The interaction between glycemic control and sleep characteristics in patients with type 1 Diabetes Mellitus

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•To determine the effect of hyperglycemic dysregulation on sleep characteristics (duration and quality), in patients with DM1 'What are the effects of controlled hyperglycemia on sleep characteristics (sleep duration and/or quality) in patients...

Ethical review	Approved WMO
Status	Pending
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON34292

Source
ToetsingOnline

Brief title
Interaction between glucoregulation and sleep in patients with DM1

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, glucose metabolism disorders

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Beurs Diabetes Fonds

Intervention

Keyword: Glucoregulation, Sleep characteristics, Type 1 Diabetes Mellitus

Outcome measures

Primary outcome

• Glucoregulation by subcutaneous continuous glucose sensor: i.e. mean night glucose

• Basal postabsorptive glucose metabolism: plasma glucose and insulin levels, endogenous glucose production (EGP), rate of appearance of glucose (Ra), rate of disappearance of glucose (Rd) of glucose measured by infusion of [6,6-2H2] glucose

• Insulin-mediated glucose metabolism by hyperinsulinemic euglycemic clamp technique: endogenous glucose production (EGP), rate of appearance of glucose (Ra), rate of disappearance of glucose (Rd) of glucose measured by infusion of [6,6-2H2] glucose, glucose infusion rate (GIR)

• Indirect calorimetry: resting energy expenditure and respiratory coefficient (RQ), glucose and lipid oxidation rates

• Objective sleep characteristics by polysomnography (PSG) : total sleep time (TST), % REM sleep, % stage 1 sleep, % stage 2 sleep, % stage 3 (SWS) sleep, % wake, apnea-hypopnea index (AHI), heart rate (HR)

• Sympathetic activity by heart rate variability (HRV) by PSG

• Subjective sleep and daytime sleepiness by validated sleep questionnaires

Secondary outcome

• Sleep-wake cycle by Actigraphy

• Diaries: caloric intake, physical activity, actigraphy

•Plasma concentrations: total cholesterol (TC), HDL-C, LDL-C, triglycerides (TG),glucose, insulin, glucagon, free fatty acid (FFA), total glycerol, leptin, cortisol, growth hormone(GH), lactate, isotope enrichment of [6,6-2H2] glucose

Study description

Background summary

Type 1 diabetes mellitus (DM1) is caused by destruction of pancreatic β-cells which results in absolute insulin deficiency. Intensive insulin therapy is essential for optimal glucoregulation, because diabetic complications are determined by the degree of long term hyperglycemia [1]. However, glucoregulation can not be normalized in patients with DM1 despite intensive insulin therapy and/or lifestyle adaption. This is reflected in relatively large variations in blood glucose levels and relatively high HbA1c levels compared to healthy subjects. [2]

Sleep duration and sleep quality are determinants of glucose tolerance:

Normal glucose regulation has a diurnal pattern with variations in glucose tolerance, in which sleep plays a key role. [3] There is a strong relation between sleep duration and glucoregulation. Partial sleep restriction during one or multiple nights induces glucose intolerance and a reduction in the acute insulin response to glucose in healthy volunteers. [4] In accordance, we demonstrated that reduction of sleep duration even for a single night reduced insulin sensitivity by ~20% in both healthy subjects and patients with type 1 Diabetes Mellitus. [5,6]
In addition to sleep duration, sleep quality is another determinant of glucoregulation. Selective suppression of slow wave sleep (SWS) in healthy subjects, without any change in sleep duration, induces marked glucose

intolerance measured by i.v. tolerance test (ivGTT), implying that interference with sleep quality impairs subsequent glucoregulation, probably secondary to increased sympathetic nervous activity. [7] The effects of controlled interference with sleep quality on insulin sensitivity measured by the euglycemic clamp method has not been performed in healthy subjects and patients with DM1.

Metabolic regulation affects sleep quality:

Patients with DM have alterations in sleep characteristics. [8,9] Lamond et al. [10] demonstrated that one-third of the patients with DM report sleep difficulties. Other studies showed that patients with DM2 have more difficulty initiating and maintaining sleep and more excessive daytime sleepiness compared with healthy controls. [11-15]

There are only a few studies on sleep patterns in patients with DM1. Jauch-Chara et al. [16] provided evidence for altered sleep architecture in patients with DM1 under non-hypoglycaemic conditions. These patients showed a tendency toward less deep sleep, with decreased amounts of slow wave sleep (SWS) during the first half of the night.

Conversely, we hypothesize that hyperglycemia in DM1 may also affect sleep characteristics. If this appears to be true, this may induce a vicious circle: metabolic dysregulation impairs sleep characteristics, and, in turn, impaired sleep quality/duration results in insulin resistance and impaired glucose intolerance.

This study aims to investigate the hypothesis :
• Hyperglycemia alters sleep characteristics (i.e. sleep duration and/or quality) in patients with DM1.
• Impaired sleep quality decreases insulin-mediated glucoregulation in healthy subjects and in patients with DM1.

Study objective

•To determine the effect of hyperglycemic dysregulation on sleep characteristics (duration and quality), in patients with DM1
'What are the effects of controlled hyperglycemia on sleep characteristics (sleep duration and/or quality) in patients with DM1?'

•Conversely, to examine the effect of decreased sleep quality on basal and insulin-mediated glucoregulation in healthy subjects and in patients with DM1
' What is the effect of selective suppression of slow wave sleep (SWS) on basal and insulin-mediated glucoregulation in healthy controls and in patients with DM1?'

Study design

Prospective intervention study

Patients with DM1 will participate 4 nights:

•First night: normal sleep with PSG in order to become accustomed to the sleep studies and to exclude patients with sleep disorders
•Normoglycemic night: normoglycemia and normal sleep with PSG to characterize normal sleep characteristics and basal and insulin mediated glucoregulation measured with the hyperinsulinemic euglycemic clamp technique.
•Hyperglycemic night: 50% reduction in basal and bolus insulin infusions to induce a hyperglycemia to assess the effect of hyperglycemia on the sleep characteristics, measured with PSG
•Night with impaired sleep quality: selective suppression of the slow-wave sleep and assess the effect on basal and insulin-mediated glucoregulation measured with the hyperinsulinemic euglycemic clamp technique.

The sequences of nights 2, 3, and 4 will be determined by balanced assignment

The healthy subjects will participate 3 nights:
•First night: normal night with PSG in order to become accustomed to the sleep studies and to exclude subjects with sleep disorders
•Control night: normoglycemia and normal sleep to characterize normal sleep characteristics and the next day subsequent basal and insulin-mediated glucoregulation measured with the hyperinsulinemic euglycemic clamp technique.
•Night with impaired sleep quality: selective suppression of the slow-wave sleep and assess the effect on basal and insulin mediated glucoregulation measured with the hyperglycemic euglycemic clamp technique.

The sequences of nights 2 and 3 will be determined by balanced assignment

Intervention

normoglycemic vs. hyperglycemic condition

normal sleep vs. selective suppression of the slow-wave sleep

Study burden and risks

Burden:

Subjects will sleep 3 (healthy controls) or 4 nights (diabetic patients) in our research centre with polysomnography; of which 2 nights of normal sleep, 1 night with hyperglycemia (only in diabetic patients), 1 night with selective suppression of the slow wave sleep. No adverse events are aspects from this.

Subsequently, the subjects will be in our hospital (after studyday 2, and 4) for 2 whole days. During these days, subjects will lie in bed and blood will be drawn from an infusion.
- Basal experiment: infusion of labeled glucose which is not radioactive en therefore no adverse effects are expected.
- Hyperinsulinemic euglycaemic clamp: infusion of insulin and labeled glucose. Blood glucose measurements will be made at regular time intervals to adjust for glucose infusion and prevent hypoglycemia.

hyperglycemic night: 50% reduction in basal and bolus insulin infusion in order to get and maintain a hyperglycemia with glucose levels between 15 and 20 mmol/L. The blood glucose levels will be carefully evaluated by the research physician during the night. No adverse events are aspects from this.

Halvering van de basale en bolus bolussen van de onderhuidse insuline pomp, waardoor er een hyperglycemie wordt bereikt. Aangezien we de patient goed instrueren om klachten van een hyperglycemie te herkennen, verwachten we geen bijwerkingen. Ook houden we de patient gedurende de gehele nacht goed in de gaten.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Informed consent
DM1 on stable continuous subcutaneous insulin infusion
HbA1c levels <8.0% during the year prior to the start of the study
Non-smoking
Age >18 and <65 years
Coffee <4 U/day
Alcohol <2 U/day

Exclusion criteria

•Presence of sleep disorders determined by validated sleep questionnaires (Pittsburg sleep quality index (PSQI), Epworth Sleepiness scale (ESS), and Berlin Questionnaire (BQ)
•Psychiatric disorders and/or use antipsychotic or antidepressant drugs at present
•Nights shifts within the last 3 months
•Pregnancy
•Chronic use of sleep medication and/or melatonin
•Use of medication known to affect glucose metabolism (e.g. prednisone, beta-blocking agents)
•Use of prokinetic drugs or aspirin
•Renal, hepatic or other endocrine disease
•Traveling across time zones < 4 weeks before the study
•History of cardiac disorders
•Difficulty to insert an intravenous catheter

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2010
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL32246.058.10