Evaluating the relationship between haemodialysis and glucose control in insulin-treated diabetic patients - a pilot study

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Primary objective: to compare glucose profiles collected by CGM on days with and without haemodialysis in a group of insulin treated diabetic patients who are on regular hemodialysis treatment. Secondary objectives: o assessment of frequency and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON39344

Source
ToetsingOnline

Brief title
CGM in DM patients on haemodialysis

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Nephropathies

Synonym
diabetes mellitus, sugar disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Abbott,De firma Abbott BV stelt gebruik van de CGM apparatuur incl. sensoren en Freestyle glucose meters kostenloos ter beschikking van deze studie

Intervention

Keyword: continuous glucose monitoring, diabetes mellitus, haemodialysis

Outcome measures

Primary outcome

Mean glucose concentration and area-under-the-curve (AUC) glucose during

24-hour periods, on days with and without haemodialysis

Secondary outcome

o frequency of glucose < 3.5 mmol/L, < 3.0 mmol/L and < 2.5 mmol/L

o frequency and severity of self-reported symptomatic hypoglycaemia

o correlation between day-to-day variations in physical activity and glucose

levels

o correlation between day-to-day variations in food intake and glucose levels

o elimination rate of insulin and/or glucose during haemodialysis

Study description

Background summary

Diabetes mellitus is a common chronic disease due to insufficiency of insulin secretion and/or increased insulin resistance. Short term complications are hypoglycaemia and hyperglycemia with or without keto-acidosis. Long-term complications can be divided into microvascular (e.g. retinopathy, nephropathy and neuropathy) and macrovascular (e.g. myocardial infarction, cerebrovascular event, peripheral arterial disease) complications. The risk of developing these acute and chronic complications is significantly reduced by optimal glycaemic

control. Diabetes is a major cause of chronic renal failure, and is the underlying disease in about 15% of patients on renal replacement therapy (haemodialysis or peritoneal dialysis). The prognosis of diabetic patients on haemodialysis is extremely poor, with 3-year survival rates of less than 30%. It has been demonstrated that better glycaemic control in diabetic patients on haemodialysis is associated with improved survival rates. However, randomised controlled trials on the impact of intensive glucose control in these patients are very limited.
Little is known about the potential influence of haemodialysis on the glycaemic control in diabetic patients, and available data are inconclusive. It has been suggested that plasma insulin is eliminated by the haemodialysis procedure, resulting in postdialysis hyperglycaemia. In contrast, mean glucose levels were found to be decreased on days with haemodialysis in two recent studies. The risk of postdialysis hypoglycaemia was even increased in one of these studies. Glucose levels in these two studies were measured with a continuous glucose monitoring (CGM) system during 2 or 4 days. CGM is a registered technique for frequent glucose measurements in the subcutaneous interstitial fluid and has the advantage of providing glucose measurements at intervals as short as 1 minute during several days.
The mechanisms behind the reported variations in glucose levels on days with and without a haemodialysis session remain to be elucidated. It is conceivable that haemodialysis may affect glycaemic control either directly (e.g. by eliminating glucose and insulin or changing insulin sensitivity) and/or indirectly (e.g. by interfering with the patients* mobility and food intake). No significant dietary changes were found in the only study examining food intake. Mobility was not monitored in any of these studies. Moreover, the patients studied were heterogeneous with respect to their diabetes treatment, which varied from diet only to oral medication or insulin therapy. Therefore, it is possible that these results are confounded by the heterogeneity of the patient groups studied.
The aim of the present study is to monitor glucose levels by CGM together with food intake and physical activity in insulin treated diabetic patients who are on regular hemodialysis treatment. Glucose monitoring will be performed both on days with and without a haemodialysis session. In addition, insulin pharmacokinetics during haemodialysis will be evaluated in a subgroup of patients. It is expected that the results of this study will contribute to optimizing metabolic control in insulin treated diabetic subjects who are on regular haemodialysis treatment.

Study objective

Primary objective: to compare glucose profiles collected by CGM on days with and without haemodialysis in a group of insulin treated diabetic patients who are on regular hemodialysis treatment.

Secondary objectives:
o assessment of frequency and severity of hypoglycaemic episodes on days with

and without haemodialysis
o describing the relationship between glucose profiles and food intake
o describing the relationship between glucose profiles and physical activity
o examining whether insulin and/or glucose is eliminated by haemodialysis

Study design

Observational invasive study.

Study burden and risks

Participants undergo regular haemodialysis treatment (usually 3 times a week for 3-4 hours). The usual schedule is either Monday-Wednesday-Friday, or Tuesday-Thursday-Saturday.

The following study procedures and tests take place.

Week 1:
o instructions on how to use a pedometer and to keep a structured diary on physical activities by a motion researcher. Pedometer is worn from 7 days before connection of the CGM device until after completion of the 5-day CGM period. The reason for starting the pedometer registration 7 days before the CGM period is to compensate for the novelty effect. New users tend to increase their walking activities during the first days of wearing the pedometer. In general, walking pattern has normalized to baseline values after one week of continued use. The pedometer and diary on physical activities are not applicable to patients who are more or less immobilised as a result of e.g. previous leg amputation or paralysis. In these patients, variations in physical activity are not expected have a significant influence on the recorded glucose profile.
o HbA1c measurement: a limited amount of blood (4 ml) is drawn. This measurement may coincide with the monthly routine laboratory measurements in these patients. In those instances, no additional blood volume is required. In all other cases, a limited amount of blood needs to be drawn. All blood samples are drawn from the fistula, and therefore, venipunctures are not required.
o instruction by dietician on how to keep a structured diary on food intake during the CGM period
o instruction by diabetic nurse on how to record hypoglycaemic events during CGM period
o instruction by diabetic nurse on how to use the Freestyle Navigator®

Week 2:
o connection of the Freestyle Navigator® on day 1 by the diabetic nurse (i.e. Monday or Tuesday).The CGM device is disconnected by the patient 120 hours later (i.e. on Saturday or Sunday, respectively). Connection of the Freestyle Navigator® takes place prior to a haemodialysis session. Consequently, the

patient who usually receives haemodialysis in the afternoon needs to perform one finger stick blood glucose measurement at nighttime for calibration of the CGM device (vide infra). Alternatively, the haemodialysis session on day 1 could be rescheduled to be performed in the morning. The choice between these two options will be left to the patient.
o calibration of CGM device with finger stick blood glucose measurements tests after 1, 2, 10, 24 and 72 h
o daily recording of insulin dose and time of administration (patient diary)
o daily recording of food intake (patient diary)
o daily recording of physical activities (patient diary) and registration of daily number of steps as counted by pedometer
o recording of hypoglycaemic events (patient diary)
o a subgroup of 10 diabetic patients participates in the pharmacokinetics study. Patients are asked in order of inclusion to participate in this pharmacokinetics study, until the required number of 10 patients has been achieved. Blood samples for determination of glucose and insulin will be drawn before, during (at one hour intervals) and directly after one haemodialysis session (4-5 blood samples of 7 ml each simultaneously from the arterial and venous side of the haemodialysis unit = 56 -70 ml in total). Dialysate will be sampled at corresponding time intervals for measurement of glucose concentration (insulin can not be measured as its concentration is below the limit of detection of the insulin immunoassay).

We consider the burden associated with this study limited. No extra study visits are required as instructions and tests are planned during regular hemodialysis sessions. Moreover, the study duration is only 12 days. A maximum of one blood sample (4 ml) is drawn for determination of HbAc. Among the 10 participants of the pharmacokinetics study, blood samples are drawn with a maximal total volume of 70 ml. All blood samples are drawn from the fistula, and therefore, venipunctures are not required. We use a CE approved CGM device. Risks associated with the Freestyle Navigator® are low and include adhesive reaction (2%) and pain or bleeding on sensor insertion (2%). The several diaries are assembled into a single, user-friendly booklet.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- insulin treated diabetes (type 1 or type 2) on haemodialysis
- age 18 years or older
- male or female

Exclusion criteria

- secondary form of diabetes
- use of oral hypoglycaemic drugs
- use of oral/parental glucocorticoids
- inability to understand written and oral instructions in Dutch and to adhere to study protocol

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-11-2010
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	06-07-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20090
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL32332.042.10

Register	ID
OMON	NL-OMON20090