Diabetes Mellitus – case studies

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Definition of diabetes (metabolic disorder)

- Chronically raised blood glucose (hyperglycaemia)
- Insulin/Glucagon
  - Insulin is responsible for lowering glucose levels
  - Glucagon is responsible for increasing glucose levels
- Two major subtypes
  - Type 1 diabetes – absolute insulin deficiency (5-15%)
  - Type 2 diabetes – impaired insulin secretion and insulin resistance (85-95%)
    - Prevalence: 8% of population
**Diagnostic criteria**

- **FPG** – fasting plasma glucose
  - DM > 7 mmol/l

- **PPG** – postprandial glucose
  - DM > 11.1 mmol/l

- **HbA1c** – glycated hemoglobin
  - DM ≥ 6.5% (48 mmol/mol)

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<tr>
<th>HbA1c (mmol/mol)</th>
<th>US/studies HbA1c (%)</th>
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Octet of pathogenesis

- Small Intestine: ↓ incretin effect
- Pancreas: ↓ insulin secretion
- Fat Tissue: ↑ lipolysis
- Kidney: ↑ glucose reabsorption
- Liver: ↑ hepatic glucose production
- Brain: Neurotransmitter dysfunction
- Muscle: ↓ glucose uptake

Hyperglycemia


Natural history of type 2 diabetes

Onset of Diabetes Years

Kendall DM, Bergenstal RM ©2003 International Diabetes Center, Minneapolis, MN. All rights reserved.
Macrovascular and microvascular complication of diabetes

Diabetes

Microvascular complications
- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy
- Limb amputation

Macrovascular complications*
- Coronary heart disease
- Ischaemic stroke
- Congestive heart failure

*The most common cause of death in patients with diabetes

Diabetes is a vascular disease

Adapted from Grobbee DE. Metabolism. 2003;52:24-8.
Lowering HbA1c Correlates to a Lower Rate of Cardiovascular Complications

Epidemiological extrapolation showing the potential benefit of a 1% reduction in mean HbA1c on cardiovascular risk factors:

- 21% Deaths related to diabetes*
- 37% Microvascular complications, eg, kidney disease and blindness*
- 14% Heart attack*
- 43% Amputation or fatal peripheral blood vessel disease*
- 12% Stroke**

*P<0.0001  **P=0.035
Stratton 2000
Treatment options

- Metformin – basal treatment
- SU derivates
- Incretins:
  - GLP-1 agonists
  - DPP-4 inhibitors (gliptins)
- SGLT2 inhibitory (gliflozins)
- Pioglitazon
- Repaglinid
- Insulins
Guidelines

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

ENTRY A1c < 7.5%
- MONOTHERAPY
  - Metformin
  - GLP-1 RA
  - DPP4-I
  - AG-I
  - SGLT-2
  - TZD
  - SU/GLN
  * If A1c > 6.5% in 3 months add second drug (Dual Therapy)

ENTRY A1c ≥ 7.5%
- DUAL THERAPY
  - GLP-1 RA
  - DPP4-I
  - TZD
  - SGLT-2
  - Basal insulin
  - Colesevelam
  - BromocriptineQR
  - AG-I
  - SU/GLN
  * If not at goal in 3 months proceed to triple therapy

ENTRY A1c > 9.0%
- TRIPLE THERAPY
  - GLP-1 RA
  - DPP4-I
  - TZD
  - SGLT-2
  - Basal insulin
  - Colesevelam
  - BromocriptineQR
  - AG-I
  - SU/GLN
  * If not at goal in 3 months proceed to or intensify insulin therapy

NO SYMPTOMS
- DUAL THERAPY OR
- TRIPLE THERAPY

SYMPTOMS
- INSULIN OR OTHER AGENTS
  - ADD OR INTENSIFY INSULIN

LEGEND
- Few adverse events or possible benefits
- Use with caution

PROGRESSION OF DISEASE

* Order of medications listed are a suggested hierarchy of usage
** Based upon phase 3 clinical trials data
New/modern drugs

• DPP4 inhibitors (gliptins)
  – Alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin

• GLP1 receptor agonists
  – Exenatide, liraglutide, lixisenatide

• SGLT2 inhibitors (gliflozins)
  – Canagliflozin, dapagliflozin, empagliflozin
Case study 1
– patient with a newly diagnosed type 2 diabetes

Family anamnesis: parents and brother – treated T2D

Personal anamnesis: 75 years, 67 kg, 164cm, hypertensis, after cataract surgery

Current diseases: during autumn 2013 spontaneously lost weight 3 kg/3 month; September 2013 polyuria especially et night hours, after checking with GP hyperglycaemia 19,6 mmol/l – sent to hospitalization in internal medicine

Which testing would you suggest?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Blood tests – glycaemia, liver function tests, lipids, thyroid hormones
  • Hyperglycaemia 19 mmol/l, glycated hemoglobin 127 mmol/mol, slight increase liver function tests, lipids and thyroid hormones normal

• Renal function
  • Mikroalbuminuria 4,0 g/l

• Blood pressure

• Abdominal ultrasound scan
  • Liver steatosis

• Eyes examinations

Which treatment would you suggest?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Intensified insulin regimen (48IU/day)
• Education – lifestyle modification – food and excercise, glycaemia self-monitoring and insulin application, complications of T2D

• There has been a satisfactory compensation of diabetes
  • Weight 60kg, BMI 22,3
  • Fasting plasma glucose 6,7 mmol/l, postprandial glucose 8,9 mmol/l

• What is the next step?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Release into outpatient care

Would you do some additional testing?
What tests?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Concentration of C-peptid

What is the parameter?
What is it says?
Case study 1
– patient with a newly diagnosed type 2 diabetes

Would you change the current treatment?
Why?
How?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Fixed combination of PAD – Janumet 50mg/1 000mg tbl. BID with Glyclada 60 mg BID

What are active ingredients/agents?
Why these drugs?
What is their mechanism of action?
What are their side effects and potential risks?
Case study 1
– patient with a newly diagnosed type 2 diabetes

• Janumet = sitagliptin (DPP-4 inhibitor) + metformin (biguanid)

• Glyclada = gliklazid (sulfonylurea)
Diabetes was compensated:

- Fasting plasma glucose 5,4-6,2 mmol/l and then 4,1-5,2 mmol/l
- Postprandial glucose up to 8,7 mmol/l and then maximally 8 mmol/l
- Glycated hemoglobin 59 mmol/mol

What is the next step?
Case study 1
– patient with a newly diagnosed type 2 diabetes

Withdrawal of sulfonylurea

With adherence to lifestyle fixed combination (DPP4i and metformin) is adequate treatment for diabetes control
Case study 2
– patient with type 1 diabetes

Family anamnesis: father – impaired glucose tolerance

Personal anamnesis: 54 years, 65 kg, 170 cm, HbA1c 7,5%, chronic pancreatitis, T1D diagnosed in 2005, hypertension without treatment, after amputation of the thumb and the second toe of the left foot, stopped smoking 2002

Current diseases: BP 135/85, long-term not-healed defect on left leg – fifth toe, hyperkalemia (6,1 mmol/l), microalbuminuria

What treatment would you suggest?
Case study 2
– patient with type 1 diabetes

• Humulin R 6-8-6 IU + Lantus 8 IU et 7 p.m.

What is the next treatment step?
Case study 2
– patient with type 1 diabetes

• Furon 40mg ½-0-0, Lusopress 20 mg 1-0-0
  • What are this mediactions? Their active ingredient and mechanism of action?

• Vitar soda a NaHCO3 patenteraly
  • What is the cause of hyperkalemia?

• Amputation of the fifth toe + ATB based on culturing + local treatment
Thank you for your attention