Training course: Pharmacotherapy in Older People

Tight glycaemic control is necessary - PRO

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x I have no potential conflict of interest to report
□ I have the following potential conflict(s) of interest to report

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<th>Type of affiliation / financial interest</th>
<th>Name of commercial company</th>
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<td>Participation in a company sponsored speaker’s bureau:</td>
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ESC
Working Group
Cardiovascular Pharmacotherapy
Tight glycemic control is necessary: Three Questions

1. Is tight glycemic control beneficial?
2. Is tight glycemic control dangerous?
3. How tight is necessary?
Type 2 DM
UKPDS

• >4000 pts with newly diagnosed T2DM
• Various interventions, including
  – intensified vs. conventional glucose lowering
• Median age 54 years (IQR 48-60 years)
• Follow-up: 10 years

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33).

UKPDS Study Group Lancet 1998;352: 837
Diabetes-Related Events
UKPDS 33 – Glucose Intervention

10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Rury R. Holman, F.R.C.P., Sanjoy K. Paul, Ph.D., M. Angelyn Bethel, M.D.,
David R. Matthews, F.R.C.P., and H. Andrew W. Neil, F.R.C.P.

ABSTRACT

BACKGROUND

During the United Kingdom Prospective Diabetes Study (UKPDS), patients with type 2 diabetes mellitus who received intensive glucose therapy had a lower risk of microvascular complications than did those receiving conventional dietary therapy. We conducted post-trial monitoring to determine whether this improved glucose control persisted and whether such therapy had a long-term effect on macrovascular outcomes.
UKPDS – Long term follow-up

LEGACY Effect! Patient patients & physicians!

Risks for Macro- and Microangiopathy

- Insulin production
- Postprandial blood glucose
- Fasting blood glucose
- Insulin sensitivity
- Normal course
- Diabetes

Macroangiopathy

Microangiopathy

Metabolic syndrome

Diabetes mellitus

0 10 20 years
Complications in Diabetes

Microangiopathy
Specific for diabetes

Macroangiopathy
Not specific for diabetes, but 3-fold risk
He died with an excellent HbA1c!
Causal?

I am blind because I was neglecting HbA1c.

Two Identical Twins
Our cases today: Two Identical Twins, age 65, British

Harold: only diabetes matters
- Type 2 Diabetes over 20 yrs
- HbA1c 7%
- LDL-C 4 mmol/l, untreated
- Blood pressure 180/105, tx
- Smoker 40 PY
- Dies of MI at age 68
- No microangiopathy

David: only the heart matters
- Type 2 Diabetes over 20 yrs
- HbA1c 10%
- LDL-C 4 mmol/l, Atorva + Ezetimib
- Blood pressure 130/85, treated
- Non-Smoker
- Blind at age 60,
  eGFR 40 ml/min
- Terrible gastroparesis
Type 1 DM: It is the same glucose!
Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes

The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group*
Cumulative Incidence of the First Occurrence of Predefined CV Disease Outcomes

First of Any of the Predefined CV Disease Outcomes

First Occurrence of Nonfatal Myocardial Infarction, Stroke, or Death from CV Disease

Intensive diabetes therapy has long-term beneficial effects on the risk of cardiovascular disease in patients with type 1 diabetes.
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ACCORD: HbA1c lowering

**Figure:**

- **Y-axis:** Glycated Hemoglobin (%)
- **X-axis:** Years
- **Legend:**
  - Standard therapy
  - Intensive therapy

**Table: No. at Risk**

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<th>Years</th>
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<th>Intensive therapy</th>
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ACCORD: Total mortality

No excessive glucose lowering!

P = 0.04

Explanation for the Failure of ACCORD and VADT

1. Up to 5 hypoglycemic drugs!
2. Hypoglycemia?
3. Weight gain?
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The Core Clinical Question: Infraphysiological Goals

No CAVEAT:
→ No J,
→ Goals

CAVEAT: Hypotension
→ Goals

CAVEAT: Hypoglycaemia
→ Goals

Risk

LDL-Cholesterol (mmol/l)

Risk

RR syst (mm Hg)

Risk

HbA1c (%)

Risk

120 130 140 150 160

6 7 8 9 10
A final remark
Prevention of Perinatal Morbidity by Tight Metabolic Control in Gestational Diabetes Mellitus

Tight glycemic control is beneficial for 2!
Conclusions and Summary

1. Tight glycemic control is beneficial for microangiopathy.
2. Tight glycemic control is beneficial for macroangiopathy only on the long-term.
3. Type I and II diabetes share same hyperglycemia!
4. Too tight is dangerous: hypoglycemia, J curve
5. J curve also for blood pressure, but not for LDL-C
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