FAFP2 Pharmaceutical care II

Seminar:
Hyperlipidemia and its management

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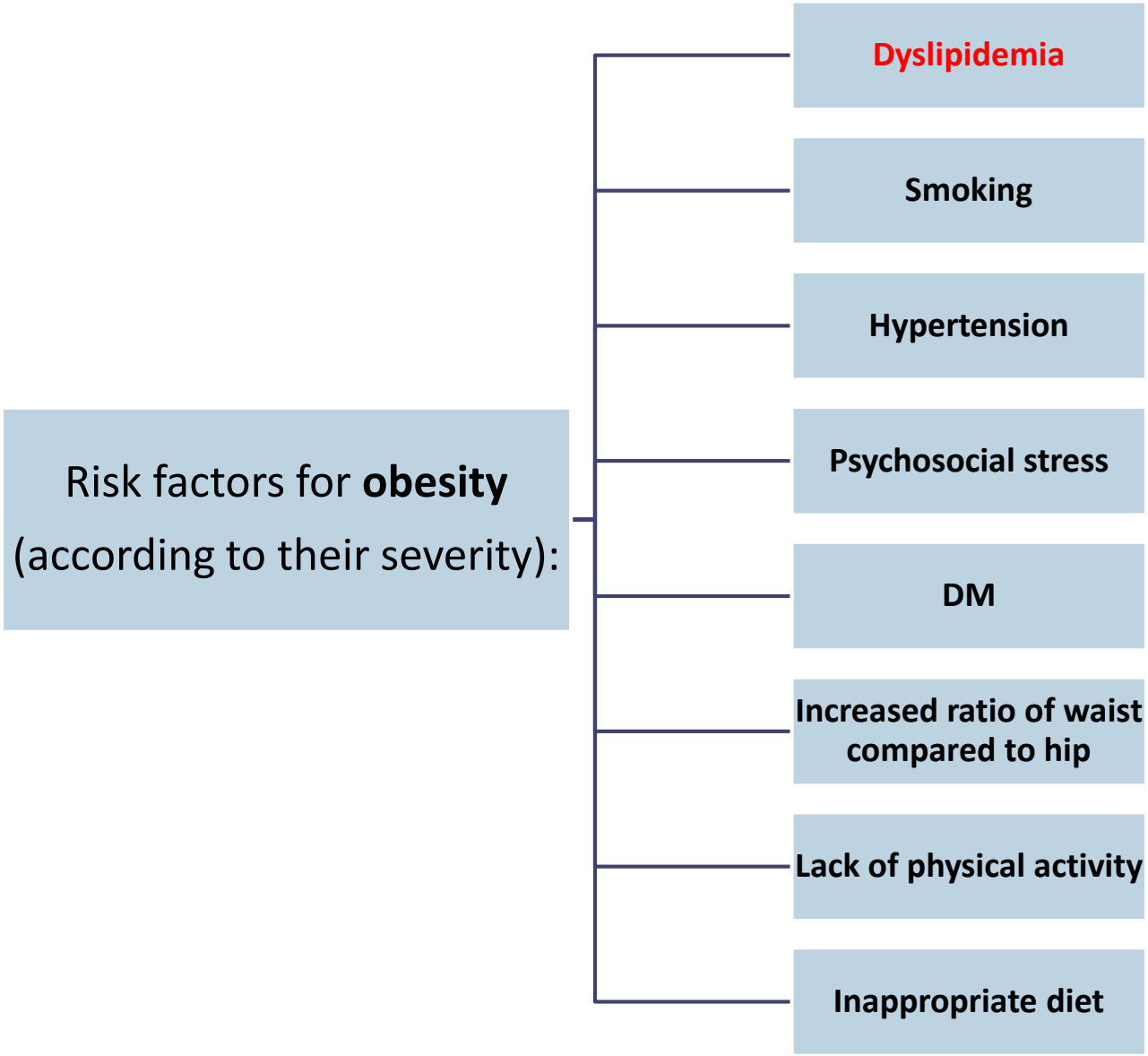
Risk factors for **obesity** (according to their severity):
Dyslipidemia
Smoking
Hypertension
Psychosocial stress
DM
Increased ratio of waist compared to hip
Lack of physical activity
Inappropriate diet

Hyperlipidemia

- cholesterol, triglycerides and phospholipids are trasported as <u>lipoproteins</u>

  - **very low-density lipoproteins** **VLDLs**
  - **low-density lipoproteins** **LDLs**
  - **intermediate density lipoproteins** **IDLs**
  - **high-density lipoproteins** **HDLs**
  - chylomicrons CM

Undesired lipoproteins:	VLDLs, LDLs	→	decrease the levels
Desirable lipoproteins:	HDLs	→	maintain levels

Lipid profile

Parameter	Optimal levels
Total cholesterol	<5.17 mmol/L
Triglycerides	<1.69 mmol/L
LDL-cholesterol	<2.58 mmol/L
HDL-cholesterol	Low >1.03 mmol/L High ≥1.55 mmol/L
Management of hyperlipidemia: - primary outcome of therapy should be to *lower LDL-cholesterol*	
Ideal *LDL:HDL ratio*	< 3 (ratio 4 and more – risk of atherogenesis is high)

Types of hyperlipidemia

Elevated plasma lipoprotein		
Combined hyperlipidemia	**plasma triglycerides >2 mmol/L** and **LDL-cholesterol >3 mmol/L**	occurs as a result of metabolic disorders (e.g. insulin resistence)
Isolated hypercholesterolemia	**LDL-cholesterol**	
Isolated hypertriglyceridemia	**plasma triglycerides**	
These three types can be combined with reduced, normal, or elevated **HDL-cholesterol**		
Familiar hypercholesterolemia	- occurs due to a genetic risk - patients at risk of developing familiar hypercholesterolemia should be monitored, including children - this can lead to early onset of coronary heart disease, atherosklerosis	

Symptoms of hyperlipidemia

- hyperlipidemia does not have any obvious symptoms

- they are usually discovered during routine examination or until it reaches the danger stage of a stroke or heart attack

Complication of hyperlipidemia

- **Atherosclerosis**
  - *accumulation of lipids, cholesterol and calcium*
  - *development of fibrous plaques within the walls of large and medium arteries*

- **Coronary Artery Disease (CAD)**
  - *narrowing of the the arteries that supply blood to the myocardium*
  - *limiting blood flow*
  - *insufficient amounts of oxygen to meet the needs of the heart*

- **Myocardial infarction (MI)**

- **Ischemic stroke**

Conditions that cause secondary hyperlipidaemia

- **Diabetes mellitus**
- **Hypothyroidism**
- **Pregnancy**
- **Alcohol abuse**
- **Chronic renal failure**
- **Hepatocelular disease**
- **Systemic lupus erythematosus**

Drugs with adverse effect to the lipoprotein profile (drugs having obesity effect)

- **Amiodarone**
- **Antipsychotics**
- **Corticosteroids**
- **Beta-blockers**
- **Diuretics**
- **Oral contraceptives**
- **Tamoxifen**
- **PAD**
- **Thyreostatics**

Drugs having antiobesity effect

- **Antidepressants** - bupropion
- **Antiepileptic drugs** - topiramate
- **Psychotropics** - aripiprazole
- **Antihypertensive** - moxonidine
- **Insulin analogue** - detemir (Levemir)

Pharmaceutical Care in Hyperlipidaemia - treatment possibilities

1. **Non-pharmacological recommendations**

2. **Pharmacotheraphy**

3. **Dietary supplements and functional foods for the treatment of dyslipidaemias**

4. **Participating in the screening of patients at risk**

1. Non-pharmacological recommendations

Lifestyle modifications to improve the plasma lipid profile

- **Quitting Smoking**
- **Weight Reduction**
- **Exercise**
- **Moderate alcohol consumption**
- **Diet:**
  - mono-unsaturated fat
  - ω-3 fatty acids - min. 1 g EPA and DHEA daily
  - vit. D - 1000-5000 IU / day

- <u>restrict</u>:
  - saturated fatty acids
  - carbohydrates with a high glycemic index

2. Pharmacotheraphy
STATINS

Effects on lipids:

- Decrease TG
- Decrease LDL-cholesterol - by **25 – 45 %** (depending on dose)
- Increase HDL-cholesterol

Combination theraphy:

Bile acid binding resins (**cholestyramine, colestipol**)

Nicotinic acid

Triple combination

Can also be combined with **fibrates**

Simvastatin

- low price, first choice
- metabolized by CYP-3A4 – high risk of drug interactions!!!

Pravastatin, fluvastatin

- unchanged CYP 3A4 (x simvastatin)
- often in combination with fibrates

Atorvastatin

Rosuvastatin

Pitavastatin

Side effects od statins

Liver

- ALT elevation

Muscle

- rhabdomyolysis - dose related!
- creatine kinase can increase 10 - 40x

Diabetes mellitus

- dysglycaemia and development of DM 2. type
- **benefit > risk** even in patients with current DM or with risk factors for possible emergence of DM

Kidney

Diarrhea

Headache

Gallstones

<u>Statins – contraindications</u>

- liver disease
- pregnancy, lactation

Drugs potentially interacting with statins metabolized by CYP3A4 leading to increased risk of myopathy and rhabdomyolysis

Anti-infective agents	Calcium antagonists	Other
Itraconazole	Verapamil	Ciclosporin
Ketoconazole	Dilthiazem	Danazol
Posaconazole	Amlodipine	Amiodarone
Erythromycin		Ranolazine
Clarithromycin		Grapefruit juice
Telithromycin		Nefazodone
HIV protease inhibitors		Gemfibrozil

FIBRATES

Effects on lipids:

- Decrease TG - by 30 – 50 %
- Little effect on LDL-cholesterol !!
- Increase HDL-cholesterol - by 10 – 15 %

Gemfibrozil

Bezafibrate

The most commonly used: micronized **fenofibrate** dose of 267 mg

EZETIMIBE

Effects on lipids:

- Decrease cholesterol
- Decrease LDL-cholesterol

- cholesterol absorption inhibitor
- inhibits intestinal uptake of dietary and biliary cholesterol without affecting the absorption of fat-soluble nutrients

- advantage:
  - it does not affect CYP 3A4

Combination with statins

NICOTINIC ACID

Effects on lipids:

- Decrease TG - by 20 %
- Decrease LDL-cholesterol - by 20 %
- Increase HDL-cholesterol - by 20 %

so-called „rule of 20 %“

- nicotinic acid derivatives

Fixed dose combination:

niacin + laropiprant

- is recommended in combination with a **statin**

3. Dietary supplements and functional foods for the treatment of dyslipidaemias

Fiber

Insoluble fibre (cellulose, lignin, psyllium)

Soluble fibre (glucomanan, galactomannan, inulin)

preferable for weight loss

Essential adequate intake of **fiber + liquid**!

- **Psyllium** 10-15 g \ day
- **Pectin** 20 to 30 g \ day
- **Glucomanan** 3-4 g \ day

Phytosterols

- sitosterol, campesterol and stigmasterol

- occur naturally in:
  - vegetable oils
  - in smaller amounts in: vegetables, fresh fruits, chestnuts, grains and legumes
  - added to: spreads and vegetable oils (functional margarine, butter and cooking oils), yoghurt and other foods

- the daily consumption of **2 g** of phytosterols can effectively lower TC and LDL-C by 7 – 10 % in humans

Monacolin and red yeast rice

- red yeast rice (RYR) is a source of *fermented pigment* that has been used in China as a food colorant and flavour enhancer

- hypocholesterolaemic effects of RYR are related to monacolins with *statin-like mechanism* - inhibition of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase

Soy protein

- soy protein has been indicated as being able to induce a modest LDL-cholesterol lowering effect when replacing animal protein foods

(this was not confirmed when changes in other dietary components were taken into account)

Dietary supplements and functional foods for the treatment of obesity

Carnitine

- involved in the transfer of **fatty acids** from the cytosol into the mitochondria where they are oxidized

- recommended daily dose: 600 – 4 000 mg daily

- carnitine is found naturally in:
  - **meat and dairy products**
  - other sources: **nuts, cereals and asparagus, broccoli, garlic and other vegetables**

(the effect on weight loss has been not shown enough!)

Coffeine

- **regulation of thermogenesis** - "thermogenic substances“: katechins
- catechins probably inhibit the enzyme system catechol-O-methyltransferase, which reduces synaptic nerve endings in the adipocytes and the process of thermogenesis itself

(real intensity and importance of this mechanism for reducing body weight been not discovered yet!)

Garcinia Cambogia

- hydroxycitric acid:
  - inhibit lipogenesis process
  - reduce the production of cholesterol and fatty acids
  - increases the production of glycogen in the liver
  - suppress appetite
  - increase production of body heat by activating the process of thermogenesis

(real intensity and effect on weight loss insufficiently proven!)

4. Participating in the screening of patients at risk

self-measurement of cholesterol levels – practical training

device: **Accutrend Triglycerides**

- for the key parameters used to detect cardiovascular disease: triglycerides
- device is suitable for professional use as well as for self-testing