¹, Germaine Cornélissen², Anatoly Masalov³, Bohumil Fiser⁴, Jarmila Siegelova⁴, Franz Halberg²

¹Scientific Center for Children's Health, Academy of Medical Sciences, Moscow, Russia ²Halberg Chronobiology Center, University of Minnesota, Minneapolis, Minnesota, USA ³Lebedev Physical Institute, Moscow, Russia, ⁴Masaryk University, Brno, Czech Republic

Background

A prolonged global solar activity cycle with a period of 16 to 18 years, reportedly associated with holes in the topology of the sun's corona and manifested in the distribution of open magnetic field structures (1), as reviewed by Nayar (2), complements the about (~) 10.5- and ~21-year Schwabe and Hale cycles of Wolf's relative sunspot numbers and their signatures in human growth and development described by Nikityuk.

Materials and Methods

We use Marquardt's approach for extended cosinor-implemented linear-nonlinear rhythmometry on data on body length at birth recorded from random samples from 25-150 babies/year in Moscow, Russia during 1874 to 1985 and shorter series from Alma Ata, Kazakstan (3-7).

Metaanalytical Problem

In body length in Moscow, a period (τ) of 20.28 years (y) with a 95% confidence interval (in parentheses) extending from 18.76 to 21.88 y is found for boys and a period of 20.78 (19.05, 22.78) y for girls. The corresponding values for Russians in Alma Ata are $\tau = 17.77$ (14.00, 20.07) y for boys and 17.75 (15.21, 21.08) y for girls. For Kazaks in Alma Ata, the τ for boys = 21.24 (18.39, 24.09) y and for girls 21.45 (15.44, 27.45) y. Without confidence intervals, uncertainties are missed: one would postulate that a signature of a global solar cycle characterizes Russian boys and girls in Alma Ata and a Hale cycle in Moscow, suggesting indeed a plausible geographic

difference. The difference between Russians and Kazaks in Alma Ata, in point estimates of τ may suggest an ethnic difference. In addition to putative ethnic and geographic differences there is also a likely effect to be anticipated from the different lengths of the time series analyzed. The confidence intervals may be questioned since the time series are non-stationary and one remedy may be to compute the periods on sections of the time series and to summarize them by population-mean cosinor. In the latter case, they will be most likely different and probably yet wider. An about 15-year cycle in premature labor in data of the senior author (IM) has the same uncertainty.

New results

By examining additional data covering 22 more years with gaps, IM prolonged an already unique Nikityuk series and confirms the main inferences drawn cautiously from the original data covering more than a century. The ubiquity in neonatal events of signatures of Schwabe and Hale cycles is thus extended to many variables of pediatric interest: incidences of toxicosis, miscarriage, anemia, respiratory infection, pyelonephritis, gestosis, premature labor, premature membrane rupture, Apgar-1, Apgar-5 scores, birth weight, height, head and chest circumference. Her work is dedicated to the memory of Boris Nikityuk (10.X.1933-30.IX.1998), the late professor and head of the Department of Anatomy and Anthropology of the Russian Academy of Physical Education, Moscow and the President-Founder of the International Academy of Integrative Anthropology.

Supported by MSM0021622402

REFERENCES

- Markov VI, Sivaraman KR. New results concerning the global solar cycle. Solar Phys 1989; 123: 367-380.
- 2. Prabhakaran Nayar SR. Periodicities in solar activity and their signature in the terrestrial environment. ILWS Workshop, Goa, February 19-24, 2006. 9 pp.
- Halberg F, Cornélissen G, Otsuka K, Syutkina EV, Masalov A, Breus T, Viduetsky A, Grafe A, Schwartzkopff O. Chronoastrobiology: neonatal numerical counterparts to Schwabe's 10.5

and Hale's 21-year sunspot cycles. In memoriam Boris A. Nikityuk. Int J Prenat Perinat Psychol Med 2001; 13: 257-280.

- 4. Cornélissen G, Halberg F. Chronomedicine. In: Armitage P, Colton T, editors. Encyclopedia of Biostatistics, 2nd ed. Chichester, UK: John Wiley & Sons Ltd; 2005. p. 796-812.
- Refinetti R, Cornélissen G, Halberg F. Procedures for numerical analysis of circadian rhythms. Biological Rhythm Research 2007; 38 (4): 275-325. <u>http://dx.doi.org/10.1080/09291010600903692</u>
- Halberg F, Cornélissen G, Katinas G, Tvildiani L, Gigolashvili M, Janashia K, Toba T, Revilla M, Regal P, Sothern RB, Wendt HW, Wang ZR, Zeman M, Jozsa R, Singh RB, Mitsutake G, Chibisov SM, Lee J, Holley D, Holte JE, Sonkowsky RP, Schwartzkopff O, Delmore P, Otsuka K, Bakken EE, Czaplicki J, International BIOCOS Group. Chronobiology's progress: season's appreciations 2004-2005. Time-, frequency-, phase-, variable-, individual-, age- and site-specific chronomics. J Applied Biomedicine 2006; 4: 1-38. http://www.zsf.jcu.cz/vyzkum/jab/4 1/halberg.pdf
- Halberg F, Cornélissen G, Katinas G, Tvildiani L, Gigolashvili M, Janashia K, Toba T, Revilla M, Regal P, Sothern RB, Wendt HW, Wang ZR, Zeman M, Jozsa R, Singh RB, Mitsutake G, Chibisov SM, Lee J, Holley D, Holte JE, Sonkowsky RP, Schwartzkopff O, Delmore P, Otsuka K, Bakken EE, Czaplicki J, International BIOCOS Group. Chronobiology's progress: Part II, chronomics for an immediately applicable biomedicine. J Applied Biomedicine 2006; 4: 73-86. <u>http://www.zsf.jcu.cz/vyzkum/jab/4_2/halberg2.pdf</u>

RENAL FAILURE AND LONG-TERM EXERCISE TRAINING – A REVIEW

Masahiro Kohzuki

Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan

INTRODUCTION

The exercise capacity of the patients with renal dysfunction declines and this phenomenon is distinctly related to the extent of renal function deterioration. It is suggested that appropriate exercise training may improve the physical strength and the quality of life in patients with chronic renal failure (CRF) besides the improvement of glucose and lipid metabolism.

PRESENT STATUS

However, it is required to consider the influence of exercise on renal function thoroughly, because acute exercise causes proteinuria and decreases renal blood flow and glomerular filtration rate. At present, there are few reports concerning the optimal intensity and duration of exercise training for patients with CRF. Moreover, there has been no definite conclusion as to whether or not chronic exercise training (EX) has any renal protective effect in animal models of CRF. Recently, the renal and peripheral effects of long-term moderate to intense exercise training in various rat models of CRF has been extensively reported. The effects of a combination of EX and rennin-angiotensin system inhibitors (ARI) on renal function were also assessed. The results indicated that moderate to intense EX and ARI can yield a renal protective effect in some models. They also suggested that the simultaneous treatment of moderate EX and ARI provided a greater renoprotective effect than treatment by ARI alone.

CONCLUSION

Further investigations will be needed to examine the mechanism of the renal protective effect of EX. A better understanding of the mechanism may lead to improved exercise strategies and the establishment of a renal rehabilitation regime for CRF patients.

Supported by MSM0021622402

REFERENCES

- Cheema B, Abas H, Smith B, O'Sullivan A, Chan M, Patwardhan A, Kelly J, Gillin A, Pang G, Lloyd B, Singh MF. Progressive exercise for anabolism in kidney disease (PEAK): a randomized, controlled trial of resistance training during hemodialysis. J Am Soc Nephrol. 2007; 18(5): 1594-601.
- 2. Davison SN. Facilitating advance care planning for patients with end-stage renal disease: the patient perspective. Clin J Am Soc Nephrol. 2006; 1(5): 1023-8.
- Dodson JL, Diener-West M, Gerson AC, Kaskel FJ, Furth SL. An assessment of health related quality of life using the child health and illness profile-adolescent edition in adolescents with chronic kidney disease due to underlying urological disorders. J Urol. 2007; 178(2): 660-5; discussion 665.
- Gaudino M, Girola F, Piscitelli M, Martinelli L, Anselmi A, Della Vella C, Schiavello R, Possati G. Long-term survival and quality of life of patients with prolonged postoperative intensive care unit stay: unmasking an apparent success. J Thorac Cardiovasc Surg. 2007; 134(2): 465-9.
- Giordano M, Tirelli P, Ciarambino T, Gambardella A, Ferrara N, Signoriello G, Paolisso G, Varricchio M. Screening of depressive symptoms in young-old hemodialysis patients: relationship between Beck Depression Inventory and 15-item Geriatric Depression Scale. Nephron Clin Pract. 2007; 106(4): 187-92.

- Molsted S, Prescott L, Heaf J, Eidemak I. Assessment and clinical aspects of healthrelated quality of life in dialysis patients and patients with chronic kidney disease. Nephron Clin Pract. 2007; 106(1): 24-33.
- Neumann ME Finding 'hope' for understanding kidney disease. Nephrol News Issues. 2007; 21(5): 64-66.

NON-INVASIVE IMAGING TECHNIQUES IN CASES OF CARDIAC FAILURE

Wolf Jean-Eric.^a, Dobsak Petr.^b, Barthez Olivier.^a, Eicher Jean-Christophe^a, Siegelova Jarmila.^b

 ^a IInd Department of Cardiology, University Hospital of Dijon, France
^b Department of Functional Diagnostics and Rehabilitation, St.Anna Faculty Hospital in Brno, Czech Republic

Introduction

Echocardiography is a traditional noninvasive "imaging" method that provides useful information for the management of heart failure. Its potential applications range from diagnosis to therapeutic decisions to the monitoring of therapy. Although great strides have been made in the understanding and treatment of heart failure, its incidence is increasing and, along with this increase, a growing number of patients are presenting with additional co-morbidities.

Recent advances in the imaging techniques helped much the diagnosis of cardiac failure (1). These modern imaging modalities combine classic echocardiography (TTE, TEE) computed tomography (CT) and MRI, are constantly used to confirm the existence, to precise the etiologies, mechanisms and prognosis of the cardiac failure. Although echocardiography is still the first line modality used, imaging is often sub-optimal especially in non-echogenic patients. Computed tomography and MRI are second line imaging modalities that have the ability to overcome the limitations of echocardiography.

The mentioned non-invasive imaging techniques allow the doctors to follow with precision their patients on treatment and to reach some therapeutic indications (implantable cardioverter-defibrillators, for instance) depending on the data obtained from the imaging technique (2).

In this short review we will present and precise their use in clinical practice summarized in the Table 1.

Methods compared

Table 1

	Echocardiography	Nuclear cardiology	СТ	MRI
Ventricular function				
-systolic	+++	+++	+?	+++
-global and regional	+++	++	+?	+++
-dyssynchrony	++	+	-	?
-diastolic	+++	+	-	?
Aetiology -ischaemic heart disease -valvular heart disease -cardiomyocardiopathy	++ +++ +	++ - -	++ + ?	++ + ++
Prognosis	++	++	?	++
Follow-up	+++	++	-	++

+ to +++ : increasing interest for the technique for each item

Discussion

The most frequently used technique for assessment of the left ventricle status in heart failure is still echocardiography (TTE or TEE). These techniques are widely available, but image acquisition depends on the operator and the acoustic window. Reproducibility is reasonable in normal ventricles, but the quantification of volumes and mass relies on geometric assumptions that do not apply to ventricles undergoing asymmetric cardiac remodeling such as in cardiomyopathy (3). Cardiovascular magnetic resonance is independent of geometric assumptions (4) and has been shown to be accurate and reproducible (5). The published reproducibility data for echocardiography and newly acquired MRI data in patients with heart failure suggested recently the improved reproducibility for MRI, leading to significant reductions in sample sizes for drug trials (6). However, there are no reports of direct comparison of reproducibility of MRI with echocardiography in the same group of patients. Thus, it should be of interest to perform a head-to-head comparison between these techniques and to determine the influence of heart size, shape, and mass on the results in

normal subjects and patients with dilated or hypertrophied hearts. The methods of nuclear cardiology such as thallium SPECT have been proposed to predict the reversibility of left ventricular dysfunction after revascularization. These techniques permit differentiation of viable from nonviable myocardium; however few studies have directly compared their accuracy in the same patients (7, 8). It is now widely accepted that the techniques used in nuclear cardiology have comparable accuracy for prediction of reversibility of global left ventricular dysfunction after revascularization (9, 10).

The combination of cardiac MRI and multi-slice CT can complement the diagnostic information obtained by echocardiography and invasive cardiac catheterization. Post-operative imaging of CHD is especially enhanced by the spin echo MRI techniques, while gradient cine-echo MRI imaging allows functional information that is not encumbered by geometric assumptions (11). Phase contrast (velocity encoding) cardiac MRI data can provide information about flow, allowing accurate determination of regurgitation and shunt volume. Gadolinium enhanced MRI or three-dimensional reconstructed images from multi-slice CT angiography allow excellent delineation of vascular structures in complex heart disease. Coronary imaging, while possible with both modalities, appears more facile with fast CT imaging (11).

Conclusion

The presented data obtained by various techniques in patients with heart failure should be interpreted in the context of locally available techniques. It is necessary to point out that there are very wide variances in several parameters such as volumes and ejection fraction between techniques used, which are most marked in comparisons using echocardiography. This suggests that cardiovascular magnetic resonance could be recommended as a preferred technique for volume and ejection fraction estimation in heart failure patients, because of its 3D approach for non-symmetric ventricles and superior image quality.

Supported by MSM0021622402

References

- Higgins CB. Which standard has the gold? J Am Coll Cardiol 19 (1992), pp. 1608– 1609.
- Habib G, Tribouilloy C, Lafitte S. The best of echocardiography in 2006. Arch Mal Coeur Vaiss. 2007 Jan;100 Spec No 1:9-17.
- Gordon EP, Schnittger I, Fitzgerald PJ, Williams P, Popp RL. Reproducibility of left ventricular volumes by two-dimensional echocardiography. J Am Coll Cardiol 2 (1983), pp. 506–513.
- Allison JD, Flickinger FW, Wright CJ, Falls DG, Prisant LM, VonDohlen TW, Frank MJ. Measurement of left ventricular mass in hypertrophic cardiomyopathy using MRI: comparison with echocardiography. Magn Reson Imaging 11 (1993), pp. 329–334
- Longmore DB, Klipstein RH, Underwood SR, Firmin DN, Hounsfield GN, Watanabe M, Bland C, Fox K, Poole-Wilson PA, Rees RS. Dimensional accuracy of magnetic resonance in studies of the heart. Lancet 1 (1985), pp. 1360–1362.
- 6. Bellenger NG, Grothues F, Smith G, Pennell DJ. Quantification of right and left ventricular function by MRI. Herz 25 (2000), pp. 392–399
- 7. Rehr RB, Mallow CR, Filipchuk NG, Peshock RM. Left ventricular volumes measured by MR imaging. Radiology 156 (1985); 285-8.
- Mogelvang J, Stockholm KH, Saunamaki K, Reimer A, Stubgaard M, Thomsen C, Fritz-Hansen P, Henriksen O. Assessment of left ventricular volumes by magnetic resonance in comparison with radionuclide angiography, contrast angiography and echocardiography. Eur Heart J 13 (1992), pp. 1677–1683.
- 9. Tamborini G, Galli CA, Maltagliati A, Andreini D, Pontone G, Quaglia C, Ballerini G, Pepi M. Comparison of feasibility and accuracy of transthoracic echocardiography versus computed tomography in patients with known ascending aortic aneurysm. Am J Cardiol. 2006 Oct 1;98(7):966-9. Epub 2006 Aug 22.
- Semelka RC, Tomei E, Wagner S, Mayo J, Caputo G, O'Sullivan M, Parmley WW, Chatterjee K, Wolfe C, Higgins CB, Interstudy reproducibility of dimensional and functional measurements between cine magnetic resonance imaging studies in the morphologically abnormal left ventricle. Am Heart J 119 (1990), pp. 1367–1373.
- Samyn MM. A review of the complementary information available with cardiac magnetic resonance imaging and multi-slice computed tomography (CT) during the study of congenital heart disease. Int J Cardiovasc Imaging. 2004 Dec;20(6):569-78.

EFFECT OF LOW VOLTAGE ELECTRICAL STIMULATION ON ANGIOGENESIS IN RAT SKELETAL MUSCLE

Makoto NAGASAKA, Masahiro KOHZUKI

The Department of Internal Medicine and Rehabilitation Science, Graduate School of Medicine, Tohoku University of Sendai, Japan

INTRODUCTION

LVES (Low voltage electrical stimulation) in skeletal muscle at a level far below the threshold of muscle contraction has been reported to promote local angiogenesis. However the mechanism underlying the promotion of local angiogenesis by LVES has not been fully elucidated.

AIM

We evaluated whether angiogenic factors, such as VEGF (vascular endotherial growth factor), HGF (hepatocyte growth factor) and FGF (fibroblast growth factor), and other disadvantageous factor, such as inflammation { IL6 (Interleukin-6)}, and hypoxia {HIF-1 α (hypoxia-inducible factor 1 α)} contribute to the local angiogenesis by LVES. Moreover there are some reports that both HVES (high voltage electrical stimulation) up-regulates VEGF and we compared the effects of LVES to that of HVES on the induction of the angiogenic factors.

ANIMALS AND METHODS

We completely excised bilateral femoral arteries of the Male Sprague-Dawley Rats. After the operation, the electrodes were implanted onto the center of the fascia of the bilateral TA (tibialis anterior) muscles, tunneled subcutaneously and exteriorized at the level of the scapulae. The rats were randomly divided into 3 groups. In the first group, the TA muscles
were continuously stimulated at a 50-Hz stimulus frequency, with a 0.1 V stimulus strength and no interval (C-LVES). In the second group, rats were stimulated with 50Hz, 0.1V stimuli at two-hour intervals (I-LVES). In the third group rats were stimulated with a 10Hz, 3V stimulus at two-hour intervals (I-HVES).

RESULTS

The VEGF levels were significantly increased in C-LVES, I-LVES and I-HVES stimulated muscles compared with that of the controls. However there was not significantly different in the VEGF level among 3 conditions. The HGF level was significantly increased only in C-LVES stimulated muscles compared with that of the controls whereas were not increased in I-LVES and in I-HVES. C:F ratio (Capillary to muscle fiber ratio) of stimulated muscles were increased about 2 fold compared with the unstimulated muscles in C-LVES and I-HVES, whereas was not increased in I-LVES. On the contrary, there was no difference in FGF, IL6, and HIF-1 α between the LVES group and control group.

CONCLUSION

In conclusion, both LVES and HVES are useful to induce VEGF and angiogenesis. Moreover LVES might be better for ischemic disease than HVES, as HVES causes discomfort and muscle atrophy.

Supported by MSM0021622402

REFERENCES

- 1. Dobsak P, Nagasaka M, Siegelova J, Kohzuki M, Imachi K, Jancik J. PROMOTION OF ANGIOGENESIS AND BLOOD SUPPLY RESTORATION IN ISCHEMIC SKELETAL MUSCLE OF RAT AFTER LOW-VOLTAGE ELECTRICAL STIMULATION. Atherosclerosis Supplements 2005; 6(1):16-17.
- Nagasaka M, Kohzuki M, Dobsak P, Fujii T, Mori, Ichie M. THE EFFECT ON ANGIOGENESIS BY CONTINUOUS ELECTRICAL STIMULATION OF SKELETAL MUSCLE OF RAT: THE CHANGE OF BLOOD FLOW BY ELECTRICAL STIMULATION (*Japanese*). Japanese Journal of Rehabilitation Medicine 2005; 41(suppl.): S291.
- 3. Nagasaka M, Kohzuki M, Ito O, Minami N, Dobsak P. THE EFFECT ON ANGIOGENESIS BY CONTINUOUS ELECTRICAL STIMULATION OF SKELETAL MUSCLE OF RAT: THE BLOOD FLOW OF HEALTHY MEN BY ELECTRICAL STIMULATION (*Japanese*). Japanese Journal of Rehabilitation 2005; 41(suppl.): S292.
- 4. Nagasaka M, Kohzuki M, Dobsak P, Imachi H, Minami N. NEW STRATEGY OF PHYSICAL THERAPY: EFFECT OF LOW-VOLTAGE ELECTRICAL STIMULATION ON ANGIOGENESIS IN RAT SKELETAL MUSCLE. In: Proceedings of the 3rd World Congress of the International Society of Physical and Rehabilitation Medicine Sao Paulo 2005. Monduzzi Editore: 845-48. ISBN 88-7587-137-X
- Nagasaka M, Kohzuki M, Fujii T, Kanno S, Kawamura T, Onodera H, Itoyama Y, Ichie M, Sato Y. EFFECT OF LOW-VOLTAGE ELECTRICAL STIMULATION ON ANGIOGENIC GROWTH FACTORS IN ISCHAEMIC RAT SKELETAL MUSCLE. Clin Exp Pharmacol Physiol. 2006; 33(7): 623-7.
- Nagasaka M, Kohzuki M, Minami N, Kanazawa M, Dobsak P, Siegelova J. LOW-VOLTAGE ELECTRICAL STIMULATION AS A NEW TREATMENT FOR ISCHEMIC DISEASE ON HYPERTENSIVE ATHEROSCLEROSIS. Journal of Hypertension 2006; 24(suppl.6): S237.

CIRCADIAN BLOOD PRESSURE VARIATION ANALYZED FROM 7-DAY MONITORING

Jarmila Siegelová, Jiří Dušek, Bohumil Fišer, Pavel Homolka, Pavel Vank, Michal Mašek, Alena Havelková, Germaine Cornelissen*, Franz Halberg*

Department of Functional Diagnostics and Rehabilitation, Masaryk University Brno, St. Anna Faculty Hospital Brno, Czech Republic, *University of Minnesota, USA

INTRODUCTION

Franz Halberg, Germaine Cornelissen and BIOCOS scientific group provided strong evidence for the need to account for day-to-day changes in blood pressure and heart rate variables in the similar way as a circadian assessment considers the hour-to-hour variability [1-5]. The evidence led to the recommendation of around-the-clock monitoring for 7 days at the outset [6,7], to be continued whenever needed, until monitoring for a lifetime becomes more readily feasible.

By 1988, major findings had been summarized in a volume of annotated illustrations [8]. Methodology had developed concomitantly under Halberg chronobiology center leadership in Minnesota University. In particular, the "sphygmochron" [9] was introduced.

The sphygmochron is a computer summary of results from chronobiological analyses performed on BP and HR data collected around the clock by ambulatory monitoring. Two approaches are possible, one parametric (model-dependent), the other non-parametric (model-independent). The parametric approach entails the least-squares fit of a two-component model consisting of cosine curves with periods of 24 and 12 hours. Estimates are obtained for the MESOR (midline-estimating statistic of rhythm), a rhythm-adjusted mean, and for the amplitude and (acro)phase of each component, measures of (half) the extent of predictable change within a cycle, and of the timing of overall high values recurring in each cycle, respectively.

The relationship between age and circadian blood pressure (BP) variation was the aim of the present study.

METHODS

One hundred and eighty-seven subjects (130 males, 57 females), twenty years to seventy seven years old, were recruited for seven-day BP monitoring. Colin medical instruments (Komaki, Japan) were used for ambulatory BP monitoring (oscillation method, 30-minute interval between measurements). Sinusoidal curve was fitted (minimum square method) and mean value and amplitude of the curve (double amplitude corresponds to the night-day difference) were evaluated every day of monitoring. Average 7-day values of the mean (M) and of double amplitude (2A) for systolic BP (SBP), diastolic BP (DBP) and heart rate (HR) were determined for each subject.

RESULTS

Mean values of MESOR (\pm SD) for the whole group of healthy people were: SBP- 127 \pm 8 mmHg, DBP – 79 \pm 6 mmHg, HR – 70 \pm 6 bpm. Mean values of double circadian amplitude were: SBP – 21 \pm 7 mmHg, DBP – 15 \pm 5 mmHg, HR – 15 \pm 6 bpm. The linear relationship between MESOR of SBP and age (r=0.341, p< 0.001) and DBP and age (r=0.384, p<0.001) was found (difference between the age of twenty years and seventy seven years: SBP - 16, DBP-12 mmHg). Double circadian amplitude of SBP and DBP was increasing with age up to 35 years, then the curve remained relatively flat up to 55 years (maximum at 45 years) and then decreased again (difference between 45 and 77 years: SBP- 13 mmHg, DBP-12 mmHg). Heart rate MESOR and double circadian amplitude were age-independent. Mean values of SBP and DBP were increasing with age up to 75 years, but night-day

difference of SBP and DBP reached the maximum value at 45 years and then decreased.



Figure 1. The circadian rhythm analysis according to non-parametric approach.

MESOR - rhythm-adjusted 24-hour mean.

Amplitude –half of total predictable change in rhythm, definied by rhythmic function fitted to data and expressed in original or relative units, e.g., as percentage of series mean or MESOR.Acrophase- Timing of peak value of the rhythm. Halberg cosinor analysis.)



Relationship between mean SBP and age

Figure 2. Relationship between MESOR of systolic blood pressure(SBP, mmHg), measured by 7 day ambulantory blood pressure monitoring, and age (years) of the subjects.



Relationship between mean DBP and age

Figure 3. Relationship between MESOR of diastolic blood pressure (DBP, mmHg), measured by 7 day ambulantory blood pressure monitoring, and age (years) of the subjects.



Relationship between MESOR HR and age

Figure 4. Relationship between MESOR of heart rate (HR, bpm), measured by 7-day ambulatory blood pressure monitoring, and age (years) of the subjects



Circadian amplitude SBP and age

Figure 5. Relationship between circadian amplitude of systolic blood pressure (SBP, mmHg), measured by 7-day ambulantory blood pressure monitoring, and age (years) of the subjects.



Circadian amplitude DBP and age

Figure 6. Relationship between circadian amplitude of diastolic blood pressure (DBP, mmHg), measured by 7-day ambulatory blood pressure monitoring, and age (years) of the subjects.



Circadian amplitude HR and age

Figure 7. Relationship between circadian amplitude of heart rate (bpm, HR), measured by 7-day ambulatory blood pressure monitoring, and age (years) of the subjects.

DISCUSSION

There is a growing body of evidence suggesting that time structures in us and around us are intrically interwoven. Most if not all components of variation found in biota are also found in the environment, and vice versa [10]. For instance, about daily changes are seen in almost every biological variable under 24-hour synchronized conditions. It has also long been known that the phase of circadian rhythms can be manipulated by changing the phase of the environmental cycles [11]. At least for the case of circadian rhythms, their genetic inheritance has been demonstrated on a molecular basis [12,13], suggesting that the influence from the environment has been acquired genetically during the course of evolution.

The mapping of chronomes should benefit our understanding of human health and disease in several ways. The study of human chronomes can serve the derivation of refined reference values to better define health and to identify pre-disease, so that prophylactic interventions can be instituted as early as possible, preferably before disease sets in [14-16]. The focus is thus put on pre-habilitation, in the hope that the need for re-habilitation will thereby be reduced [17,18,19].

Several studies [20, 21] comparing the classification of patients based on single office measurements with that based on ambulatory monitoring for one to seven days suggest that the incidence of misdiagnosis is around 40%, in keeping with the 48% response to placebo in the Australian Therapeutic Trial [22,23]. Comparison of circadian characteristics from day to day in records spanning at least two days further indicates the shortcomings of monitoring limited to a single 24-hour span [24,25,26]. Prolonging the monitoring from one to two days reduces the uncertainty in the estimation of circadian parameters by about 35% [27], whereas further information on the biological week [28,29,30,31] requires monitoring for at least 7 days, the current recommendation of BIOCOS for everybody at the outset [32]. It is now widely accepted that prognosis of target organ damage is by far superior when it is based on around the clock monitoring than on single office measurements [33,34,35].

The mistaken impression that the circadian variation in blood pressure and heart rate is sufficiently stable to be approximated by a single 24-hour profile stems in large part from the use of statistical methods on groups of subjects rather than focusing on the individual patient. Correlation analyses applied to large groups of subjects with a wide range of average values emphasize similarity. Statistical analyses focusing on individual differences observed from one profile to another, however, yield information more likely to help the patient in need of treatment [24]. Several case reports document this point [16, 36, 37,38, 39]. Continued monitoring is the most logical solution.

An important distinction needs to be made between lessons learned from large clinical trials and their application for the individual patient. Differences and trends uncovered in studies on groups, even when each subject provides only one or a few measurements, cannot be similarly assessed in medical practice when a decision needs to be made for treating the individual patient. In order to be able to reach an informed decision for the given patient, serial rather than single data should be collected. When time series are available, it becomes possible to assess risk elevation or the response to treatment for that particular patient.

Our study made possible not only to confirm the increase of systolic and diastolic blood pressure with age but also to describe the age dependence of the circadian amplitude. Mean values of SBP and DBP were increasing with age up to 75 years, but night-day difference of SBP and DBP reached the maximum value at 45 years and then decreased.

Supported by MSM0021622402

REFERENCES

- Halberg F. Some physiological and clinical aspects of 24-hour periodicity. J-Lancet (Minneapolis) 73: 20-32, 1953.
- 2. Halberg F. Chronobiology. Ann Rev Physiol 31: 675-725, 1969.
- 3. Cornélissen G, Halberg E, Halberg Francine, et al. Chronobiology: a frontier in biology and medicine. Chronobiologia 16: 383-408, 1989.
- Halberg F, Cornélissen G. Chronobiology, rhythms, clocks, chaos, aging, and other trends. In: Maddox G. (ed.) Encyclopedia of Aging, 3rd ed. Springer, New York, 2001, pp. 196-201.
- Halberg F, Cornélissen G, Otsuka K, et al., International BIOCOS Study Group. Crossspectrally coherent ~10.5- and 21-year biological and physical cycles, magnetic storms and myocardial infarctions. Invited presentation, NATO Advanced Study Institute on Space Storms and Space Weather Hazards, Crete, Greece, June 19-29, 2000. Neuroendocrinol Lett 21: 233-258, 2000.

- Halberg F, Cornélissen G, Wall D et al. Engineering and governmental challenge: 7day/24-hour chronobiological blood pressure and heart rate screening. Biomedical Instrumentation & Technology 36: Part I, 89-122, Part II, 183-197, 2002.
- Cornélissen G, Delmore P, Halberg F. Health Watch 3. University of Minnesota/Medtronic, Minneapolis, MN, 31 pp., 2004.
- Halberg F, Cornélissen G, Halberg E, Halberg J, Delmore P, Shinoda M, Bakken E. Chronobiology of human blood pressure. Medtronic Continuing Medical Education Seminars, 1988, 4th ed., 242 pp.
- Halberg F, Bakken E, Cornélissen G, et al. Chronobiologic blood pressure assessment with a cardiovascular summary, the sphygmochron. In: Blood Pressure Measurements (Meyer-Sabellek W, Anlauf M, Gotzen R, Steinfeld L, eds), Steinkopff Verlag, Darmstadt, FRG, 1990, pp. 297-326.
- Halberg F, Cornélissen G, Otsuka K, Watanabe Y, Delyukov A, Gorgo Y, Zhao ZY, Weydahl A, Sothern RB, Siegelova J, Fiser B, Dusek J, Syutkina EV, Perfetto F, Tarquini R, Singh RB, Rhees B, Lofstrom D., Lofstrom P, Sonkowsky R, Johnson PWC, Schwartzkopff O, International BIOCOS Study Group. Cross-spectrally coherent ~10.5- and 21-year biological and physical cycles, magnetic storms and myocardial infarctions. Neuroendocrinoogy Letters 2000; 21: 233-258.
- 11. Halberg F. Chronobiology. Annual Reviews of Physiology 1969; 31: 675-725.
- 12. Pennisi E. Multiple clocks keep time in fruit fly tissues. Science 1997; 278: 1560-1561.
- Plautz JD, Kaneko M, Hall JC, Kay SA. Independent photoreceptive circadian clocks throughout *Drosophila*. Science 1997; 278: 1632-1635.
- Halberg F, Cornélissen G, Carandente A, Bakken E, Young E. Chronobiologic perspectives of international health care reform for the future of children. Chronobiologia 1993; 20: 269-275.
- 15. Cornélissen G, Delmore P, Bingham C, Rutledge G, Kumagai Y, Kuwajima I, Suzuki Y, Kuramoto K, Otsuka K, Scarpelli PT, Tarquini B, Cagnoni M, Garcia L, Zaslavskaya RM, Syutkina E, Carandente F, Rapoport SI, Romanov YA, Tamura K, Bakken E, Halberg F. A response to the health care crisis: a 'health start' from 'womb to tomb'. Chronobiologia 1993; 20: 277-291.
- 16. Cornélissen G, Otsuka K, Halberg F. Blood pressure and heart rate chronome mapping: a complement to the human genome initiative. In: Chronocardiology and Chronomedicine: Humans in Time and Cosmos, Otsuka K, Cornélissen G, Halberg F (eds.), Life Sciences Publishing, Tokyo, 1993, pp. 16-48.

- Cornélissen G, Halberg F, Schwartzkopff O, Delmore P, Katinas G, Hunter D, Tarquini B, Tarquini R, Perfetto F, Watanabe Y, Otsuka K. Chronomes, time structures, for chronobioengineering for "a full life". Biomedical Instrumentation & Technology 1999; 33: 152-187.
- 18. Halberg F, Cornélissen G, Wall D, Otsuka K, Halberg J, Katinas G, Watanabe Y, Halhuber M, Müller-Bohn T, Delmore P, Siegelova J, Homolka P, Fiser B, Dusek J, Sanchez de la Peña S, Maggioni C, Delyukov A, Gorgo Y, Gubin D, Carandente F, Schaffer E, Rhodus N, Borer K, Sonkowsky RP, Schwartzkopff O. Engineering and governmental challenge: 7-day/24-hour chronobiologic blood pressure and heart rate screening: Part I. Biomedical Instrumentation & Technology 2002; 36: 89-122.
- 19. Halberg F, Cornélissen G, Wall D, Otsuka K, Halberg J, Katinas G, Watanabe Y, Halhuber M, Müller-Bohn T, Delmore P, Siegelova J, Homolka P, Fiser B, Dusek J, Sanchez de la Peña S, Maggioni C, Delyukov A, Gorgo Y, Gubin D, Carandente F, Schaffer E, Rhodus N, Borer K, Sonkowsky RP, Schwartzkopff O. Engineering and governmental challenge: 7-day/24-hour chronobiologic blood pressure and heart rate screening: Part II. Biomedical Instrumentation & Technology 2002; 36: 183-197.
- Kumagai Y, Kuwajima I, Suzuki Y, Kuramoto K, Otsuka K, Cornélissen G, Halberg F. Untenable acceptance of casual systolic/diastolic blood pressure readings below 140/90 mm Hg. Chronobiologia 1993; 20: 255-260
- Schaffer E, Cornélissen G, Rhodus N, Halhuber M, Watanabe Y, Halberg F. Outcomes of chronobiologically normotensive dental patients: a 7-year follow-up. J American Dental Association 2001; 132: 891-899.
- 22. Management Committee. Australian National Blood Pressure Study: The Australian Therapeutic Trial in Mild Hypertension. The lancet (June 14) 1980: 1261-1267.
- Halberg F, Cornélissen G, Halberg E, Halberg J, Delmore P, Shinoda M, Bakken E. Chronobiology of human blood pressure - Medtronic Continuing Medical Education Seminars, 1988, 4th ed., 242 pp.
- Cornélissen G. Instrumentation and data analysis methods needed for blood pressure monitoring in chronobiology. In: Scheving LE, Halberg F, Ehret CF (eds). Chronobiotechnology and Chronobiological Engineering. Dordrecht, The Netherlands: Martinus Nijhoff, 1987, pp. 241-261.
- 25. Tamura K, Wu J, Cornélissen G, Halberg F. Agreement between consecutive ambulatory 24-hour blood pressure and heart rate profiles in Japanese hospital staff. Progress in Clinical and Biological Research 1990; 341A: 263-272.

- 26. Watanabe Y, Cornélissen G, Halberg F, Bingham C, Siegelova J, Otsuka K, Kikuchi T. Incidence pattern and treatment of a clinical entity, overswinging or circadian hyperamplitudetension (CHAT). Scripta medica 1997; 70: 245-261.
- 27. Halberg F, Scheving LE, Lucas E, Cornélissen G, Sothern RB, Halberg E, Halberg J, Halberg Francine, Carte J Jr, Straub KD, Redmond DP. Chronobiology of human blood pressure in the light of static (room-restricted) automatic monitoring. Chronobiologia 1984; 11: 217-247.
- 28. Carandente F, Cornélissen G, Halberg F Further data and analyses. Chronobiologia 1994; 21: 311-314.
- Halberg F, Cornelissen G, Raab F, Schaffer E, Siegelova J, Fiser B, Dusek J, Prikryl P, Otsuka K. Automatic physiologic 7-day monitoring and chronobiology. Japanese J of Electrocardiology 1995; 15 (Suppl. 1): S-1-5 - S-1-11.
- Siegelova J, Homolka P, Dusek J, Fiser B, Cornélissen G, Halberg F. Extracircadian-tocircadian variance transpositions early and vice versa late in life in the human circulation. Proceedings, 1st International Symposium, Workshop on Chronoastrobiology & Chronotherapy (Satellite Symposium, 7th Annual Meeting, Japanese Society for Chronobiology), Kudan, Chiyodaku, Tokyo, 11 Nov 2000, pp. 58-60.
- Singh RB, Cornélissen G, Siegelova J, Homolka P, Halberg F. About half-weekly (circasemiseptan) pattern of blood pressure and heart rate in men and women of India. Scripta medica 2002; 75: 125-128.
- Halberg F, Smith HN, Cornélissen G, Delmore P, Schwartzkopff O, International BIOCOS Group. Hurdles to asepsis, universal literacy, and chronobiology—all to be overcome. Neuroendocrinology Letters 2000; 21: 145-160.
- Mancia G, Gamba PL, Omboni S, Paleari F, Parati G, Sega R, Zanchetti A. Ambulatory blood pressure monitoring. J Hypertension (Suppl) 1996; 14: S61-S66.
- Mallion JM, Baguet JP, Siche JP, Tremel F, De Gaudemaris R. Clinical value of ambulatory blood pressure monitoring. J Hypertension 1999; 17: 585-595
- Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. Hypertension 2000; 36: 894-900.
- 36. Halberg F, Cornélissen G, International Womb-to-Tomb Chronome Initiative Group. Resolution from a meeting of the International Society for Research on Civilization Diseases and the Environment (New SIRMCE Confederation), Brussels, Belgium,

March 17-18, 1995: Fairy tale or reality? Medtronic Chronobiology Seminar #8, April 1995, 12 pp. text, 18 figures.

- Cornélissen G, Halberg F. Impeachment of casual blood pressure measurements and the fixed limits for their interpretation and chronobiologic recommendations. Annals. New York Academy of Sciences 1996; 783: 24-46.
- Cornélissen G, Halberg F, Hawkins D, Otsuka K, Henke W. Individual assessment of antihypertensive response by self-starting cumulative sums. J Medical Engineering & Technology 1997; 21: 111-120
- 39. Halberg F, Cornélissen G, Otsuka K, Katinas GS, Schwartzkopff O, Halpin C, Mikulecky M, Revilla M, Siegelova J, Homolka P, Dusek J, Fiser B, Singh RB. Chronomics detects altered vascular variabilities constituting risks greater than hypertension: with an illustrative case report. In: Mitro P, Pella D, Rybar R, Valocik G (eds). Proceedings, 2nd Congress on Cardiovascular Diseases, Kosice, Slovakia, 25-27 April 2002. Bologna: Monduzzi Editore, 2002, pp. 223-258.

ANALYSIS OF BAROREFLEX FUNCTION BY MEANS OF MATHEMATICAL MODEL

Bohumil Fišer, Jarmila Siegelová, Jiří Dušek, Michal Pohanka, Michal Mašek, Josef Barák, Jiří Moudr, Germaine Cornelissen, Franz Halberg

Dept Physiology, Dept. Functional Investigations and Rehabilitation, Faculty of Medicine, Masaryk University, Brno

INTRODUCTION

It is generally believed that the primary function of baroreflex is a short time stabilization of blood pressure. Reevaluation of all functions of baroreflex by means of simple mathematical model of circulation was the aim of the present study.

METHODS

The simple mathematical model of circulation consists of three equations:

CO = (AP - VP) / TPR, M = Ca * AP + Cv * VP, CO = k * VP, where CO = cardiac output, AP = arterial pressure, VP = venous pressure, TPR = total peripheral resistance, M = total volume of blood in arterial and venous beds, Ca = arterial bed capacity (0.006 l/mmHg), Cv = venous bed capacity (0.6 l/mmHg), k = constant proportional to myocardial contractility (1). The following states are modeled: 1. Rest (AP = 100 mmHg, CO = 5l/min, M = 3.6 l = total blood volume – volume of blood in heart and lungs). 2. Immediately after baroreceptors denervation (increase in blood pressure 50 mmHg caused by increased TPR). 3. Several days after baroreceptors denervation (return of blood pressure to the original level caused by natriuresis and by corresponding decrease in blood volume). 4. Physical exercise before baroreceptors denervation (increase of cardiac output to 20 l/min at constant blood pressure, k and TPR are calculated, other values equal to rest values). 5. Physical exercise several days after baroreceptors denervation (TPR and k equal to values at exercise before denervation).

RESULTS

The results are seen in Table 1.

		Rest		Exerci	se
	Before	Immediately			Exercise
	denervation	after	days after	Exercise before	after
AP mmHg	100	150	100	100	72.6
CO l/min	5	4.5	3	20	13.1
M 1	3.6	3.6	2.4	3.6	2.4
TPR					
mmHg*min/l	19	32.3	32.3	4.75	5.3
Κ					
l/(min*mmHg)	1	1	1	4	4
VP mmHg	5	4.5	3	5	3.3

Despite the same value of cardiac contractility indicator k and the same decrease of TPR caused by vasodilatation in working muscles as before denervation the cardiac output is one third lower after baroreceptors denervation. This demonstrates the disadvantage of baroreceptor denervation and so the main function of the baroreflex.

DISCUSSION

The elimination of baroreflex by cutting of baroreceptors efferents in animal experiments elicits immediately an increase in blood pressure of approximately 50 mmHg. Blood pressure returns to the original level by means of natriuresis during few days. The trade off is a decrease of blood volume, which causes the decrease of cardiac output during exercise. This indicates that the primary function of baroreflex is the vasodilatation by suppression of activity of vasomotor level nerves. Therefore blood volume is held on a sufficiently high level.

The baroreceptors cannot measure the absolute values of blood pressure. The baroreceptors resetting during the night serves to the recalibration (2). The set point is approximately 50 mmHg under the value of blood pressure at which the suppression of vasomotor activity is completely abolished. The combined action of baroreflex control and endocrine humoral blood pressure by kidneys secure relatively low blood pressure at blood volume sufficiently high for increased cardiac output during exercise. Relatively low blood pressure decreases the oxygen consumption of heart muscle and protects the brain vessels. The latter function is more important. Blood pressure in giraffe is much higher than in man and other mammals without negative consequences. The importance of brain blood vessels protection demonstrates the localization of baroreceptors in vessels conducting blood to the brain. The brain perfusion is fine tuned by autoregulation during several seconds. We have demonstrated this reaction in man several years ago (3). This autoregulatory reaction disappears in hypertensives (4). It is seen not only from our study, but also the observation of inadequate perfusion of brain in hypertensives after abrupt decrease of blood pressure by antihypertensive treatment demonstrates this fact. The low baroreflex gain insufficiently protects the human body from increase in blood pressure caused by psychological stress or by obesity. We have demonstrated in children and young adults that low baroreflex gain and obesity are two independent risk factors for high blood pressure (5). This study also solved "the egg and hen problem". Low baroreflex gain was observed also in white coat hypertension, it means before the increased blood pressure remodeled the carotic sinus wall (6).

CONCLUSION

In conclusion, the model simulation revealed the common regulation of blood pressure and blood volume by baroreflex and kidneys as a primary function of baroreflex. The second important function is protection of brain vessels against the loss of autoregulatory ability, which is important for adequate supply of the brain with oxygen and nutrition. Baroreflex maintains adequate protection against hypertension in primitive civilizations but at obesity and/or psychological stress the low baroreflex gain is an independent risk factor for hypertension.

Supported by MSM0021622402

REFERENCES

- Fišer B. Teoretické problémy terapie hypertenze řešené pomocí jednoduchého matematického modelu. Čas. Lék. Čes. 115,1976,(33-34), p.1008-1011.
- Siegelová, J., Fišer, B., Dušek, J., et al. 24-hodinové monitorování krevního tlaku u pacientů s esenciální hypertenzí. Vnitř Lék, 1993, 39, p. 183-190.
- Savin E., Siegelova J., Fišer B., Bonnin P.: Intra- and extracranial artery blood flow velocity during sudden blood pressure decrease in humans. Eur. J. Appl. Physiol. 76, 1997, 289-293.
- Siegelová J., Fišer B., Dušek J., Al-Kubati M.: Die Baroreflexsensitivitätsmessung bei Patienten mit essentieller Hypertonie: Einfluss von Enalapril. Nieren und Hochdruckkrankheiten 24(1), 1995: p. 20-22.
- Honzíková N., Nováková Z., Závodná E. Paděrová J., Lokaj P., Fišer B., Balcárková P., Hrstková H. Baroreflex sensitivity in children, adolescents, young adults with essential and white–coat hypertension. Klinische Paediatrie, 218, 2006, (4), p. 237-242.
- Cornélissen G., Delcourt A., Toussaint G.et al. Opportunity of detecting pre-hypertension: world wide data on blood pressure overswinging. Biomedicine and pharmacotherapy,59, 2005; Suppl. 1: p. 152 – 157.

FUNCTIONAL IMPAIRMENT AND QUALITY OF LIFE IN PATIENTS AFTER ACUTE STROKE

Martina Tarasová, Jana Nečasová, Robert Mikulík,

Michal Pohanka, Mohsin Kaid Ali Hashim, Lenka Drliková, Barbora Bártlová, Eva Nosavcovová, Nabil Abdulah Ibrahim Al-Mahmodi, Abdul Karim Al Fadhli, Farag Hassan Anbais, Ashref Ali Erajhi, Petr Pospíšil, Lumír Konečný, Jarmila Siegelová

Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ

INTRODUCTION

Stroke is a leading cause of disability among elderly people. In addition to physical, emotional and social consequences, the economic impact of stroke is tremendous. The incidence of stroke increases markedly with age ageing populations expose an increasing number of people to the risk of stroke in western countries (13).

Little is known about the effectiveness of long-term stroke physiotherapy. There are no generally accepted guidelines that determine the optimal timing, intensity or duration of rehabilitation. We have not found any data what kind of physiootherapy is most beneficial and resource-efficient for the patients with residual disabilities living in their homes. Several reports have addressed the need for psychological support and enhancing social activities in order to reach the ultimate goal in stroke rehabilitation. Many stroke patients fail to resume full lives, and a major negative impact of stroke on family functioning is not an infrequent phenomenon. Therefore, stroke rehabilitation requires a long-term perspective, extending to several years after the onset of stroke (13).

The role of rehabilitative efforts has been widely recognized as being essential in the acute stage of stroke. The beneficial effects of stroke unit rehabilitation have been well documented by several workers. Treatment of acute stroke patients in stroke units has been shown to reduce mortality, length of hospital stay, discharge rate to nursing homes and cost. Functional recovery has been significantly greater and more rapid in a stroke unit in comparison with general wards. Treatment in stroke units has increased the proportion of patients able to live at home long after their stroke (14).

When we speak about quality of life, we usually pursue the impact of the disease of a person on his or her physical or mental health, way of life and sense of contentment with life (8).

The definition of quality of life is based on the Maslow's theory of hierarchy of needs, i.e. fulfilment of basic physiological needs (need of satiation, sleep, easing the pain) is the condition of stimulation and fulfilment of more subtle needs (need of security, need of relationship with other people, need of self-esteem) (8). Quality of life is regarded as a multidimensional quantity and usually it is defined as "subjective evaluation of own living situation". It includes therefore not only the sense of physical health and absence of symptoms of the disease or treatment, but, in global approach, also mental health, social functioning, religious and economic aspects, etc. (9). Other factors influencing quality of life include age, sex, polymorbidity, family situation, preferred values, economic situation, education, religiosity, cultural background, etc. Overall quality of life is then a complex of the above-mentioned factors (10, 11).

The question which factors influence quality of life and have an impact on activities of daily life in different situations and circumstances is studied systematically in many countries of the world and widely published. With questionnaires enabling quality of life conditioned by health state to be marked, we have available a tool allowing us to quantify and assess the condition of our patients (Health Related Quality of Life – HRQOL) before our therapeutic and nursing interventions as well as after them (2). By means of the short-form HRQOL questionnaires - SF-36 we can evaluate the results of medical and social interventions (3). The short form of the questionnaire (Short Form 36 Health Subject Questionnaire, SF 36) is the most frequently applied generic questionnaire. This questionnaire is a tool being used often for evaluation of quality of life in various branches of medicine due to its good informative value. The assessment is carried out in 8 domains or categories, namely physical activity, physical role, pain, general health evaluation, vitality, social activity, emotional role, mental health (7, 2).

AIM

The first aim of this study was as to evaluate the questionnaire of quality of life (participation) - Index of overall quality of life (SF-36 short-form) in patients after acute stroke (CMP) with moderately serious and light affection according to FIM (Functional independence measure) who were hospitalized in the Ist neurological clinic of St. Anna Teaching Hospital in Brno.

The second aim was to answer the question whether quality of life depends on functional impairment of patients with stroke tested by means of Functional Impairment measure (FIM), which was measured in the period when they were released from the clinic.

METHODS

Characteristic of the patients with stroke

The set consisted of 40 patients of average age $60,1 \pm 11,8$ years (range 30 - 88 years), with the diagnosis I 60 - I 69, generally affected central nervous system (CNS) with impairment of motor functions, with moderately serious functional affection according to FIM, who were hospitalized with acute stroke in the Ist Neurological clinic of St. Anna Teaching Hospital in Brno. The set consisted of 20 women of average age 59.6 ± 12.4 years and of 20 men of average age 61.5 ± 11.3 years.

The questionnaire FIM was originally given to 96 patients who were instructed to send it back to the clinic within 1 - 2 months after their hospitalization in the Ist neurological clinic for the subsequent statistical data processing, only 40 questionnaires were answered, i.e. approx. 42 %.

In the course of hospitalization in the clinic the whole set was subjected to evaluation of impairment by means of the test Functional independence measure (FIM) – measurement of functional independence.

The average time of hospitalization was 13.2 ± 6.5 days (with a minimum of 3 days and maximum of 34 days) and 34 patients were allowed home, 6 were transferred to facilities for subsequent care.

Methods of evaluation

At the beginning of rehabilitation care and at the finishing of hospitalization disability of patients was tested by means of Functional independence measure (FIM).

Patients were intensively treated with drugs and physiotherapeutic procedures based on specialized methods of physiotherapy based on neurophysiological approach. There are following methods used:

Conventional - range of motion/strengthening exercises, training in mobility for functional independence

Neurodevelopmental Training (NDT) - also known as the *Bobath* technique. This technique was developed in the 1940s and the principle is to reduce muscle spasticity by focusing on normal patterns of movement.

Proprioceptive neuromuscular facilitation (Knott & Voss) - relies on quick stretching and manual resistance of muscle activation of the limbs in functional directions, which often are spiral and diagonal in direction.

Brunnstrom technique - facilitates synergistic patterns of movement that develop during recovery from *hemiplegia* (paralysis of one side of the body). Development of flexor and extensor synergies is encouraged during early recovery with the hope that synergic activation of muscles will transition into voluntary activation of movements

Rood technique - modifies movement with cutaneous sensory stimulation

When these approaches to stroke recovery are compared to each other, no one method appears to be more effective than another. However, NDT alone may require prolonged periods of time to produce functional results which may be accomplished faster in conjunction with other methods. Some rehabilitation facilities also incorporate biofeedback into their program to complement other types of therapy (15).

The patients being released from the clinic were given the questionnaire Index of overall quality of life (SF-36) as a device assessing participation with the instruction to send it back to the clinic within 1 - 2 months after their hospitalization in the Ist Neurological clinic for the subsequent statistical data processing. The evaluation was carried out in 8 above-mentioned categories.

Numerical expression of dimensions of quality of life – individual dimensions influencing quality of life are based on the questionnaire SF-36 and are calculated as average values of specific questions from the questionnaire being structured in the particular way. These dimensions have the values from 0 to 100. A lower value means generally a worse value of the given dimension and decreases overall quality of life, a higher value means generally a better value of the given dimension and increases overall quality of life.

The study was approved by the local ethical commission, the examined patients signed informed approval.

Statistical processing

Statistical processing was made by using the program Microsoft Excel, version 2002 and the program Statistica, version 7. The results are presented as the average and the standard

deviation ($x\pm$ SD). The values of individual dimensions were determined by means of the program SF-36® Health Survey Scoring Demonstration (12). Then we determined correlation coefficient and statistical significance in selected relations.

RESULTS

The functional condition evaluation by means of FIM at the beginning of rehabilitation care (admission) and at the releasing from the clinic (discharge) is presented in the whole set (40 patients), in the sets of women (20 patients) and men (20 patients), in the patients under 70 years of age (25 patients) and in the patients of 70 and more years of age (15 patients).



Graph 1. Evaluation FIM at the beginning of care (admission) and at the releasing from the clinic (discharge); *p < 0.05

The file of 40 delivered questionnaires of quality of life SF 36 was subdivided, because of comparison, into subgroups according to age (age over 70 and under 70 years) and according to sex (sets of women and men).

Evaluation of individual items in the questionnaire quality of live SF 36:

Table 1 Values of individual categories in quality of live SF 36 and general physical and

mental health in the whole set.

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
average	45.8	29.4	54.8	46.9	46.4	53.8	45.8	58.8	35.4	42.6
SD	± 30.9	± 36.6	± 28.6	± 19.9	± 21.2	± 30.5	± 41.8	± 18.1	± 10.9	± 9.7

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

Table 2 Values of individual categories in quality of live SF 36 and general physical and mental health in the set of **women**.

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
average	43.8	35	50.1	47.2	46.8	51.9	56.7	58.6	34.3	43.9
SD	± 32.4	± 40.1	± 26	± 20.3	± 19.4	± 33.3	± 43.4	± 19.8	± 11.3	± 9.2

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

Table 3 Values of individual categories in quality of live SF 36 and general physical and mental health in the set of **men**

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
average	47.8	23.8	59.4	46.6	46	55.6	34.9	59	34.3	43.9
SD	± 30.2	± 32.9	± 31	± 20	± 23.4	± 28.2	± 38.2	± 16.8	± 11.3	± 9.2

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

Table 4 Values of individual categories in quality of live SF 36 and general physical and mental health in the set of **patients under 70 years of age**

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
average	47.6	32	54.7	46.3	45.2	50.5	45.3	56.3	36.4	41.1
SD	± 33.6	± 37.9	± 31	± 22.3	± 24.1	± 30.1	± 41.8	± 19.6	± 11,5	± 10.2

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

Table 5 Values of individual categories in quality of live SF 36 and general physical and mental health in the set of **patients of 70 and more years of age**

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
average	42.7	25	54.8	47.8	48.3	59.2	46.7	62.9	33.9	45.2
SD	± 26.9	± 35.4	± 25.2	± 15.8	± 15.9	± 31.5	± 43.3	± 15.3	± 10.2	± 8.4

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

It is shown from the results that our patients after stroke evaluated worse their physical health items than their mental health. In all the sets being monitored, the patients evaluated role of physical state, i.e. restriction of physical functioning because of the health state, as the worst item of quality of life. The item Mental Health was evaluated as better one.

Evaluation of individual parameters in the studied sets

Table 6 Comparison of the results of evaluation of individual parameters in quality of live SF

36 in the studied sets

	whole set	women	men	age to 70 years	age 70 and more
	х	х	х	х	years
					Х
PF	45.8	43.8	47.8	47.6	42.7
RP	29.4	35	23.8	32	25
BP	54.8	50.1	59.4	54.7	54.8
GH	46.9	47.2	46.6	46.3	47.8
VT	46.4	46.8	46	45.2	48.3
SF	53.8	51.9	55.6	50.5	59.2
RE	45.8	56.7	34.9	45.3	46.7
MH	58.8	58.6	59	56.3	62.9
PCS	35.4	34.3	34.3	36.4	33.9
MCS	42.6	43.9	43.9	41.1	45.2

Explanation: x - average, SD - standard deviation, PF - Physical Functioning, RP - Role-Physical, BP - Bodily Pain, GH - General Health, VT - Vitality, SF - Social-Functioning, RE - Role-Emotional, MH - Mental Health,. PCS - Physical Component Summary, MCS - Mental Component Summary

Elderly patients (70 and more years of age) evaluated their Physical Component Summary as the worst one. The greatest differences are apparent in perception of "Role-Emotional" in the sets of men and women; the difference is 21.8 in favour of women with better subjective perception. Then quite a big difference (11.2) was recorded in the category "Role-Physical", that is evaluated better by women, and "Bodily Pain", being better tolerated by men with the difference 9.3. Similar results, without major differences between individual sets, were found in the items "Vitality" and "General Health".

We answered also the question whether quality of life in our set being tested depends on the final functional condition of patients with stroke tested by means of FIM when they were released from the clinic and whether general physical health correlates with mental health. The results of correlation analysis are presented in Table 7.

Table 7 Dependence of final functional condition according to FIM on index of general mental and physical health SF 36

	FIM x PCS	FIM x MCS	PCS x MCS
	correlation coefficient	correlation coefficient	correlation coefficient
	r	r	r
whole set	0.175 NS	0.053 NS	0.485**
set of women	0.123 NS	0.096 NS	0.557*
set of men	0.237 NS	-0.015 NS	0.469*
set under 70	0.197 NS	0.067 NS	0.685**
Set of 70 and more	0.074 NS	-0.355 NS	0.112 NS

Explanation: FIM - Functional independence measure, PCS - Physical Component Summary, MCS - Mental Component Summary, r - correlation coefficient, NS - not statistically significant, * statistically significant p < 0.05, ** statistically significant p < 0.01

There is no correlation between FIM and SF 36. Correlation between PCS and MCS shows that physical health in younger patients influences significantly mental health. In patients over 70 years of age we have not found a significant correlation, influence of physical health on mental health is not important.

DISCUSSION

Evaluation of quality of life becomes an integral part of studies monitoring on a long-term basis health state of patients in various branches of medicine, with the conception of quality of life including a wide range of life perception (7).

Even if evaluation of the degree of impairment is of an essential significance for assessment of seriousness of the stroke, it cannot implicate all main factors influencing quality of life. Not only health state, but also social and economic conditions, mental health, fulfilment of aims in life, culture and value system in various geographical conditions are ranked among them. Quality of life is a subjectively perceived standard of life by which people assess their physical, emotional and social abilities (4).

Our results show that patients after stroke reach a lower number of points in subjective evaluation of quality of life in all aspects, as it was expected in generic disorders bringing on disability (6).

As to the age and quality of life, elderly patients arrived at worse evaluation almost in all items; it can be caused by development of the disease, higher number of associated complications in higher age, impaired ability of adaptation, lower motivation, etc.

As to the differences between sexes, we found them mostly in the parameter "Role-Emotional"; women evaluated this item by 21.8 points better than men, and in "Role-Physical" where evaluation of women was better by 11.2 in comparison with men. Also perception of pain was worse in women (a difference against men was 9.3).

In the other parameters there were not significant differences in the monitored sets.

As to the evaluation of dependence of functional condition of patients with CMP tested by means of FIM when they were released from the clinic and quality of life evaluated according to SF 36, a statistically significant relation was not possible to be demonstrated.

As the questionnaire SF-36 is a simple and cheap device for determination of quality of life, the information provided by this questionnaire could be used both before the specific therapy and after it for determination of changes in quality of life by way of changes in points of patients, concurrently with clinical measurements of seriousness of the disease (1).

The main reason of evaluation of quality of life in patients is assessment of the treatment effect. In available foreign literature we can notice the effort to assess the treatment effect in a more complex way, not only according to somatic and laboratory markers, but also by means of evaluation of quality of life. In our conditions evaluation of quality of life is carried out mainly on account of the research and is not a usual part of the treatment. Our study shows that there is no connection between functional condition of patients and subjectively perceived quality of life. That is why a complex evaluation of quality of life requires combination of both questionnaire methods (FIM and SF 36).

CONCLUSION

According to our results there is no correlation between the Functional independence measure (FIM) and Index of overall quality of life (SF-36 short-form). Correlation between Physical Component (PCS) and Mental Component Summary (MCS) shows that in younger patients physical health influences significantly mental health. In patients over 70 years of age we have not found a significant correlation, the effect of physical health on mental health is not significant.

Supported by MSM0021622402

LITERATURE

- Kvalita života u pacientů s Charcot-Marie-Tooth chorobou, in. 2005, 65, p.922-924.
 http://websiska.cz/ct/dokumenty/vysledky studie u italskych pacientu s CMT.pdf
- Petr, P.: Dotazník SF-36 o kvalitě života podmíněné zdravím (The SF-36 Questionnaire of the Health related Quality of Life). Kontakt, 2000, 2(1): p. 26-29.
 Petr, P., a kol..:Regionální standard Kvality života podmíněné zdravím (The Regional Standard of Health Related Quality of Life). Kontakt 2001, 3 (3): p. 146-150.
- 3) Last, J. M.: A dictionary of epidemiology III, Ed. Oxford Univ. Press, 1995, 180 p.
- 4) Kolektiv autorů: Životní styl a obezita longitudiální epidemiologická studie prevalence obezity. ČLS JEP, Česká obezitologická společnost. Praha, 2006, 63 p.
- Kalová, H. et al.: Kvalita života u chronických onemocnění ve světle novějších modelů zdraví
- Slováček, J. et al.: Kvalita života nemocných jeden z důležitých parametrů komplexního hodnocení léčby. Vojenské zdravotnické listy, ročník LXXIII, 2004, 1, p. 6-9.
- 7) Zittoun, R. et al.: Assessment of quality of life during intensive chemotherapy bone marrow transplantation. *Psychooncology*, 1999, vol. 8, no. 1, p. 64–73.
- Quality of Life for Patients with Chronic Illness. http://www.nih.gov/ninr/about/legislation/chronic illnesss.htm
- Stáblová, A.: Kvalita života dialyzovaných nemocných. UK FTVS Praha, Laboratoř sportovní motoriky. *www.ftvs.cuni.cz*
- 10) Curtis, J.R., et al.: Measure of the Quality of Dying and Death: Initial Validation Using After-Death Interviews with Family Members. *J. Pain Sympt. Management*, 2002, 24, 1, p. 17–31.
- 11) SF-36® Health Survey Scoring Demonstration
 http://www.sf-36.org/ SF-36® Health Survey Scoring Demonstration.htm
- 12) Pitkänen,K.: Stroke rehabilitation in the elderly. A controlled study of the effectiveness and costs of a multidimensional intervention. Series of Reports, No 52, Department of Neurology, University of Kuopio. 2000.
- 13) Indredavik B, Bakke F, Slordahl SA, Rokseth R, Håheim LL: Stroke unit treatment: 10-year follow-up. Stroke 1999; 30: 1524-1527.
- 15) Rehabilitation of Motor Deficit after stroke –Untertanding stroke rehabilitation. In:

http://www.medifocushealth.com/NR020/Approaches-to-Stroke- Rehabilitation Rehabilitation-of-Motor-Deficits-after-Stroke.php

Summary

The aim of this study was to evaluate the questionnaire of quality of life (SF-36 short-form) in patients after acute stroke and to compare the results with Functional Impairment Measure (FIM).

Methods: We examined 40 patients with acute stroke by means of questionnaire FIM and the questionnaire of quality of life (SF-36 short-form).

Results and conclusion: We have not found after rehabilitation any correlation between FIM and index of quality of live in patients after acute stroke. The correlation between physical component and mental component according to FIM summary was found in younger patients under 70 years of age.

Key words: stroke, quality of life, physiotherapy, functional impairment measurement

WATER IMMERSION AND PHYSIOTHERAPY IN PATIENTS WITH PARKINSON DISEASE

Petr Pospíšil,^{1,2} Lumír Konečný,^{1,2}, Marie Zmeškalová², Hana Srovnalová³, Ivana Rektorová³, Eva Nosavcovová², Michaela Sosíková², Petr Dobšák^{1,2}, Jarmila Siegelová^{1,2},

Dept. of Functional Diagnostics and Rehabilitation¹, Department of Physiotherapy², Dept. of

Neurology³, Medical Faculty, Masaryk University, St. Anna Faculty Hospital in Brno,

Czech Republic

INTRODUCTION

Rigidity, postural instability, bradykinesis and tremor are well known basic symptoms of Parkinson's disease (PD). Higher incidence of cardiovascular diseases belongs to other characteristics that are, together with respiratory complications, the most common cause of death in PD (1, 2).

Positive effect of exercise therapy was reported repeatedly (3, 4, 5, 6). Aerobic exercise therapy in a swimming pool with warm water is also recommended. However, there is no evidence on cardiovascular parameters reaction to water immersion in PD patients in scientific literature sources. We have already shown the reaction of cardiovascular parameters in patients with cardiovascular disease in our previous study (7).

AIM

Elucidation of reaction of cardiovascular parameters to water immersion of lower parts of the body and thorax in patients with PD was the aim of the present study.

METHODS

9 patients with the diagnosis of PD were examined at the Dept. of Neurology, St. Anna Faculty Hospital in Brno, Czech Republic. Stable medication without changes during the last month, Hoehn and Yahr Score < 3 and suitability for exercise therapy in the swimming pool were assessed as entrance criteria of this study.

Basic statistic parameters of the tested group of PD patients are presented as mean values \pm standard deviations (SD): age 71 \pm 7 years, duration of disease 7 \pm 3 years, Hoehn and Yahr score 2.2 \pm 0.7.

Exercise therapy in the swimming pool was realized with the frequency of once a week for the period of 12 weeks. Each exercise therapy unit lasted 40 minutes. It consisted of 10 minutes of outdoor warm-up phase and 30 minutes of aerobic exercise in the swimming pool aimed at balance improvement, rigidity and hypokinesis management, muscular imbalances and other gross and fine motor skills improvement. This phase was followed by 15 minutes of relaxation in supine position in a dry wrap.

Systolic (SBP) and diastolic (DBP) blood pressure and heart rate (HR) were measured. Mercury manometer was used for the measurement of blood pressure, Polar tester for the measurement of heart rate, rate x product (RPP) was calculated. The first measurement was performed 7 minutes after having a shower (5 minutes of rest in sitting position followed by 2 minutes of still standing), the second measurement was performed immediately after water immersion (32.5 °C) up to the level of the heart, the third measurement after 2 minutes of water immersion and the last measurement at the peak of work load during exercise therapy in the swimming pool. Subjective perception of work load intensity was evaluated according to Borg's Rate of Perceived Exertion (8).

All the data were examined in the phase of clinical improvement of patients ("on" state) without changes of regular anti-parkinsonian medication.

Kolmogorov-Smirnov test was used for normality verification, Pair T-test for dependent samples to reveal changes caused by immersion into warm water (StatSoft, Inc., version 7). The study was approved by the Ethical Committee of Medical Faculty, Masaryk University

and all participating patients signed their written consent.

107

RESULTS

In comparison to the values of initial examination (standing out of water) there was a significant decrease of values of heart rate and diastolic blood pressure in the second examination performed immediately after water immersion. Systolic blood pressure did not increase significantly. Rate x pressure product did not change significantly (Table 1).

Table1: Compa	• •	• ,•	1.	1 0	1 • 1•	1 0		•
I ablal · Compo	pricon of	avamination	raculto	hotoro on	1 immodia	tolv ot	tar watar i	mmorgion
			ICSUILS	UCIDIC and	i mmuua	iciv ai	ici waici i	IIIIICISIOII
rear and the second sec						J		

SI	3P	DI	BP	H	R	R	PP
1 st	2 nd	1 st	2 nd	1 st	2 nd	1 st	2 nd
measure- ment	measure- ment	measure- ment	measure- ment	measure- ment	measure- ment	measure- ment	measure- ment
	ment	ment	ment		ment	ment	ment
122±13	120±9	83±9	76±7	78±8	72±9	96±13	87±11
N.	.P.	*p≤0.05			0.05	N.	.P.
Annotation: 1 st measurement before water immersion							

2nd measurement immediately after water immersion

The same trend was also present after 2 minutes of still standing in the swimming pool. In comparison to the initial values (standing out of water) there was a highly significant decrease of values of heart rate, diastolic blood pressure and rate x pressure product in the third examination performed after 2 minutes of still standing in the swimming pool (Table 2).

Table 2: Comparison of examination results before water immersion and after 2 minutes of still standing in the swimming pool

SI	3P	DBP		HR		R	PP
1^{st}	3 rd	1 st	3 rd	1 st	3 rd	1^{st}	3 rd
measure-	measure-	measure-	measure-	measure-	measure-	measure-	measure-
ment	ment	ment	ment	ment	ment	ment	ment
122±13	119±7	83±9	73±8	78±8	67±7	96±13	80±12
N.P. **p≤0.01			<u><0.01</u>	*p≤	0.05	**p<	<u>≤0.01</u>
Annotation: 1. measurement before water immersion							

3. measurement after 2 minutes of still standing in water

At the peak of exercise therapy work load there was a significant increase of systolic blood pressure and rate x pressure product in comparison to the values of examination 3 performed after 2 minutes of still standing in the swimming pool (Table 3). The values of
diastolic blood pressure, heart rate and rate x pressure product approximated to the values of initial examination in standing out of water (Table 4).

SI	BP	DBP		HR		RPP	
3 rd measure- ment	4 th measure- ment						
119±7	129±7	73±8	80±7	67±7	75±12	80±12	97±18
*p≤	0.05	N.P.		N.P.		*p≤0.05	

Table 3: Comparison of examination results after 2 minutes of water immersion and at the peak of exercise therapy work load

Annotation:3rd measurementafter 2 minutes of still standing in water4th measurementat the peak of exercise therapy work load

Table 4: Comparison of examination results before water immersion and at the peak of exercise therapy work load

SI	3P	DBP		HR		RPP	
1 st	4 th						
measure-							
ment							
122±13	129±7	83±9	80±7	78±8	75±12	96±13	97±18
N.	P.	N.	P.	N.	P.	N	.P.

Annotation:1st measurementbefore water immersion4th measurementat the peak of exercise therapy work load

The exercise therapy work load was evaluated with the use of Borg's Rate of Perceived Exertion. The rating fluctuated between 11 and 14 from the maximum of 20 in all examined patients.

DISCUSSION

There is no agreement in opinions on the impact of water immersion on blood pressure. We found scientific sources describing decrease of systolic and diastolic blood pressure in thermo-neutral bath of $34-35^{\circ}C$ (8) and hypo-thermal bath of $32^{\circ}C$ (9) as well as sources declaring mild increase of systolic blood pressure and no changes of diastolic blood pressure in thermo-neutral ($34.5^{\circ}C$) bath and decrease of diastolic blood pressure in hypo-thermal bath of $30^{\circ}C$ (10). Some studies found no changes of blood pressure during thermo-neutral bath (11, 12).

In our group of examined PD patients we found statistically significant decrease of diastolic blood pressure in thermo-neutral bath of 32.5°C. Systolic blood pressure increased only in the course of exercise unit.

Water immersion in PD patients leads to decrease of resting heart rate known as diving reflex. The intensity of sympathetic activity decrease and vagal activity increase depends mainly on the depth and speed of immersion and on water temperature (11, 12). Intensive reaction may cause extreme bradycardia and sudden death. (13). Activity of reninangiotensin system also decreases (14, 9). In our group of PD patients the decrease of heart rate was present immediately after water immersion and lasted during the course of exercise therapy unit. The similar results were described by Fardy et al. (15) in the study with healthy subjects.

No other clinically relevant negative aspects of PD exercise therapy in the swimming pool were found during the course of 12 weeks of exercise therapy.

Regular controlled group or individual rehabilitation is recommended to the majority of PD patients (5). Elderly patients can benefit from rehabilitation as well as younger subjects (6).

CONCLUSION

Thermo-neutral (32.5°C) water immersion and up to the level of heart caused statistically significant decrease of heart rate and diastolic blood pressure in patients with Parkinson disease. This trend lasted for the period of exercise therapy unit in the water. The increase of systolic blood pressure and heart rate was detected only at the peak of exercise therapy work load in water when the values approximated those of initial examination before water immersion.

We have not observed any subjective inconveniences and any clinical manifestations of possible haemodynamic pathological changes during exercise therapy in our study.

We consider group form of controlled hydro-kinesitherapy a suitable and safe supplement to classic exercise therapy unit in the frame of neurorehabilitation. Further research on a larger group of PD patients is necessary to prove the results of this study.

Supported by MSM0021622402.

REFERENCES

1. Helly, M.A., Morris, J.G.L., Traficante, R., Reid, W.G.J. et al. The Sydney multicentre study of Parkinson's disease: Progression and mortality at 10 years. Journal of neurology, Neurosurgery and Psychiatry, 1999, 67/3, p. 300-308. (fulltext)

2. Gorell, J.M., Johnson, C.C., Rybicki, B.A. Parkinson's disease and its comorbid disorders: An analysis of Michigan mortality data, 1970-1990. Neurology, 1994, 44, p. 1865-1868.

3. Ellis, T. et al. Efficacy of a physical therapy program in patients with Parkinson's disease: A randomized controlled trial. Archives of Physical Medicine and Rehabilitation, 2005, 86/4, p. 626-632.

4. Cees, J.T. et al. The effects of physical therapy in Parkinson's disease: a research synthesis. Archives of Physical Medicine and Rehabilitation, 2001, 82/4, p. 509-515.

5. Lun, V. et al. Comparison of the effects of a self-supervised home exercise program with a physiotherapist-supervised exercise program on the motor symptoms of Parkinson's disease. Movement Disorders, 2005, 20/8, p. 971-975.

6. Reuter, I. Engelhardt, M. Exercise training and Parkinson's disease. Placebo or essential treatment?

The Physician and Sportsmedicine, 2002, 30/3, p. 43-50.

 Borg, G. Psychophysical bases of perceived exertion. Med Sci Sports Exercise, 1982, 14, p. 377-381.

8. Henschel, H.D. Vergleichende Untersuchungen zur Behandlung mit Kohlensaurenbader. Arch Phys Ther (Leipzig), 1962, 14, p. 327-334.

9. Šrámek, P., Šimečková, M., Janský, L. Human physiological responses to immersion into water of different temperatures. Eur J. Physiol, 2000, 81 (5), p. 436 – 442.

10. Park, K.P., Choj, J.K., Park, Y.P. Cardiovascular regulation during water immersion. Appl Human Sci, 1999, 18 (6), p. 233-241.

11. Mano, T., Iwase, P., Saito, M., et al.: Neural and humoral controlling mechanism of cardiovascular functions in man under weightlessness simulated by water immersion.
Acta Astronaut 1991; 23: 31 – 33.

12. Miwa, C., Sugiyama, Y., Mono. T. et al. Spectral characteristics of heart rate and blood pressure variabilities during head-out water immersion. Environ Med, 1966, 40 (1), p. 91 - 94.

13. Lin, Z.C. Applied physiology of diving. Sports Medicine, 1988, 5, p. 41 – 56.

14. Gabrielsen, A., Pump, B., Bie, P.et al. Atrial distension, haemodilution and acute control of renin release during water immersion in humans.

Acta Physiol Scand, 2002, 174 (2), p. 91 -99.

15. Fardy, P.P., Franklin, B.A., Porcari, J.P., Verrill, D.E. Training techniques in cardiac rehabilitation. Human Kinetics, 1998, p. 88-105.

PHYSIOTHERAPY AND CIRCADIAN BLOOD PRESSURE VARIABILITY

Alena Havelková, Jarmila Siegelová, Bohumil Fišer, Leona Mífková, Veronika Chludilová, Jaroslava Pochmonová, Pavel Vank, Michal Pohanka, Jiří Dušek, Germaine Cornélissen*, Franz Halberg*

Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ, *Halberg Chronobiology Center, University in Minnesota, USA

INTRODUCTION

High blood pressure is number one in risk factors of cardiovascular diseases and civilization diseases in general that are known as yet.

It seems that the repeated single measurements of blood pressure in the medical practice is no longer sufficient for the determination of optimal treatment of patients with heart diseases. Ambulatory monitoring of blood pressure opens new possibilities in prevention, screening, diagnostics and therapy of chronically ill patients. Blood pressure is a biological parameter showing, in spite of numerous regulation mechanisms, considerable variability beat-to-beat, within 24 hours and also in longer time intervals (weekly, monthly) (Siegelová et al. 1993, Siegelová and Fišer 2005, Homolka 2006). 24-hour monitoring contributed in recent years significantly to the progress in diagnostics and therapy of cardiovascular diseases. In combination with the knowledge of pharmacokinetics and pharmacodynamics of antihypertensive medicines it offers other possibilities of medical treatment (Souček, Kára et al. 2002; Siegelová et al. 2004). A longer lasting (7 days at least) monitoring increases validity of obtained information with observing biological rhythms of blood pressure. The knowledge of chronobiology of circadian cycles of physiologic functions initiates a modern trend in medicine, i.e. intervention before the manifestation of clinical symptoms of the disease (Siegelová and Fišer 2005, Halberg et al. 2006, Watanabe et al. 2006).

1

Monitoring of blood pressure response to physical load is well-founded not only in exercise diagnostics of hypertonic patients and of patients with cardiovascular and other internal diseases, but also in setting up and checking an optimal training program that should be beneficial to improvement or stabilization of their health state. Cardiovascular rehabilitation is perceived as a process helping the patients with heart diseases in retaining their optimal physical, mental, working and emotional state. Its principles are based on the assumption that the adaptation of cardiovascular system to physical load is conditioned by regular, particularly dynamic endurance activities of adequate kind and intensity (Placheta et al. 1999).

PURPOSE

The objective of this study was to find if there is a relationship between the day time when cardiovascular rehabilitation was running in the patients after myocardial infarction and an average daily value of systolic and diastolic blood pressure at 7-day ambulatory monitoring.

METHODS

The set being monitored consisted of ten patients after myocardial infarction of age (63 ± 6.3) and ejection fraction (43 ± 12.3) %.

The patients underwent phase II of cardiovascular rehabilitation (controlled ambulatory rehabilitation program) lasting two to three months with the frequency of two times or three times in a week at the Department of Functional Diagnostics and Rehabilitation of St. Anna Teaching Hospital.

In the course of rehabilitation they went through 7-day ambulatory monitoring of blood pressure. During BP recording they did not interrupt their pharmacotherapy.

The seven-day blood pressure monitoring was made by using the instrument TM - 2421 of the Japanese firm AD on the principle of oscillometric analysis. During the time of monitoring the patients carried the recording instrument in the case on the body and

cuff with the measuring probe above a. brachialis. The instrument measured blood pressure for 7 days repeatedly every 30 minutes from 5 to 22 h and once in an hour from 22 to 5 h. If a value that was not very probable from the point of view of the setting-up of the instrument was recorded, another check measurement was made (Siegelová et al. 2004).

The measured BP values for every patient from the monitored set were statistically processed in the form of arithmetic means. The profiles of BP in the days without cardiovascular rehabilitation (hereafter in the days without exercises) and in the days with cardiovascular rehabilitation (hereafter in the days with exercises) in individual time intervals were obtained as arithmetic mean of the values in every hour of individual days with denying the individuality of persons in the monitored set.

The average SBP and DBP and their standard deviations (SD) in the given days were determined by the calculation of arithmetic mean of these values. These average values were compared by means of two-factor analysis of variance without repetition (ANOVA). Concrete differences between the averages from the days without exercises and the averages of the values in the time intervals when cardiovascular rehabilitation was running in individual groups of patients, were tested by the paired t-test.

RESULTS

Table 1 gives the average of BP profiles in the days without exercises and with exercises that were obtained from arithmetic means of SBP and DBP for every hour of individual days regardless of individual differences between the patients in the monitored set.

The calculated value F (ANOVA) for SBP highly exceeds the critical value for the significance level $\alpha = 0.01$. It was proved that there are statistically conclusive differences between the daily averages of SBP in the monitored groups. The differences of averages in individual groups of the days with exercises in comparison with the group of days without exercises were tested by paired t-test.

The average value of SBP in 24 h in the group of patients doing exercises from 9 a.m. to 10.15 a.m. is statistically highly conclusively higher ($\alpha = 0.01$) in comparison with

the group of days without exercises (133 or 120 mm Hg). The average value of SBP in 24 h in the group of patients doing exercises from 1.30 p.m. to 2.45 p.m., however, is statistically conclusively lower ($\alpha = 0.05$) (115 or 120 mm Hg). The averages of the remaining two groups and of the group without exercises are identical. It is interesting that in all groups with exercises lower minimal values of SBP were found than in the group without exercises.

The calculated value F (ANOVA) for DBP also highly exceeds the critical value for the significance level $\alpha = 0.01$. It was proved that there are statistically conclusive differences between the averages of individual monitored groups. The results of paired t-test demonstrate the statistically highly conclusively higher values in the groups of days when the exercises were running from 7.30 a.m. to 8.45 a.m. and from 9 a.m. to 10.15 a.m. ($\alpha = 0.01$) and statistically highly conclusively lower values in the group of days when the patients were doing exercises in the afternoon from 1.30 p.m. to 2.45 p.m. ($\alpha = 0.01$) in comparison with the average of values in 51 days without cardiovascular rehabilitation (71, 75, 63 or 69 mm Hg).

Table 1: 24-hour profile of systolic and diastolic blood pressure [mm Hg]
obtained as arithmetic mean of values of the patients

	with exerc		with exercises time [h]							
			7:30-	8:45	9:00-	10:15	10:30	-11:45	13:30	-14:45
Ν	5	1	1()	3	3	6		3	
[mmHg]	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
X	120	69	120	71**	133**	75**	120	67	115*	63**
SD	5.9	4.0	11.9	5.6	12.0	10.2	12.9	6.3	12.8	6.3
X _{max}	128	75	152	83	158	91	142	81	136	74
X _{min}	110	62	99	62	108	57	97	56	94	48
t _{calculated} .			0.221	3.448	5.317	4.029	0	1.657	2.795	6.183
Fcalculated	16.371	23.662								

- n number of monitored days
- x arithmetic mean SD standard deviation

x_{max}, x_{min} - maximal and minimal average circadian value of blood pressure

- * statistically conclusive difference at the significance level $\alpha = 0.05$
- ** statistically conclusive difference at the significance level $\alpha = 0.01$
- t criterion of paired t-test $t_{(0.05)} = 2.068 t_{(0.01)} = 2.807$
- F criterion of analysis of variance $F_{(0.05)} = 2.471 F_{(0.01)} = 3.530$

DISCUSSION

The diagnosis based on one clinical measurement of BP is wrong in about 40 % of the cases compared to 24-hour ambulatory monitoring. The 48-hour record furthermore reduces uncertainty in assessment of blood pressure parameters by 35 % in comparison with 24-hour monitoring. Halberg et al. (2006) and Watanabe et al. (2006) tend to a long-term monitoring of blood pressure for the sake of increasing validity of the obtained data and optimization of the therapy. They recommend a 7-day recording of blood pressure to cover the biological week.

The nature of the reaction of cardiovascular system to exercises depends on intensity, type and duration of physical load and also on individual characteristics of organism and on external influences. Even a moderate load affects tonus of vegetative nervous system by reducing activity of n. vagus and stimulation of sympathicus occurs. Autonomous nervous regulations with predomination of sympathicus at a high intensity of the load bring about increasing of heart rate, peripheral resistance of vessels, secretion of catecholamins and blood pressure. After the termination of the load sympathetic activity decreases and parasympathetic activity increases with latency.

Systolic blood pressure at the dynamic load of low and moderate intensity quickly achieves a steady state (130 - 170 mm Hg), diastolic pressure does not show substantial changes or slightly decreases. The load of submaximal and maximal intensity leads to gradual increasing of systolic pressure. Diastolic blood pressure is mostly decreasing, but in some cases is also increasing. Both blood pressure parameters react to static (isometric) load by increasing (Placheta et al. 2001).

This study confirms the blood pressure reaction to the load, both in the interval of proceeding exercises and in the whole circadian cycle. Systolic blood pressure was increasing at the time of rehabilitation, sometimes, however, also within two hours after the termination of exercises. The reaction of diastolic pressure at the load is less specific in physiological conditions. Regularity in the curves of diastolic pressure in individual persons being tested is also difficult to be found.

Both foreign literature and the studies carried out in St. Anna Teaching Hospital prove positive influence of cardiovascular training on the prognosis of heart diseases. Mífková et al. (2005) assess successfulness of the rehabilitation program depending on how early rehabilitation is started (already during hospitalization), on the length of duration of individual phases of the training, and on frequency of arranging individual exercise units. The content of individual phases of the rehabilitation program was also a subject of the discussion (Chaloupka et al. 2006, Mífková et al. 2006).

For example, according to Jančík (2005), it is not the time devoted to exercises or the particular type of exercises, but intensity of the load that is decisive for a direct influence on prognosis of cardiovascular diseases, without any regard to the type of exercises being done by the patient.

This study adds to the above-mentioned facts, concerning cardiovascular rehabilitation, the information that, apparently, the effect of the complex therapy of heart diseases depends also on the time of day when the patients perform the rehabilitation program.

The tested persons were divided in this study into four groups differing in time intervals of rehabilitation. It was proved that the time of exercises influences the average value of blood pressure during the circadian cycle. Cardiovascular training taking place in the morning increased statistically conclusively the average 24-hour value of blood pressure in comparison with the days without exercises. Exercises arranged in the afternoon decreased statistically conclusively the average 24-hour value of blood pressure

Influence of exercises on circadian variability of blood pressure was investigated also by Homolka (2006); he states that the exercises of an aerobic nature done in the evening by patients with hypertension caused abnormal fluctuation of circadian values of blood pressure contributing to CHAT (Circadian-Hyper-Amplitude-Tension). He did not find any abnormalities in the days without exercises and with exercises done in the morning and in the afternoon. Effective complex therapy of high blood pressure and cardiovascular rehabilitation as an integral part of it are a basic condition for the decrease of morbidity and mortality caused by cardiovascular diseases and their complications. Our studies show that the time of day when the load is applied influences average 24-hour values of blood pressure.

CONCLUSION

It was proved that there is a statistically highly conclusive dependence of SBP and DBP values on the day time when the patients went through cardiovascular rehabilitation.

Supported by MSM0021622402

LITERATURE

- Halberg, F., Cornélissen, G. & Schwartzkopff, O. (2006). Seven day blood pressure measurement: Contraversion in single 24-h profiles of blood pressure and heart rate. In Halberg, F., Kenner, T., Fišer, B., Siegelová, J. Noninvasive Methods in Cardiology. s. 10 – 26.
- Homolka, P. (2006). Cirkadiánní variabilita krevního tlaku u pacientů s esenciální hypertenzí. Brno: LF MU. 149 s.
- Chaloupka, V., Siegelová, J. & Špinarová, L. (2006). Rehabilitace nemocných s kardiovaskulárním onemocněním. Cor Vasa, 48 (7 – 8).
- Jančík, J. (2005). Rehabilitace po infarktu myokardu a revaskularizace u starších nemocných. Vnitřní lékařství, 51 (4), s. 388 – 389.
- Mífková, L., Kožantová, L. & Siegelová, J. (2005). Kombinovaný trénink u pacientů po akutním infarktu myokardu. Medicina Sportiva Bohemica a Slovaca, 14 (3), s. 115 – 123.

- Mífková, L., Siegelová, J. & Vymazalová, L. (2006). Intervalový a kontinuální trénink v kardiovaskulární rehabilitaci. Vnitřní lékařství, 52 (1), s. 44 – 50.
- Placheta, Z. (1999). Zátěžová diagnostika v ambulantní a klinické praxi. Praha: Grada.
- Siegelová, J. & Fišer, B. (2005). Diagnostika hypertenze současnost a budoucnost. Vnitřní lékařství, 51 (S 3), s. 50 – 53.
- Siegelová, J., Fišer, B. & Dušek, J. (1993). 24-hodinové monitorování krevního tlaku u nemocných s esenciální hypertenzí. Vnitřní lékařství, 39 (2), s. 183 – 190.
- Siegelová, J., Fišer, B. & Dušek, J. (2004). Nové trendy v monitorování krevního tlaku. Postgraduální medicína, 6 (5), s. 474 – 477.
- 11. Souček, M. (2002). Klinická patofyziologie hypertenze. Praha: Grada.
- Watanabe, Y., Katinas, G. & Cornélissen, G. (2006). Time course of blood ressures over 18 years analyzed separately by day and by week. In Halberg, F., Kenner, T., Fišer, B., Siegelová, J. Noninvasive Methods in Cardiology. s. 42 – 46.

SUMMARY

The objective of this study was to find if there is a relationship between the time when cardiovascular rehabilitation was running in the patients after myocardial infarction and an average daily value of systolic and diastolic blood pressure at 7-day ambulatory blood pressure monitoring.

Systolic and diastolic pressure significantly increased in the patients who underwent cardiovascular rehabilitation in the morning from 9.00 a.m. to 10.15 a.m., and it significantly decreased in those who did their physical exercise in the afternoon from 1.30 p.m. to 2.45 p.m., compared to the blood pressure value in the days without rehabilitation.

KEY WORDS

Blood pressure, ambulatory blood pressure monitoring, circadian variability, chronobiology, cardiovascular rehabilitation.

FITNESS IN MULTIPLE SCLEROSIS

Lumír Konečný¹, Petr Pospíšil¹, Michal Dufek², Lenka Drlíková¹, Farag Hassan Anbais¹, Ashref Ali Erajhi¹, Petr Dobšák¹, Pavel Vank¹, Jarmila Siegelová¹

¹ Department of Functional Diagnostics and Rehabilitation and ²1st Neurological Department, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ

INTRODUCTION

Multiple sclerosis (MS) is chronic system auto-immune disease bringing about functional neurological deficit on the basis of dissemination of demyelinisation focuses in CNS area (1). At the beginning of the disease appears already also axon involvement that is probably a cause of persisting neurological deficit. Maximum axon loss occurs in the first years of the disease (period with minimal disability and clinical finding) and, as a result of depletion of functional reserves of CNS, a substantial deceleration in conduction of nerve impulse develops. Another axon loss brings on an irreversible disability already (2). Demyelinisation and axon involvement are localized particularly in periventricular area, in brain-stem, cerebellum, lateral and posterior cords of spinal chord. Predominant manifestations include central pyramidal symptoms, cerebral, stem and sensitive signs, disorders of autonomous regulation, continence, etc. (3). Multiple sclerosis also attacks basic physiologic response to load by demyelisating processes (4, 5). Functional changes in skeletal musculature, particularly reduction of the number of fibres of the type I, reduction of oxidative abilities and prevailing anaerobic activity of skeletal extrafusal fibres (6) are ranked among other pathophysiological processes. Increasing health troubles lead to secondary signs of physical decondition with a gradual reduction of muscular mass, appearance of functional troubles and further reduction of cardiorespiratory fitness (7). However, it is probably caused by deconditioning in consequence of the lack of physical activities. The restriction of

physical activities in MS patients was confirmed (8). It could be primarily caused by muscle weakness and fatigue (9). It is suggested that aerobic exercises and strengthening may help to prevent secondary changes partially caused by deconditioning (10). Controlled exercising activity represents a significant element influencing physical decondition and course of MS disease (4, 11, 12, 13, 14). Assessment of functional condition of cardiorespiratory and metabolic activity and of determination of functional reserves could help to set up optimal individual rehabilitation workload with an adequate intensity (11, 12, 13, 14, 15).

PURPOSE

The study was aimed to analyse physical fitness, metabolic and hemodynamic functions in the set of patients with MS and comparison of the measured results with actual standards, investigation of fatigue and independence.

METHODOLOGY

The examined set consisted of patients from neurological outpatient clinic for MS of 1st Neurological Department, St. Anna Teaching Hospital and patients in Brno-town. The patients were tested in the clinically stabilized disease condition. They confirmed by signature of "Informed approval of the patient" their participation in the study. The study was approved by appropriate ethical commission of St. Anna Teaching Hospital in Brno. Evaluation of clinical disability, independence and fatigue was carried out before the exercise examination.

Exclusion criteria of contraindications for going through spiroergometry and ability of the patient to undergo the examination on bicycle ergometer were the criteria for inclusion. The patients with internal, metabolic and other diseases, which could influence validity of the exercise test results, were excluded.

We use following tests for clinical functional impairment:

EDSS (Kurtzke's Expanded Disability Status Scale) (16) is a standard scale for evaluation of clinical disability in patients with MS. It is a neurological examination with evaluation by 0.5 point, in interval from 0 (no functional disorder or impairment) to 10 (death due to MS), MS impact on 8 basic functional systems.

FIM (Functional Independence Measure) (17) is a scale for evaluation of independence in basic daily activities. Evaluation applies to locomotive skills, mental functions, and general degree of independence. Possible range is 18 – 126 points.

MFIS (Modified Fatigue Impact Scale) (18) is a questionnaire including subjective assessment of fatigue impact on physical condition (MFISp), cognitive (MFISc) and psychosocial functions (MFISps). It contains 21 questions with evaluation of 0 - 4 points (0 – on fatigue impact on the function; 4 – almost permanent fatigue impact). Possible range is 0 to 84 points.

Examinations of physical fitness and oxygen transport system:

Symtom limited spiroergometry was carried out in standard conditions (15) on bicycle ergometer (system for the analysis of respiratory gases, MedGraphics, USA). The load was measured out in 2 min intervals by 20 W. The examination determined functional parameters: peak work capacity (W_{peak}), peak work capacity per kg of body mass (W_{peak} . kg⁻¹), peak oxygen consumption (VO_{2peak}), peak oxygen consumption per kg of body mass (VO_{2peak} . kg⁻¹), pulse oxygen (VO_2 . SF⁻¹), minute ventilation (VE), relative ventilation (VE . kg⁻¹). Then resting and highest achieved values of systolic pressure (SBP_{rest} and SBP_{peak}) and diastolic pressure (DBP_{rest} and DBP_{peak}), and resting and highest achieved values of heart rate (HR_{rest} and HR_{peak}) were recorded. The resulting values were mathematically processed and compared with actual standards IBP for Czechoslovak healthy population (International Biologic Program, 1977) (19). Statistical data analysis (program STATISTICA for Windows - ver.7.7) was carried out by means of Wilcoxon test for non-paired values and correlation analysis (Spearman, r, P < 0.05) of individual parameters.

RESULTS

35 patients with diagnosed MS disease were examined - 28 women (80 %) and 7 men (20 %) of mean age 49.1 \pm 10 years. The degree of disability according to EDSS was 3.0 \pm 1.2 (medium degree of disability). In 17 patients we found a relapse-remittent (RR) form of the disease, in 16 patients a secondarily progressive (SP) and in 2 patients a primarily progressive (PP) form of the disease. In the questionnaire MFIS the patients assessed their fatigue on average as moderate to medium, with an approximately identical influence of physical and cognitive decondition. Independence, tested by the

scale FIM, achieved the upper limit of the scale range, i.e. minimal limitation of independence in doing common daily activities. General characteristic of the set and evaluation of the disease activity are given in Table 1.

Table 1 Basic anthropometric data and data defining MS disease in the set beingexamined (the values are expressed as mean \pm SD)

	Achieved value	Min. and max.
	Acmeveu value	values
Clinical disablility (EDSS)	3.0 ± 1.2	0 - 10
Fatigue (MFIS)	32.3 ± 17.9	0 - 84
MFISp – physical	16.8 ± 8.9	0 - 36
MFISc – cognitive	12.7 ± 8.4	0 -40
MFISps – psychosocial	2.7 ± 2.3	0 - 8
Independence (FIM)	116.3 ± 10.9	18 - 126
Body mass index (BMI)	24.7 ± 4.6	
Length of disease MS (years)	15.4 ± 12.5	
Age (years)	49.1 ± 10.0	

Parameters of physical fitness and metabolic functions

Statistical evaluation of mean values found in examinations indicated a significant decrease of most parameters of functional fitness in patients from the monitored set in comparison with actual IBP standards. The given finding demonstrates a significantly lower functional fitness in MS patients. A detailed survey of the results and statistical evaluation is in Table 2.

Table 2 Measured values of spiroergometric parameters in comparison with the CzechIBP standard (the values are expressed as mean \pm SD)

Spiroergometric	Measured	Value according to	Statistical
parameters	value	IBP standard	significanc
			e
W _{peak} (W)	89.0 ± 34.1	176.3 ± 28.4	***
$W_{peak.} kg^{-1} (W . kg^{-1})$	1.29 ± 0.4	2.5 ± 0.3	***
HRpeak	$140,8 \pm 23,8$	177.7 ± 7.5	***

VO _{2peak} (ml O ₂)	1432.9 ± 474.4	2021.1 ± 320.4	***
VO_{2peak} . kg ⁻¹ (ml O_2)	20.6 ± 5.9	28.5 ± 3.2	***
VO_{2peak} , SF^{-1} (ml.tep ⁻¹)	9.9 ± 3.0	$11.4 \pm 0,02$	*
VE (L.min ⁻¹)	$44,9 \pm 18,6$	78.3 ± 12.5	***
VE.kg ⁻¹ (L.min ⁻¹ .kg ⁻¹)	0.7 ± 0.3	1.11 ± 0.14	***
RER	1.0 ± 0.1	1.1 ± 1.8	**
* D : 0.05 ** D : 0.001	*** D . 0.0001		

* P < 0.05 ** P < 0.001 *** P < 0.0001

Hemodynamic parameters

Average resting values of systolic blood pressure at rest (SBP_{rest}) were 125.4 ± 15.1 mmHg, of diastolic blood pressure at rest (DBP_{rest}) 82.3 ± 9.1 mmHg and heart rate at rest (HR_{rest}) 72.8 ± 12.6 pulses.min⁻¹. The following factors participated in termination of the exercise test: suddenly appearing total fatigue, probably due to MS (36 %), fatigue of musculature of lower extremities (48 %), and achieving of hypertonic reaction of BP (16 %). Statistical evaluation showed, however, significantly lower values of peak heart rate at the lower achieved maximum performance and significantly higher values of DBP_{max} (97.2 ± 21.4 mmHg) at the peak of the load in comparison with actual Czech standards IBP. As to SBP_{max} values, no statistical significance was proved. A rather low value of HR_{max} and increased values of DBP_{max} could indicate a decreased level of physical performance and pathological (hypertonic) reaction of DBP is a response of organism to physical loading by a dynamic form. Decrease of SBP in the restitution phase showed normal values on average. Survey of the results is in Table 3.

Hemodynamic	Measured	Value according to	P level
parameters	Value	IBP standard	(Wilcoxon)
SBP _{max} (mmHg)	186.0 ± 27.7	177.9 ± 8.0	NS
DBP _{max} (mmHg)	97.2 ± 21.4	77.5 ± 8.6	***
HR _{max} (pulse.min-1)	140,8 ± 23,8	177.7 ± 7.5	***

Table 3 Measured values of hemodynamic parameters in comparison with Czech IBPstandards (the values are expressed as mean \pm SD)

After statistical evaluation correlation analyses between neurological impairment (EDSS), MFISp, FIM and parameters of functional fitness and metabolic functions were carried out. General results of the analysis are in Table 4. The most important relation was found between spiroergometric parameters and EDSS, and then in the subscale MFISp. The assumption of the close relation between the scales FIM and MFIS has been proved (r = -0.56, P < 0.001). In our set we have not found any relation between FIM and EDSS (r = -0.05, NS), between EDSS and MFIS (r = 0.28, NS), we have only found a small dependence between EDSS and the length of the disease (r = 0.35, P <0.01). All correlation analyses were carried out, however, on a statistically small sample of patients.

	Length of	EDSS	MFIS	MFISp	FIM
	the disease				
W _{peak} (W)	-0,30	*** -0,67	* -0,41	** -0,50	0,08
$W_{peak.} kg^{-1} (W \cdot kg^{-1})$	-0,27	*** -0,58	* -0,42	** -0,49	0,10
HRpeak	* -0,37	** -0,48	* -0,39	* -0,38	0,08
VO_{2peak} (ml O_2)	-0,24	** -0,64	** -0,43	** -0,56	0,12
VO_{2peak} . kg ⁻¹ (ml O ₂)	-0,15	** -0,47	* -0,38	** -0,48	0,13
VO_{2peak} SF ⁻¹ (ml.tep ⁻¹)	-0,10	** -0,48	-0,14	-0,31	-0,11
$VE(L.min^{-1})$	-0,32	** -0,48	* -0,41	** -0,51	0,12
$VE.kg^{-1}$ (L.min ⁻¹ .kg ⁻¹)	-0,21	* -0,36	* -0,42	** -0,49	0,20
* P < 0.05 ** P < 0.0	1 *** P < 0	.001			

Table 4 Correlation between parameters of the spiroergometry and selected clinical parameters (the values are given as Spearman coefficient r),

DISCUSSION

A significant decrease of parameters of cardiorespiratory fitness in comparison with normal population is documented in a number of studies (4, 11, 12, 13, 20, 21). Many of them are resumed in the study of Motl et al. (22). As to the Czech studies published in the world, especially the study of Řasová et al. (23) presents comprehensive results of spiroergometric measurements made on the sample of 112 patients with MS; in the majority of the cases we are in accordance with the results and conclusions of this study. The results of our measurement represent the choice of the population of MS patients with quite a low degree of subjectively perceived fatigue (MFIS 32.3 ± 17.9), a high degree of independence (FIM 116.3 ± 10.9 , 74 % of patients did not use any aids to locomotion), and a relatively low degree of EDSS (3.0 ± 1.2) (24). The results of our study showed a statistically very significant limitation of functional capacity of cardiorespiratory system and physical fitness in comparison with actual standards applicable to Czechoslovak population (19). The patients in the set with MS manifested a rather low tolerance of dynamic load and a quite a low ability of achieving maximal values of physical performance (23, 21). This fact also corroborates a preliminary termination of the test. It can be explained by the block of conduction of nerve impulses increasing with the increasing load (2, 21). Under the load two patients suffered heart rhythm disorders that were not too grave and were not the reason for interrupting the test. The pressure reaction of the examined set to the dynamic load showed hypertonic reaction DBP_{max} at the load peak. This reaction can be explained by a higher vascular resistance and a lower vascular elasticity in consequence of the long-time physical inactivity and by a higher mean age of the set (15). Our results also imply the correlation between the degree of neurological impairment (EDSS), MFISp and spiroergometric parameters. The achieved results are limited by the size of the set. New rehabilitation methods demonstrate decreasing fatigue (MFIS) and reduction of clinical impairment (EDSS) on the basis of increasing cardiorespiratory fitness (4,11,12). According to Zálišová et al. (25) physical condition and fatigue can be influenced by suitably chosen rehabilitation and fatigue should not be taken as the load limit. The results of the exercise test therefore represent, last but not least, a significant contribution to the prediction of the load measured out optimally, mainly objectively and relevantly, in rehabilitation programs for MS patients with quite a low degree of clinical impairment.

CONCLUSION

The results of spiroergometry showed that in the examined set of MS patients there is a very low tolerance of physical load and a rather low capacity of the transport system. The study demonstrates the correlation between the results of the spiroergometry and clinical functional impairment according to EDSS and fatigue according to MFIS questionnaire.

Supported by MSM0021622402.

LITERATURE

- HAVRDOVÁ, E. (2002). Roztroušená skleróza. Praha: Triton, 3.vyd. 110s., ISBN 80-7254-280-X.
- HAVRDOVÁ, E. (2004). Význam včasné léčby roztroušené sklerózy mozkomíšní. Neurologie pro praxi; č.5, s. 291-294.
- BAREŠ, M. (2002) Evokované potenciály v diagnostice roztroušené sklerózy mozkomíšní. Neurologie pro praxi č. 5, s. 244 – 248.
- MOSTERT, S., KESSELRING, J. (2002) Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. Multiple Sclerosis; 8(2):161-68.
- PONICHTERA-MULCARE JA. (1993) Exercise and multiple sclerosis. Med Sci Sports Exerc; 25: 451/65.
- DE HAAN, A. (2000) Contractile properties and fatigue of quadriceps muscles in multiple sclerosis. Muscle Nerve; 23:1534-41.
- TANTUCCI C., MASSUCCI M. et al. (1996) Energy cost of exercise in multiple sclerosis patients with low degree of disability. Mult Scler; 2: 161/67.
- 8. ALEXANDER V., KENT-BRAUN JA. (1997) Quantitation of lower physical activity in persons with multiple sclerosis. Med Sci Sports Exerc: 517/23.
- FISK JD., PONTEFRACT A. (1994) The impact of fatigue on patient with MS. Can J Neurol Sci: 21: 9/14.
- 10. KENT-BRAUN J, SHARMA KR. et al. (1994) Effect of exercise on muscle activation and metabolism in MS. Muscle & Nerve 17: 1162/69.
- 11. PETAJAN, JH., GAPPMAIER, E., WHITE, AT. (1996). Impact of aerobic training on fitness and quality of life in multiple sclerosis. Ann Neurol; 39(4):432-41.

- 12. ROMBERG, A., VIRTANEN, A. (2004). Exercise capacity, disability and leisure physical activity of subjects with multiple sclerosis. Mult. Sclerosis; 10(2):212-18.
- SCHAPIRO RT, PETAJAN JH et al. (1988) Role of cardiovascular fitness in multiple sclerosis: A pilot study. J Neuro Rehab 2: 43/49.
- ZÁLIŠOVÁ K, HAVRDOVÁ E. (2001) Effect of aerobic load and rehabilitation on patients with multiple sclerosis - pilot study. Multiple Sclerosis-Clinical and Laboratory Research 7: 116.
- PLACHETA, Z., SIEGELOVÁ, J. (1999). Zátěžová diagnostika v ambulantní a klinické praxi, Praha: Grada, 1. vyd., 286 s., ISBN 80-7169-271-9
- 16. KURTZKE, J. (1983). Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology, č. 33, s. 1444 1452.
- VAŇÁSKOVÁ, E. (2004). Testování v rehabilitační praxi cévní mozkové příhody. NCO NZO, vyd. 1., 65 str. TZ 57-852-04
- Multiple Sclerosis Council for Clinical Practice Guidelines (1998). Fatigue and multiple sclerosis. Washington DC: Paralyzed Veterans of America.
- SELIGER, V., BARTŮNĚK, Z., ROTH, Z. (1977). Metody a výsledky celostátního výzkumu fysické zdatnosti obyvatelstva. Praha: Karolinum.
- 20. FOGLIO K, CLINI E. et al. (1994) Respiratory muscle function and exercise capacity in MS. European Resp Journal 7: 23/28.
- 21. PONICHTERA-MULCARE JA, MAHEWS T. et al. (1995) Maximal aerobic exercise of individuals with multiple sclerosis using three modes of ergometry. Clincal Kinesiology 49: 4/13.
- 22. MOTL, RW, MCAULEY. E., (2005). Physical activity and multiple sclerosis: a meta-analysis. Multiple sclerosis, II, 459-463.
- ŽASOVÁ, K., BRANDEJSKÝ, P., HAVRDOVÁ, E. (2005). Spiroergometric and spirometric parameters in patients with multiple sclerosis. Multiple Sclerosis; 11: 213-221.
- 24. VALACHOVIČOVÁ I. (2001). Návrh metodického postupu rehabilitácie u pacientov s diagnózou sclerosis multiplex. Rehabilitácia; 34:199-203.
- 25. ZÁLIŠOVÁ, K. (2001). Effect of aerobic exercises applied in the frame of complex physiotherapeutic program on fatigue in multiple sclerosis. In Rehabilitácia, roč. 2001, č.34 (4), s. 229-231.

SUMMARY

The aim of this study was to analyze the physical fitness, the functional parameters, fatigue and independence in a group of patients with multiple sclerosis (MS), and to compare the measured results with applicable standards.

Patients and methods: We examined 35 MS patients with clinically active form of MS (age 49.1 \pm 10.0 years, 28 women, 7 men, mean duration of MS 15.4 \pm 12.5 years, EDSS 3.0 \pm 1.2) who participated in spiroergometric examination. All the patients underwent a symptom-limited spiroergometry on bicycle (load 20 W increasing every 2 min) in order to evaluate the following parameters of functional capacity: maximal oxygen comsumption (O_{2peak} -ml O₂,VO_{2peak}.kg⁻¹, -ml O₂. kg⁻¹), maximal work load (W_{peak} -watts, W_{peak} kg⁻¹ -watts.kg⁻¹). We measured hemodynamic parameters – heart rate (HR) and blood pressure (SBP and DBP). The registered data were compared with Czech standards (IBP standards – International Biologic Program, Seliger et al., 1977). The patients were also tested for fatigue (questionnaire MFIS) and functional independence measure (FIM).

Results: The results showed a significant reduction of functional capacity, namely in the values of parameters of spiroergometry (P<0.05, Wilcoxon paired) VO_{2peak} (1432.9 ± 474.4 ml O₂), VO_{2peak}.kg⁻¹ (20.6 ± 5.9 ml O₂.kg⁻¹), W_{peak} (89.0 ± 34.1 watts) and W_{peak} kg⁻¹ (1.29 ± 0.4 watts.kg⁻¹) at the exercise peak. Correlations between clinical testing (EDSS), fatigue (MFIS) and spiroergometric data (Spearman coefficient) were obtained.

Conclusions: The examined patients with MS have a low exercise tolerance and a rather low capacity of the transport system. Spiroergometric parameters depend on the degree of clinical disability and subjectively evaluated fatigue.

* * *

PHYSIOTHERAPY LASTING THREE MONTHS IN PATIENTS AFTER STROKE

Barbora Bártlová, Eva Nosavcovová, Marcela Nováková, Lenka Drlíková, Abdul Karim Al Fadhli, Farag Hassan Anbais, Ashref Ali Erajhi, Leona Dunklerová, Jarmila Siegelová

Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, Brno

INTRODUCTION

At present there are living in the Czech Republic almost 1,4 million citizens at the age of 65 years and older than 65 years (i.e. 13.6 % citizens of the Czech Republic). More than 18 % of the citizens are older than 60 years and 2.5 % of them are older than 80 years. Among the causes of morbidity in old age the cardiovascular system diseases are number one, whereas strokes are the third most frequent cause of death. In our country there is still one of the highest numbers of stroke in the world. The annual incidence of ischemic ictus is in the range of $550 - 570/100\ 000\ citizens$ in our country, the annual ischemic ictus mortality is $70 - 80/100\ 000\ citizens$. With regard to the fact that the phenomenon "ageing of old population" appears in all EU countries and that atherosclerosis is present in 90 % people over 75, further considerable increase of these figures can be expected (1,8,11,13).

AIM OF THE STUDY

The aim of our study was to evaluate the results of subsequent physiotherapy and ergotherapy in 65 patients with diagnosis I60 - I69, in general affection of central nervous system on the basis of vascular disease with motor activity disorder and cognitive functions, and evaluation of independence measure in basic daily activities by

means of the test of functional examination (Functional Impairment Measure, FIM) and Barthel test (BT).

SET OF EXAMINED PATIENTS

In 2005 we had 1064 treated 205 patients who were hospitalized in the unit of long lasting physiotherapy. These patients with diagnosis I 60 - 69 had CNS affection on the basis of vascular disease with motor activity disorder. Individual physiotherapy and ergotherapy was prescribed to these patients.

After three months of therapy, the patients were discharged:

43 of them were discharged to home care	62 %
22 of them were discharged to social service institutions	. 31 %
5 of them were moved to emergency ward	7 %

FIM test and BT were evaluated in 65 patients from the total number of 70, who completed the physiotherapy and ergotherapy and were discharged to home care or to institutions for social services. In five patients who were moved to emergency ward these programs were not finished, and that is why this group was excluded from further processing.

The average age of these patients was 71 years and median age was 74 years. The average age of the patients discharged to home care was 72 years and that of the patients discharged to social service institutions was 68 years. The age distribution of all 65 patients can be seen in graph 1.



Graph 1. The age distribution of 65 patients with stroke

Duration of physiotherapy and ergotherapy in our ward on average was 56 days, intensity of rehabilitation was 1 hour of individual physiotherapy and half an hour of ergotherapy 5 days in a week.



Graph 2. Duration of hospitalization in patients with stroke

METHODOLOGY

We used for our purposes FIM test and Barthel test evaluating independence in basic everyday activities and are therefore suitable for monitoring of progress of the treatment and therapeutic procedures.

FIM test – or measurement of functional independence, evaluates 18 activities in 6 categories: 1. Self attendance, 2. Control of sphincters, 3. Displacements, 4. Mobility, 5. Communication, 6. Social abilities. Each item has a scale consisting of seven points, when 1 means full assistance and 7 full independence. The total score can be 18 - 126 points (2,5,6,7,10).

Barthel test - test of basic everyday activities evaluates 10 activities:

- 1. Eating, drinking,
- 2. Dressing,
- 3. Taking a bath,
- 4. Personal hygiene,
- 5. Incontinence of defecation,
- 6. Incontinence of urination,
- 7. Ability to Use WC,

- 8. Displacement from the bed to the chair,
- 9. Walking on even ground,
- 10. Climbing stairs.

Individual items are evaluated either in three degrees of dependence – does not accomplish (0), accomplishes with assistance (5) and accomplishes independently without assistance (10), or in two degrees of dependence – does not accomplish (0), accomplishes independently or with assistance (5), or in four specific degrees according to circumstances (0,5,10,15). The total score can be therefore 0 - 100 points (2, 3, 4, 6, 12, 13).

As Barthel test does not contain evaluation of cognitive components, we used only the evaluation of motor function score of FIM test to compare the results with FIM test.

RESULTS

We compared the results of motor score of FIM test and the results of Barthel test at the beginning of rehabilitation and at then discharge in the whole set of 65 patients, and then separately in the subgroup of 43 patients who were discharged home and 22 patients discharged to social service institutions.

	FIM input	FIM output	Barthel input	Barthel output
Means of the whole set	46±23	58±24**	42±30	55±30**
Discharged home	54±21	67±19*	53±28	67±24*
Discharged to social service	31±17	40±23*	22+22	32±27*
institutions	51±17	40123		32127
* p < 0,05, ** p < 0,01				

For evaluation of functional state of input and output parameters of both tests we used Wilcoxon paired test and the results showed statistically significant improvement of the function at the level p < 0.01 in both functional tests in all groups.

Input and output results of both tests can be seen in graphs 3 and 4.



Graph 3. Results of functional state (FIM test) before and after 3-month rehabilitation of patients with stroke



Graph 4. Results of functional state (BT) before and after 3-month rehabilitation of patients with stroke

DISCUSSION

The measured results show that a long-term rehabilitation of patients with stroke leads to a substantial improvement of their independence in basic daily activities, which eases their re-integration into normal life. These people can then leave the hospital and go home. If their functional limitation does not allow it and they must go to a social service institution, any improvement of their self attendance needs the help of the staff nursing.

Expectations after stroke vary. Some patients die in spite of all possible care, the least affected patients return to their original health state in the course of several hours or days. Then, however, there are many patients who will have some sequential problems. Here different tests of basic everyday activities can be applied in a large extent, both as indicators of the rehabilitation progress, and as an advice to a problematic part of self attendance, necessity of prescribing compensatory aids or adjustment of the flat (9, 11, 13).

CONCLUSION

By means of functional tests (BT and FIM test) we demonstrated successfulness of three-months rehabilitation in patients after CMP. Physiotherapy and ergotherapy are indicated in all patients, regardless of the measure of functional impairment.

Supported by MSM0021622402

LITERATURE

- 1. Beneš, Vl. (2003). Ischemie mozku. Praha: Galén.
- 2. Grünerová, M. (2005). Neurorehabilitace. Praha: Galén.
- Guth, A. (1995). Vyšetrovacie a liečebné metodiky pre fyzioterapeutov. Bratislava: LIEČREH
- 4. Kalvach, P. (1997). Mozkové ischemie a hemoragie. Praha: Grada.

- Kelly, P.J., Stein, J., Shafqat, S., Eskey, C., Doherty, D., Chang, Y., Kurina, A., and Furie, K.L. (2001). Functional Recovery After Rehabilitation for Cerebral Stroke, Feb 2001; 32: 530 - 534.
- Kwon, S., Hartzema, A.G., Duncan, P.W., Min-Lai, S. (2004). Disability Measures in Stroke: Relationship Among the Barthel Index, the Functional Independence Measure, and the Modified Rankin Scale Stroke, Apr 2004; 35: 918 - 923.
- Malý, M. (2001). Testovanie funkčnej sebestačnosti. Rehabilitácia, 34,2001 Med J Aust; 177(8):452 – 456.
- 8. Nebudová, J. (1998). Cévní mozkové příhody minimum pro praxi. Praha: Triton.
- 9. Országh, J., Káš, Sv. (1995). Cévní příhody mozkové. Praha: Brána.
- 10. Švestková, O. (2004). Možnosti posouzení funkčních schopností, aktivit a participací. Autoreferát doktorandské práce. Praha: Univerzita Karlova.
- 11. Tarasová, M., Ošmerová, J., Svoboda, L., Vohlídalová, I., Vank, P., Frajhi, F.A., Karim, A.F.A., Sosíková, M., Siegelová, J. (2005). Testování funkčního stavu pacientů po cévní mozkové příhodě. Hradec Králové: Univerzita Hradec Králové
- Vaňásková, E. (2004). Testování v rehabilitační praxi cévní mozkové příhody. Brno: NCONZO.
- 13. Weber, P. (2000). Minimum z klinické gerontologie. Brno: IDVPZ.

SUMMARY

FUNCTIONAL RESULTS OF REHABILITATION LASTING THREE MONTHS IN PATIENTS AFTER STROKE

The aim of this study was to evaluate the questionnaire Functional Impairment Measure (FIM) and Barthel test in patients after stroke before and after three months of rehabilitation and ergotherapy.

Methods: We examined 65 patients after stroke by means of questionnaire FIM and Barthel test.

Results and conclusion: We have found after rehabilitation and ergotherapy by means of FIM and Barthel test improvement of functional state in our patients. Rehabilitation and

ergotherapy are indicated in all patients with stroke without any regard to functional state.

Key words: stroke, quality of life, rehabilitation, functional impairment measurement

EXERCISE TRAINING IN OBESE PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE

Jaroslava Pochmonová, Leona Mífková, Veronika Chludilová, Hana Svačinová, Pavel Vank, Michal Pohanka, Nabil Abdulah Ibrahim Al-Mahmodi, Mohsin Kaid Ali Hashim, Abdul Karim Al Fadhli, Farag Hassan Anbais, Ashref Ali Erajhi, Petr Pospíšil, Lumír Konečný, Jarmila Siegelová

Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ

INTRODUCTION

Physiotherapy in patients with chronic ischemic heart disease is an essential part of the treatment (1, 2, 3, 4, 5). Some patients, in addition to ischemic heart disease, are also obese and their habitual exercise activity can be lower than in patients without obesity. To indicate properly the exercise treatment in patients with ischemic heart disease with obesity, we have studied the physical performance at the maximum symptom-limited load in patients with chronic ischemic heart disease and obesity.

AIMS OF THE STUDY

The study was aimed at evaluation of twelve-week combined training on physical performance (expressed as maximal achieved performance and performance converted to 1 kg of the body mass), on indicators of capacity of the transport system (expressed as maximal oxygen intake) and on quality of life in patients with ischemic heart disease with regard to their body mass and possible obesity.

METHODOLOGY

The set of 88 examined patients with chronic ischemic heart disease was divided into three groups according to the value of BMI. The first group included patients with BMI up to 25, in the second group with BMI 25.1 - 30 and in the third group with BMI over 30; basic characteristics of the set are given in Tables 1 - 3.

 Table 1. Basic characteristic of the group of patients with BMI up to 25

Number (n)	16
Age (years)	60.9±8.9
EF (%)	47.7±12.6
BMI (kg.m ²)	23.9±1.2

Table 2. Basic characteristic of the group of patients with BMI 25,1 - 30

Number (n)	50
Age (years)	63.0±9.6
EF (%)	49.0±9.5
BMI (kg.m ²)	27.3±1.6

Table 3. Basic characteristic of the group of patients with BMI over 30

Number (n)	22
Age (years)	62.4±10.8
EF (%)	48.9±9.7
BMI (kg.m ²)	31.9±2.6

The patients put on exercise therapy for ischemic heart disease had to comply with the following criteria: they did not suffer acute myocardiac infarction or attack of nonstable angina pectoris in the period of three months before starting the exercises, no patient had any valvular defect or heart failure and treated hypertension.

The patients with serious dysrhythmia, with signs of hemodynamic instability, with severe ischemiaof left ventricul at rest or under load were excluded. The patients with uncontrolled hypertension and diseases ruling out exercise therapy also were not included into the set.

Examinations made within the framework of this study. Before starting exercise therapy all patients were submitted to entrance examination of symptom-limited spiroergometry. In addition to the basic clinical examination (to exclude contraindications of the load examination) their ejection fraction of left ventricle was determined by Doppler echocardiography with the instrument SONOS 5500 (Hewlett Packard).

Evaluation of the transport system function was realized by means of spiroergometric load test on bicycle ergometer. The twelve-lead electrocardiogram was recorded by the instrument Cardiovit CS 100 – Schiller. Ventilation-respiration values were determined by gas analyzer Pulmonary Function System 1 070 – MedGraphics CPX/D, USA, equipped with software for their analysis and evaluation.

The examination was carried out in morning hours and the patients were noticed in advance that they should take the morning dose of their usual medication. Each patient was given the reason of examination and expected results. From the beginning of the load test twelve-lead EKG at rest was monitored. In the course of 2 to 5-minute phase of adaptation sitting on the ergometer because of stabilizing the parameters, rest values of heart rate (HR) and blood pressure (BP) were read.

The protocol with progressive load without interruptions up to the symptom-limited maximum was determined for the examination (6). ECG record was taken and the examined patient assessed his subjective perception of the load intensity (rating of perceived exertion - RPE) and his blood pressure (BP) was measured by auscultation method by means of a mercury manometer. Respiratory parameters in exhaled air ware determined by means of a breath gas analyser in real time breath-to-breath. On the basis of the measured values the arithmetic mean was calculated for every 30 seconds of load.

Seattle Angina Questionnaire. At the beginning and after the completion of the rehabilitation program the patients were given Seattle Angina Questionnaire (SAQ) to be filled out for finding out their subjective perception of health state and quality of life. The questionnaire is divided into five sections (further and in the results SAQ 1-5) and contains nineteen items altogether (7, 8, 9, 10).

Section 1 (SAQ 1) The patient indicates how the chest pain or anginous pain during the last four weeks restricted him in performing activities given in the section. The activities are arranged according to their physical strenuousness.

Section 2 (SAQ 2) It deals with comparison of the present health state with the period four weeks ago as to the frequency of anginous troubles in performing routine daily activities.

Section 3 (SAQ 3) The patient indicates how many times a day or a week he had anginous troubles in the last month in comparison with the same period four weeks ago and how many times he had to take nitroglycerin because of them.

Section 4 (SAQ 4) It concerns subjective perception of the treatment and satisfaction of the patient with it.

Section 5 (SAQ 5) The last part should convey how the patients perceive quality of their life with the disease and its possible fatal end.

The study was approved by local ethical committee and the patients signed their informed approval.

The results were presented as average \pm standard deviation, statistical evaluation was made by using Student T-test and Wilkoxon test.

RESULTS

In patients with chronic ischemic heart disease with BMI up to 25 we have found **statistically significant increase** of maximal symptom-limited performance (Wmax), statistically significant increase of maximal heart rate (HRmax), maximal oxygen consumption (VO₂max), MET, questionnaire of quality of life with regard to usage of nitroglycerin at anginous pain (SAQ 3), as it is given in Tables 4, 5, 6.

Table 4. Results of symptom-limited spiroergometry before exercise therapy in individual groups of patients with chronic ischemic heart disease divided according BMI

	BMI to 25 (1 st group)	BMI 25,1 – 30 (2 nd group)	BMI over 30 (3 rd group)	Statistical significance
HR maximal	121.0±13.6	113.5±16.8	109.1±19.1	NS
W maximal (W)	114.7±34.9	109.5±29.6	121.4±39.3	NS
SBPmax mmHg	204.7±35.5	193.7±25.2	198.8±29.2	NS
DBPmax mmHg	101.7±10.3	106.2±13.2	121.4±39.3	NS
VO ₂ max (ml/min)	1649±389	1643±373	1833±493	NS
VO ₂ max/kg	22.4±5.3	19.5±4.4	19.1±4.9	*
SAQ 1	85.8±16.8	78.1±20.2	78.6±15.7	NS
SAQ 2	77.1±19.0	77.5±22.1	83.0±22.7	NS
SAQ 3	83.3±17.2	82.8±16.0	84.5±16.3	NS
SAQ 4	91.6±17.1	85.9±17.4	90.5±11.3	NS
SAQ 5	70.0±19.6	63.7±17.8	71.1±14.5	NS

In the column statistical significance *, +, o - p < 0.05, **, ++, oo - p < 0.01; BMI: up to 25 versus 25.1 -30: *; up to 25 versus over 30: +, 25.1 30 versus over 30: o. Statistical significance of the difference before rehabilitation and after it is given next to the relevant value (* p < 0.05, ** p < 0.01)

Table 5 Results of symptom-limited spiroergometry after rehabilitation in individual groups of patients with chronic ischemic heart disease

	BMI to 25 (1 st group)	BMI 25,1 – 30 (2 nd group)	BMI over 30 (3 rd group)	Statistical significance
HR maximal	133.9±17.6*	114.1±19.5	109.4±21.5	NS
W maximal (W)	133.9±39.0*	118.3±32.8*	126.2±39.0	NS
TKs max mmHg	209.0±30.2	198.2±26.2	211.4±25.2*	NS
TKd max mmHg	106.0±15.7	106.0±15.1	126.2±39.0	NS
VO2 max (ml/min)	1964±470**	1756±424	1921±457	**
VO2 max/kg	26.5±6.4*	20.8±5.2*	20±4.4	NS
SAQ 1	88.8±15.3	83.0±16.6*	85.8±14.2**	NS
SAQ 2	85.3±16.0	85.0±16.2*	89.0±16.5	NS
SAQ 3	88.3±14.7*	87.7±15.4**	89.2±12.4*	NS
SAQ 4	93.3±12.3	92.7±10.9**	93.3±8.1	NS
SAQ 5	72.9±18.0	71.2±18.5**	80.0±14.0**	NS

In the column statistical significance *, +, o - p < 0.05, **, ++, oo - p < 0.01; BMI: up to 25 versus 25.1 -30: *; up to 25 versus over 30: +, 25.1 30 versus over 30: o. Statistical significance of the difference before rehabilitation and after it is given next to the relevant value (* p < 0.05, ** p < 0.01) We have achieved considerably different results in the studied groups. It follows from what was given above, that the patients with a normal body mass attained significant improvement in maximal achieved physical performance, in maximal achieved heart rate and maximal oxygen intake. In the patients with overweight we demonstrated significant increase of maximal achieved physical performance and maximal oxygen intake related to kilogram of body mass. In the patients with obesity we achieved significant decrease of systolic pressure and heart rate at rest.

By evaluation of individual items of the questionnaire SAQ we have found out that in the group of the patients with BMI up to 25 significant improvement was achieved in frequency of anginous pain and necessity of taking nitroglycerin. In the overweight group the patients indicated significant improvement in all items of the questionnaire SAQ. In the group of obese patients improvement was indicated in the questionnaire items concerning occurrence of anginous pain (SAQ 1), general perception of quality of life (SAQ 5) and also SAQ 3.

DISCUSSION

Regular combined exercise training of a suitable intensity results in adaptation of organism to the load, in increase of physical performance and capacity of the transport system and in quality of life.

In the presented study we were dealing with the role of obesity in this process of rehabilitation. Individual groups differed only in the body mass index before the beginning of rehabilitation process. The exception was maximal transport capacity for oxygen, that was lower in the group of obese patients; it can be easily explained by a lower proportion of muscular mass and bigger proportion of adipose tissue mass. Comparison of individual groups after the completion of exercise therapy brought the same results. This fact demonstrates that in all body mass groups there are considerable inter-individual differences. We also did not find out any differences in subjective evaluation of quality of life before exercise therapy and after its completion.

Comparison of individual objective indicators and of subjective evaluation before physiotherapy and after it gives a different view. Substantial increase of quality of life
along with improvement of maximal physical performance and maximal capacity of oxygen transport system occurs in the group of patients with overweight. In the patients with normal body mass and in the patients with obesity we can observe less noticeable, but statistically significant improvement of subjectively evaluated indicators. Only in the patients with a normal body mass this subjectively perceived condition is accompanied by increase of maximal physical performance. This was not found in obese patients.

Our results show that the body mass influences considerably a subjectively perceived degree of disablement influenced by training. The reality that in obese patients their physical performance has not been improved is probably due to the fact that their overweight represents such a strain on the organism, that probably their ischemic heart has not enough additional reserves which would appear with increased maximal physical performance. The conclusions following from our study are not pessimistic in the case of obese patients, however. Even if their physical performance has not been improved, improvement of subjectively experienced quality of life turned out, and it is more important for the therapy. It seems that intensive pressure on decreasing the body mass could bring about still more favourable results of exercise training for the patient.

CONCLUSION

The paper aims at evaluation of the impact of the twelve-week combined training on quality of life, physical performance and capacity of the transport system of the patients depending on their body mass.

On the basis of the input symptom-limited spiroergometry and of the same examination carried out after the termination of the training we have proved that the twelve-week combined exercise training in patients with chronic ischemic heart disease resulted in increasing their physical performance and capacity of the transport system, particularly in the patients with the body mass index lower than 30. As to the patients with the body mass index higher than 30, we have not observed any increase of physical performance. We have found, however, that all groups of patients subjectively experienced improvement of their quality of life. We have thus shown that even if the rehabilitation training does not lead to improved physical performance, it can bring about subjectively experienced improvement of quality of life.

Supported by MSM0021622402

REFERENCES

- 1. CHALOUPKA, V., SIEGELOVÁ, J. ŠPINAROVÁ, L. a kol. 2006. Rehabilitace u nemocných s kardiovaskulárním onemocněním. *Cor Vasa*. 48: K 127-45.
- JANČÍK, J. DOBŠÁK, P. SVAČINOVÁ, H. SIEGELOVÁ, J. PLACHETA, Z. 2002. Zátěžová vyšetření u nemocných s chronickým srdečním selháním. *Kardiol. Revue, roč. 3.,* s. 175-179.
- JANČÍK, J. VANK, P. MÍFKOVÁ, L. CHLUDILOVÁ, V. FIŠER, B. SIEGELOVÁ, J. – EICHER, J. CH. 2004. Aerobní trénink kombinovaný se silovými prvky u nemocných s chronickou ischemickou chorobou srdeční: vliv na variabilitu srdeční frekvence. In *Optimální působení tělesné zátěže a výživy*. Hradec Králové: Gaudeamus, s. 213-216, ISBN 80-7041-666-1
- MARTINÍK, K. 2005. Individuální výběr nemocných pro silový trénink u nemocných po akutním infarktu myokardu se sníženou ejekční frakcí levé komory – editioral. *Vnitřní lékařství, roč. 51., č. 1.,* s. 13-16.
- NIEDERLE, P. 2004. Rehabilitace a trénink u kardiaků. In ASCHERMANN, M. et al. *Kardiologie*. Praha: Galén, s. 1421-1424.
- 6. PLACHETA, Z. SIEGELOVÁ, J. ŠTEJFA. et al. 1999. Zátěžová diagnostika v ambulantní a klinické praxi. Grada Publishing, s. 51-178, ISBN 80-7169-271-9
- DRAGOMIRECKÁ, E. ŠKODA, C. 1997. Kvalita života. Vymezení, definice a historický vývoj pojmu v sociální psychiatrii. Č. S. Psychiatrie, roč. 93, č.2, s. 102-108.
- SLOVÁČEK, L. SLOVÁČKOVÁ, B. JEBAVÝ, L. BLAŽEK, M. KUČEROVSKÝ, J. 2004. Kvalita života nemocných – jeden z důležitých parametrů komplexního hodnocení léčby. *Vojenské zdravotnické listy, roč. 73, č.1,* s. 6-9.

- SLOVÁČEK, L. Kvalita života a ischemická choroba dolních končetin. *Interv Akut* Kardiol 2006;5:207–210
- PAYNE, J. A KOL. 2002. Zdraví: hodnota a cíl moderní medicíny. Praha: Triton, s. 9-12, s. 54-64, ISBN 80-7254-293-1

SUMMARY

The paper deals with evaluation of the impact of the 12-week combined exercise training on quality of life, physical performance and capacity of the transport system of patients with chronic ischemic heart disease (n = 88) depending on the body mass of the patients.

On the basis of the input spiroergometric examination and of the same examination carried out after the termination of the training we have proved that the 12-week combined exercise training in patients with chronic ischemic heart disease resulted in increasing their physical performance and capacity of the transport system, particularly in the patients with the body mass index lower than 30. As to the patients with the body mass index higher than 30, we have not observed any increase of physical performance. We have found, however, that all groups of patients subjectively experienced improvement of their quality of life. We have thus shown that even if the rehabilitation training does not lead to improve physical performance, it can bring about subjectively experienced improvement of quality of life.

KEY WORDS

Quality of life, combined training, cardiovascular rehabilitation, chronic ischemic heart disease, obesity

EXERCISE TRAINING IN MEN AFTER CORONARY ARTERY BYPASS SURGERY

Veronika Chludilová, Leona Mífková, Jaroslava Pochmonová, František Várnay, Michal Pohanka, Nabil Abdulah Ibrahim Al-Mahmodi, Mohsin Kaid Ali Hashim, Jaroslava Pochmonová, Abdul Karim Al Fadhli, Farag Hassan Anbais, Ashref Ali Erajhi, Alena Havelková, Jarmila Siegelová

Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ

INTRODUCTION

Cardiovascular rehabilitation is a universally accepted part of the complex care of patients with cardiovascular disease (1). It increases physical fitness, improves quality of life (2-4) and decreases cardiovascular mortality (5,6). Dynamical endurance aerobic activities (walking, cycling, jogging, swimming, etc.) are the basis of cardiovascular rehabilitation programs (7-9). As a certain level of muscular strength that can be diminished in patients with ischemic heart disease (9,10) is necessary for a number of working and recreational activities, usefulness of resistance training as an adjuvant component of rehabilitation programs for cardiac patients has been considered (9). In spite of a concern as to cardiovascular safety of resistance training, resistance exercises proved to be a safe part of cardiovascular rehabilitation (1, 9-16).

PURPOSE OF THE STUDY

The purpose of the study was to examine the effect of 12-week controlled out-patient rehabilitation program on muscle strength and selected indicators of physical fitness and performance and to verify safety and effectiveness of combination of aerobic and resistance training in patients after coronary artery bypass surgery (ACB).

SET OF PATIENTS

10 men after ACB aged 64 ± 7 years, with mean ejection fraction of left ventricle 49 ± 11 %, who were at least 6 weeks (40 ± 28 weeks) after the surgery, were included into the study. All subjects gave their informed approval.

METHODOLOGY

Methods of examination

Before the beginning of exercise training (RHB) program and after its completion we made symptom-limited spiroergometry to symptom-limited maximum (Pulmonary Function System 1070, MedGraphics, USA). The examination was started by monitoring resting ECG in lying and sitting position (Schiller CS 100), followed by 3-minute adaptation in sitting position on ergometer. Load was increased every 2 minutes by 20 W to symptom-limited maximum. Anaerobic threshold was determined from the course of changes of ventilation-respiration parameters. The values of load, heart rate and RPE for the training were determined at the anaerobic threshold level.

Before the beginning of resistance training (i.e. in the 3rd week of RHB program) we made isometric test ("handgrip", DHG-SY3, Recens) to verify blood pressure response to isometric load. In the case of a normal response the entrance 1-RM test (one repetition maximum test) was made in three exercises of resistance training. The test was repeated in the 6th week and in the 12th week of RHB program.

Rehabilitation program

The outpatient controlled RHB program lasted 12 weeks altogether with frequency three times a week. The training unit lasted 60 minutes and consisted of several phases (table 1).

Table 1. Composition of the training unit

$1^{st} - 2^{nd}$ week only aerobic training	3 rd – 12 th week combined training
10 min warm-up phase	10 min warm-up phase
40 min aerobic phase	25 min aerobic phase
10 min relaxation phase	15 min resistance training
	10 min relaxation phase

Warm-up phase was aimed at preparing cardiovascular and motor system to further load, prevention of muscular-skeletal lesion. It consisted of dynamical endurance exercises (simple floor gymnastic exercises, exercises gymnastic apparatus) and stretching of muscle groups with a tendency to shortening.

Aerobic phase was effected on a bicycle ergometer (Ergoline REHA E900) controlled by the program ErgoSoft+ for Windows. The aerobic training intensity was determined at the anaerobic threshold level.

Resistance training was realized on multifunctional muscle conditioning machines TK-HC COMPACT. 4 exercises were done (bench press, pull down, leg extension on the machine and sitting-lying positions). Resistance training intensity was determined by the method 1-RM and training loads were determined in percents of maximum: 30-60 % 1-RM (each week increase by 10 %). The number of sequences was 3 - 5 with the number of repetitions 10x. Before starting the resistance training, the patients were thoroughly informed about proper breathing and technique of doing exercises.

Modified Schultz autogenic training was used for relaxation.

In the course of the whole training monitoring of heart rate, blood pressure and degree of RPE, during the aerobic phase and in 1-RM test also ECG was carried out.

RESULTS

The effect of 12-week controlled out-patient rehabilitation program showed in patients after coronary artery bypass surgery a statistically significant increase of symptom-limited oxygen intake and oxygen intake converted to kg of body mass (evaluated also at anaerobic threshold level Table 2) was recorded.

Table 2. Parameters of aerobic capacity in patients after coronary artery bypass surgery before and after 12-week controlled out-patient rehabilitation program

	Before RHB	After RHB	р
$VO_2SL (ml.min^{-1})$	1452 ± 292.2	1789 ± 459.6	>0.05
VO_2SL/kg (ml.min ⁻¹ .kg ⁻¹)	16.5 ± 3.32	20.3 ± 5.94	>0.05
VO₂ANP (ml.min ⁻¹)	1003 ± 191.5	1151 ± 220.1	>0.01

 VO_2SL = symptom-limited oxygen intake, VO_2ANP = oxygen intake at anaerobic threshold level

Symptom-limited performance and performance converted to kg of body mass (evaluated also at anaerobic threshold level Table 3) were also increased.

Table 3. Performance parameters in patients after coronary artery bypass surgery before and after 12-week controlled out-patient rehabilitation program

	Before RHB	After RHB	р
WSL (W)	89 ± 16.6	123 ± 36.2	>0.05
WSL/kg (W.kg ⁻¹)	1.0 ± 0.25	1.4 ± 0.49	>0.05
WANP (W)	46 ± 13.5	66 ± 18.6	>0.05

WSL = symptom-limited performance, WANP = performance at anaerobic threshold level

Muscle strength of the groups being trained was also considerably increased (table 4).

 Table 4. Performance in 1-RM test in patients after coronary artery bypass surgery before and after 12-week controlled out-patient rehabilitation program

	Before RHB	After RHB	р
Bench press (kg)	31 ± 9.4	38 ± 6.9	>0.01
Pull down (kg)	29 ± 8.7	35 ± 7.5	>0.01
Leg extension (kg)	30 ± 9.3	36 ± 8.7	>0.01

Statistical processing was made in the programs Microsoft Excel and Statistica, version 7. Distribution was tested by Lillefors modification of Kolmogorov-Smirnov test of normality. Some parameters had normal distribution Wilcoxon test was used for all parameters.

Our results in patients after coronary artery bypass surgery showed statistically significant increase of capacity of the transport system (1441 \pm 307.7 vs. 1768 \pm 482.2 ml.min⁻¹), physical performance (90 \pm 17.3 vs. 120 \pm 37.4 W) and muscular strength (bench press 30 \pm 9.8 vs. 36 \pm 9.1 kg, pull down 30 \pm 9.4 vs. 37 \pm 6.6 kg, leg extension 30 \pm 8.6 vs. 36 \pm 7.8 kg) was recorded.

DISCUSSION

After thoracotomy the capacity for physical performance of the patients is limited. Healing of the lesion takes 4 - 6 weeks on average. The first 3 months after the surgery physical strain causing tangential acting of forces and pressure on the sternum region should be contraindicated. Before starting the resistance training the attending physician must confirm that sternum is stable (4, 17-19). If there are no postoperative complications and the patient is compensated from cardiologic point of view, effortless muscle conditioning exercises directed at lower extremities can be started even sooner (20).

From the study of Maiorany et al. it follows that mere resistance training does not lead to the increase of symptom-limited oxygen intake. The authors monitored in their study, apart from other things, influence of 10-week resistance training on muscle strength in 26 men after ACB. The training unit included warm-up phase and stretching (5 min), resistance training (36 min) and relaxation phase (5 min). The patients did 12 exercises altogether (7 for upper extremities, 4 for lower extremities and 1 exercise for strengthening of abdominal muscles). At the beginning of the training the patients completed 1 cycle (so called "round") of exercises with intensity 40 % of maximal voluntary contraction (MVC) with the ratio of effort and rest 1:1 (30 s effort and 30 s rest). The number of repetitions was 10 - 15. Intensity in the first 2 weeks was increasing in such a way that the number of cycles increased to 2 - 3, according to capabilities of the patient. From the 2nd week all patients were already doing exercises with 40 % of MVC in 3 cycles, by the 4th week intensity was increased to 50 % of MVC, from the 6th week the ratio of effort and rest was changed to 2:1 (40 s effort and 20 s rest), from the 8th week intensity was increased to 60 % of MVC. This study confirmed that resistance training of a low to medium intensity in suitably chosen patients is safe and represents an effective stimulus for the increase of muscle strength of big muscular groups in men after ACB (21).

After the group of men went through the 12-week training with combined load, we also observed a considerable increase of muscle strength of the trained muscular groups. Due to combination of resistance and aerobic training also aerobic capacity and load tolerance were substantially increased.

Combination of aerobic and resistance training with intensity at anaerobic threshold level seemed in practise to be safe and adequately physiologically effective on condition of a correct choice of patients and their careful continuous checking.

Provided that safe limits are complied with, combined training associates positive effects of aerobic and resistance exercise and seems to be optimal for the group of patients we have been monitoring. A favourable effect of the training continues only if the patient pursues regular exercising. If no regular physical exercise follows after the rehabilitation program, the values of aerobic capacity and physical performance return to the level before the training approximately within the time as long as was the time of duration of the regular training.

CONCLUSION

12-week combined training in men after coronary artery bypass surgery resulted in increasing oxygen capacity transport by 23 %, physical performance by 38 % and muscle strength by 20 %.

Supported by MSM0021622402.

LITERATURE

- Chaloupka V, a kol. Rehabilitace u nemocných s kardiovaskulárním onemocněním. *Cor Vasa*.2006; 48: K 127-45.
- Izawa K, et al. Improvement in physiological outcomes and health-related quality of life following cardiac rehabilitation in patients with acute myocardial infarction. *Circ* J. 2004; 68(4):315-320.
- 3. McKelvie RS, et al. Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). *Am Heart J*.2002; 144(1):23-30.
- 4. Pollock ML, et al. Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription. *Circulation*.2000;101:828-833.
- 5. Špaček R, a kol. Infarkt myokardu.1. vyd.Praha: Galén, 2003.
- 6. Špinar J, a kol. Ischemická choroba srdeční.1. vyd. Praha:Grada Publishing, 2003.
- Clausen JP. Circulatory adjustments to dynamic exercise and effect of physical training in normal subjects and in patients with coronary artery disease. *Prog Cardiovasc Dis* 1976;18:456-495.

- Thompson PD. The benefits and risks of exercise training in patients with chronic coronary artery disease. *JAMA*. 1988; 259:1537-1540.
- 9. Balady GJ, et al. Cardiac rehabilitation programs. Circulation.1994;90:1602-1610.
- 10. McCartney N, et al.Maximal isokinetic cycle ergometry in patients with coronary artery disease. Med Sci Sports Exerc.1989;21:313-318.
- Mífková L, a kol. Kombinovaný trénink u pacientů po akutním infarktu myokardu. Med Sport Boh Slov.2005;14(3):115-123.
- 12. Atkins JM, et al. Incidence of arrhytmias induced by isometric and dynamic exercise. *Br Heart J*.1976;38:465-471.
- Vincent KR, et al. Resistance training for individuals with cardiovascular disease. J Cardiopulm Rehabil. 2006;26:207-216
- 14. Jančík J, a kol. Srovnání účinku aerobního a kombinovaného tréninku s tréninkem s posilovacími prvky na ukazatele funkční zdatnosti u srdečního selhání. *Cor Vasa*. 2004;4:32
- 15. Chludilová V, a kol. Dvanáctitýdenní rehabilitační program u nemocných s ICHS: kombinace aerobního a silového tréninku. *Optimální působení tělesné zátěže a výživy*, Hradec Králové 2005;197-201.
- 16. Mífková L, a kol. Účinek řízeného ambulantního rehabilitačního programu u pacientů s chronickou ischemickou chorobou srdeční na vývoj svalové síly. *Optimální působení tělesné zátěže a výživy*, Hradec Králové 2004, 222-225.
- 17. Sparing PB, et al. Strength training in a cardiac rehabilitation program: a six month follow up. *Arch Phys Med Rehabil*.1990;71:148-152.
- McCartney N, et al. The role of resistance training in patients with cardiac disease. *J Cardiovasc Risk*.1996;3:160-166.
- Fletcher GF, et al. Exercise standards for testing and training. A statement for healthcare professionals from the American Heart Association. *Circulation*. 2001;104:1694-1740.
- Bjarnason-Wehrens B, et al. Recommendations for resistance exercise in cardiac rehabilitation. Recommendations of the German federation for cardiovascular prevention and rehabilitation. *Euro J Cardiovasc Prev Rehabil*.2004; 11(4):352-361.
- Maiorana AJ, et al. A controlled trial of circuit weight training on aerobic capacity and myocardial oxygen demand in men after coronary artery bypass surgery. J Cardiopulm Rehabil. 1997;17:239-247.

SUMMARY

The purpose of the study was to examine the effect of 12-week controlled out-patient rehabilitation program with combined load on muscle strength and selected indicators of physical fitness and performance and to verify safety of the program in men after coronary artery bypass grafting (CABG). Nine men after CABG aged 64 ± 7 years, with mean ejection fraction of left ventricle 50 ± 12 % were included. Before the rehabilitation program and after it symptom-limited spiroergometry was made up to symptom-limited maximum. The training intensity was determined at the level of anaerobic threshold. Isometric test ("handgrip") was made before the beginning of resistance training. If the response was normal, 1-RM test (one repetition maximum test) was made. Statistically significant increase of capacity of the transport system (1441 ± 307.7 vs. 1768 ± 482.2 ml.min⁻¹),physical performance (90 ± 17.3 vs. 120 ± 37.4 W)and muscular strength (bench press 30 ± 9.8 vs. 36 ± 9.1 kg, pull down 30 ± 9.4 vs. 37 ± 6.6 kg, leg extension 30 ± 8.6 vs. 36 ± 7.8 kg) was recorded.

KEY WORDS

Cardiac exercise therapy, aerobic training, resistance training, coronary artery bypass surgery

FUNCTIONAL EVALUATION IN CHILDREN WITH CEREBRAL PALSY AFTER 6-MONTH THERAPY

Lenka Drlíková¹, Mohsin Kaid Ali Hashim²,

Abdul Karim Al Fadhli², Farag Hassan Anbais², Ashref Ali Erajhi², Petr Pospíšil², Lumír Konečný², Helena Zemanová¹, Jarmila Siegelová²

¹ The Home for Handicapped Children and Young Adults Kociánka, Department of Functional Diagnostics and Rehabilitation, Faculty of Medicine, Masaryk University, St. Anna Teaching Hospital, Brno, CZ

INTRODUCTION

Cerebral palsy is a syndrome characterized by disorder of postural tonus, coordination of movements and senses. It is therefore a sensory motor disease originating on the basis of non-progressive immature brain damage. (1). The syndrome has been existing for many years already in both more and less advanced communities with a relatively constant incidence of 2-5 per mil. The reason of fluctuation in this range has not been reliably demonstrated yet. (2) With regard to the fact that this disease does not reduce substantially the life-span, cerebral palsy is an important social problem. It requires lifelong assistance that is often necessary, costs of repeated orthopaedic operations and compensatory aids, rehabilitation treatment, brings about problems with professional engaging, and last but not least, affects quality of life of the patients. (2,3)

There are many studies monitoring the changes connected with different kinds of both intervening and non intervening therapies. The most frequently evaluated criteria include changes in the base (4,5), range of movements (4), changes in balance (6). The studies monitoring different approaches in the therapy of these patients have controversial results. (7,8,9)

AIM

The aim of the study is to compare possibilities of evaluation of changes of the functional state of children with cerebral palsy by means of the tests: "Gross Motor Function Measure" (GMFM) (10) and 100-point test "Barthel Index" (ADL) evaluating 10 the most important self attendance activities (11, 12). We monitor the functional state change after 6 months and we evaluate the changes for individual groups of patients. The results of the study are preliminary ones.

METHODS

We examined 15children with cerebral palsy at the age 5- 16 years, average age was 11.94 ± 4.12 years. Individual CP forms percentages were as follows: spastic 93 %, non-spastic 7 %, diplegia 47 %, hemiplegia 13 %, quadruplegia 33 %, ataxia 7 %. We used the test Gross Motor Function Measure - GMFM and the test of daily activities Barthel index.

The children were treated by methods of comprehensive rehabilitation using Bobath concept (33.3 %), in some cases exercises on analytic basis (66.6 %) prescribed by their doctor were used.

After 6 months of the prescribed therapy the same examination was repeated.

GMFM test includes evaluation of 88 items divided into 5 sections – 1. lying and rolling, 2. sitting, 3. crawling and kneeling, 4. standing, 5. walking, running and jumping. It evaluates skills of the child in individual items by using a 4-point scale on the quantitative basis. A healthy child at the age of five years should comply with all items. The protocol of the study was approved by the local ethical commission.

Barthel index ADL test evaluates 10 most important self attendance activities. It is used for assessment of the patient's independence. The need of supervising means a certain degree of dependence. We record what the patient is really doing, not what is his potential.

We expressed the results as average values (\pm SD). We evaluated also correlation between the first and the second examinations. We used a Wilcoxon test for paired values for the evaluation of our results.

RESULTS

In the first evaluation by GMFM in children with cerebral palsy as a whole reached the total score from 21 to 97 %, in the second evaluation after 6 months the group in GMFM test reached the score in the range 25- 99 %. The results of the test GMFM1 (before the treatment) showed 58.8 ± 23.1 points and after 6 months GMFM2 showed 63.6 ± 22.8 points, which is statistically significant improvement (p < 0.01).

In ADL test the same group of children with cerebral palsy reached the total score 20-100 %, on average 60 ± 32 %. In ADL test made after six months the total score was 25-100 %, on average 64 ± 31 %; the second measurement was statistically significant (p<0.05). We evaluated several parts of GMFM test, individual items of GMFM tests are in Table 1.

Table 1. GMFM test of children with cerebral palsy in first examination and examination after 6 months in individual items A to E of GMFM (A = lying and rolling, B = sitting, C = crawling and kneeling, D = stand, E = walking, running and jumping)

n = 15	А	В	С	D	Е
1 st examination	63.6±22.8	91.9±8.3	77±25.6	44±40.3	56.8±34.2
2 nd examination	58.8±23.1	93.4±6	78.9±26.2	41.4±39.2	59.4±34.1

The differences in individual items are not statistically significant.

We have not proved an improvement after 6 months in individual items of GMFM test.

Our results showed after the therapy lasting half a year in children with cerebral palsy a statistically significant improvement both in GMFM test and ADL test. Individual items of GMFM were not substantially changed.



Graph No. 1 Correlation between first and second examination using "Gross Motor Function Measure" (GMFM) in the measurement made before and after six months PT treatment

DISCUSSION

Our results in children with cerebral palsy of the scores achieved in individual tests being presented are in accordance with the results of our sample of 30 CP children already published (13), and also with other studies dealing with these problems (10, 11, 12). The test GMFM, compared to Barthel index, proves to be an identically sensitive test evaluating the results after 6-month rehabilitation.

Our study is limited by the fact that the syndrome is non-homogenous, and if we want to form homogenous groups, we are limited by an insufficient number of subjects. Obtaining more valid data means extension of the study to a longer period, which will also enable statistical evaluation of various forms of the disease and different therapeutic methods.

CONCLUSION

After the therapy of children with cerebral palsy, lasting half a year a statistically significant improvement both in GMFM test and ADL test was achieved. Individual items of GMFM were not substantially changed.

Supported by MSM0021622402

LITERATURE

1. Chmelová I. DMO. Zpráva ze semináře. Available from: http://www.mnof.web4u.cz/drs/s20030318/dmo.php

2. Kraus J. a kol. Dětská mozková obrna. Grada. Praha, 2005. ISBN 80-247-1018-8

Jankovský J. Ucelená rehabilitace dětí s tělesným a kombinovaným postižením. Triton.
 Praha, 2006. ISBN: 80-7254-730-5

4. Galarza M., Fowler E.G., Chipps L., Padden T.M., Lazareff J.A. Functional Assessment of Children with Cerebral Palsy Following Limited (L4-S1) Selective Posterior Rhizotomy - A Preliminary Report. Acta neurochirurgica 2001; 143 (9): 865- 872.

5. Lucareli P.R.G., Lima M.O., Lucarelli J.G.A., Lima F.P.S. Changes in joint kinematics in children with cerebral palsy while walking with and without a floor reaction ankle-foot orthosis . Clinics 62, 1. Available from: <u>http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1807-</u> 59322007000100010&lng=eneng&nrm=iso&tlng=eneng

6. Rose J, Wolff DR, Jones VK, Bloch DA, Oehlert JW, Gamble JG. Postural balance in children with cerebral palsy. Dev Med Child Neurol 2002; 44 (1): 58-63.

7. Krigger K. Cerebral Palsy: An Overview. Am Fam Physician 2006; 73: 91-102.

 8. Sankar C., Mundkur N., Cerebral palsy - definition, classification, etiology and early diagnosis. Indian J Pediatr [serial online] 2005; 72: 865-868. Available from: <u>http://www.ijpediatricsindia.org/article.asp?issn=0019-</u> 5456;year=2005;volume=72;issue=10;spage=865;epage=868;aulast=Sankar

9. Tsorlakis N., Evaggelinou C., Grouios G., Tsorbatzoudis C. Effect of intensive neurodevelopmental treatment in gross motor function of children with cerebral palsy. Dev Med Child Neurol 2005; 47 (4):287-289

 Russel D., Rosenbaum P., Gowland C., Hardy S., Lane M., Plews N., Hc Gawin H., Cadman D., Jarvis S. Gross Motor Function Measure Manual. Hamilton: Mc Master University. Second edition 1993, 112.

11. Mahoney FI, Barthel D. Functional evaluation: the Barthel Index. *Maryland State Med Journal* 1965;14:56-61.

12. Masur H. Scales and Scores in Neurology. Quantification of Neurological deficits in Research and Practice. New York: Thieme 2004; s. 392-393.

Drlíková L., Pospíšil P., Konečný L., Chludilová V., Siegelova J., Fišer B., Pochmonova J., Erajhi A.A., Abais F.H., Hashim M.K.A., Al-Fadhli A., Al- Mahmodi N.A.I., Vank P. Functional Impairment in children with cerebral palsy In: Noninvasive methods in cardiology. NCONZO, Brno 2006.

Summary

Introduction: Cerebral palsy is a syndrome connected with immature brain damage. This disease means a serious social and economic problem. There are lots of studies concerned with treatment of cerebral palsied individuals, but their results are dissimilar. Aims: The aim of this study is to compare functional changes using two different methods - Gross Motor Function Measure (GMFM) and Barthel Index (BI). GMFM consists of 88 tasks divided into 5 sections. BI evaluates everyday activities of the patient. Results: We examined 15 children 5-16 years old (average age was 11.94±4.12 years). The percentages of groups of different CP forms were as follows: spastic 93 %, non-spastic 7 %; diplegia 47 %, hemiplegia 13 %, quadruplegia 33 %, ataxia 7 %. The children were treated according to principles of comprehensive rehabilitation treatment (5 of them using Bobath concept, 10 of them with analytic approach). The group was tested before the treatment and after 6 months of the treatment. The correlation between both measurements was high.

Our results showed improvements in both tests, GMFM and ADL, after 6 months lasting rehabilitation treatment.

Key words: cerebral palsy, rehabilitation, functional evaluation, Gross Motor Function Measure, Barthel index

NÁZEV:	NONINVASIVE METHODS IN CARDIOLOGY
EDITOR:	F. HALBERG, T. KENNER, B. FIŠER, J. SIEGELOVÁ
VYDAL	
A VYTISKL:	NÁRODNÍ CENTRUM OŠETŘOVATELSTVÍ A NELÉKAŘSKÝCH ZDRAVOTNICKÝCH OBORŮ V BRNĚ VE SPOLUPRÁCI S MASARYKOVOU UNIVERZITOU BRNO
VYDÁNÍ:	PBVNÍ
	PRVNI
POČET STRAN:	162
VYŠLO:	BRNO 2007
VÝR. ČÍSLO:	82/2007
TIRÁŽNÍ ZNAK:	57-864-07