Evaluation of two insulin regimens for control of glucocorticoid induced hyperglycemia during chemotherapy

Published: 12-02-2014
Last updated: 24-04-2024

Primary Objective: Compare achievement of glycemic control in SSI therapy and NPH insulinGlycemic control is defined as the proportion of glucose measurements within target range (Fasting target glucose 3.9 * 7.8 mmol/l. Random target glucose 3.9-10...

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

Summary

ID

NL-OMON41445

Source
ToetsingOnline

Brief title
GLUCON-chemo

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Glucocorticoid induced hyperglycemia, High blood glucose caused by anti-inflammatory medication

Research involving
Human

Sponsors and support

Primary sponsor: Slotervaartziekenhuis

Source(s) of monetary or material Support: stichting klinisch wetenschappelijk onderzoek Slotervaart ziekenhuis.

Intervention

Keyword: chemotherapy, Glucocorticoid induced hyperglycemia, insulin

Outcome measures

Primary outcome

For each subject, we calculate the fraction of glucose measurements within

target range during a chemotherapy cycle (a continuous variable). The mean

difference of this fraction between treatment cycles is the outcome variable.

Secondary outcome

Regarding glycemic control:

o Difference in average daily blood glucose after 24h of treatment

o Difference of proportion of subjects within target range in each treatment

condition

o Difference in average number of blood glucose measurements per treatment day

o Difference in average insulin daily dose per treatment day

o Difference in proportion of measurements above and lower than target range

o Incidence of severe hypoglycemia

Treatment satisfaction: patient preference for treatment regimen in third

chemotherapy cycle

Clinical outcomes: incidence of common (hyperglycemia related) chemotoxicity

o Incidence of oral candidiasis

o Pooled incidence of all G3-4 chemotoxicity

Study description

Background summary

Glucocorticoids are a causative factor for hyperglycemia in patients receiving chemotherapy in malignant disease. Hyperglycemia during chemotherapy is associated with increased chemotoxicity. Especially nonhematologic chemotoxicity is more common in patients who develop hyperglycemia during glucocorticoid containing chemotherapy.
Glucocorticoids are synthetic adrenal glucocorticoid hormones that inhibit pro-inflammatory gene expression. By influencing gene expression, glucocorticoids can induce DNA fragmentation and apoptosis, and are therefore a key element in therapy against hematologic neoplasms. Besides its antineoplastic effects, glucocorticoids are used as an adjuvant in treatment of neoplasm- or therapy-related symptoms like nausea, pain and edema. Depending on the specific neoplasm and chemotherapy, dosing and scheme of glucocorticoids can vary between 10mg till 500mg prednisone-equivalent daily, on a continuous or intermittent base.
Depending on the dose and duration of glucocorticoid therapy, 40-98% of nondiabetic patients on glucocorticoid-containing chemotherapy develop hyperglycemia. In patients diagnosed with diabetes, this rate is even higher. Glucocorticoid induced hyperglycemia (GCIH) has a specific pattern, with normal or near to normal fasting glucose, and pronounced postprandial hyperglycemia. Hyperglycemia is minimal present during night and early morning, probably by suppression of early morning endogenous cortisol peak GCIH may lead to severe glucose excursions, but in most cases glucose levels return to normal when glucocorticoid therapy has finished.
Counteracting acute, GCIH is usually achieved by insulin therapy. Insulin is suitable for acute GCIH because the effect sets in within minutes till hours, depending on the specific type of insulin. Evidence for specific schemes of insulin therapy for GCIH is scarce, and reports are limited to non-randomized or retrospective studies, pilot studies, case-reports and expert opinions. Best described regimens are sliding scale insulin (SSI) therapy and once daily administration of intermediate acting insulin.
In SSI therapy, insulin is dosed according to the current grade of hyperglycemia. Drawbacks of SSI therapy are failure to prevent glucose excursions and thereby high glucose variability. Furthermore, it carries the need for frequent measurements and insulin administrations.

The rationale for the use of intermediate acting insulin in glucocorticoid induced hyperglycemia is based on a parallel in duration of action of intermediate acting insulin and the pattern of glucocorticoid induced

hyperglycemia. Once daily administration of intermediate acting insulin has a duration of action of 14-18 hours. When administered in early morning, concurrent with the morning dose of glucocorticoids, it covers the period from approximately 7:00am untill 21:00pm-1:00am. This period parallels the part of a natural day in which glucose metabolism is mostly affected by glucocorticoid therapy.

In this study, we aim to determine whether intermediate acting basal insulin or SSI results in superior glycemic control during glucocorticoid containing chemotherapy. For this study we will recruit patients with GCIH and prescribe them premeal aspart insulin in a sliding scale regimen and once daily NPH insulin in random order during consecutive cycles of chemotherapy. Besides our primary objective of glycemic control, we compare safety, patient satisfaction and clinical outcomes between the two treatment strategies.

Study objective

Primary Objective:
Compare achievement of glycemic control in SSI therapy and NPH insulin

Glycemic control is defined as the proportion of glucose measurements within target range (Fasting target glucose 3.9 * 7.8 mmol/l. Random target glucose 3.9-10 mmol/l) after 24h of treatment

As a secondary objective, we compare patient satisfaction, clinical outcomes and toxicity.

Study design

Randomized open label cross-over study.
Subjects will be consecutively treated by NPH insulin once daily and by short acting insulin in a sliding scale regimen. The order of the treatment regimens will be determined by randomization.

Intervention

Subjects will be consecutively treated by (A) NPH insulin once daily and by (B) short acting insulin in a sliding scale regimen. The order of the treatment regimens will be determined by randomization.

Dosing of NPH (A)
0.01 IU insulin per mg prednison-equivalent per kg bodyweight, with a dose reduction of 40% in case of age >70years old or kidney failure (eGFR < 60ml/min)

Dosing of short acting sliding scale insulin (B)
capillary glucose 7.8-12 mmol/l --> 2 supplemental units of short acting insulin

capillary glucose 12.1-17 mmol/l --> 4 supplemental units of short acting insulin
capillary glucose *17.1 mmol/l --> 6 supplemental units of short acting insulin

Study burden and risks

Both study treatments are currently already prescribed in regular care for glucocorticoid induced hyperglycemia. Glycemic control is likely to improve due to treatments and increased counselling. All subjects will receive both treatment regimens.
The burden of participation consists of 1 venipuncture (only if HbA1c and creatinin are not determined in routine laboratory within 3 months before start of study treatment), and 1 randomization visit to the outpatient clinic (we try to schedule the randomization visit subsequent to a regular visit to the outpatient clinic). Potential risk is the occurrence of hypoglycemia, as is present in any (new or adjusted) insulin therapy. We will account for this risk by supplying all subjects with dietary advice, and education how to prevent, recognize and treat hypoglycemia.

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

- Glucocorticoid induced hyperglycemia in previous cycle of chemotherapy that required therapy initiation or adjustment
- Duration of glucocorticoid cycles 4-10 consecutive days and * 4 glucocorticoid-free days between 2 cycles
- Age * 18 years & written informed consent
- Prednisone-equivalent dose of * 12,5mg
- At least 2 more cycles of chemotherapy to receive

Exclusion criteria

history of hypo-unawareness, continuous tube or parental feeding, continuous (maintenance) systemic glucocorticoid therapy

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-06-2014

Enrollment:	26
Type:	Actual

Ethics review

Approved WMO Date:	12-02-2014
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	18-04-2014
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	22-04-2014
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	21-11-2014
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	12-01-2015
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)

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	NL47135.048.13

Study results

Date completed:	23-02-2016
Results posted:	23-02-2016
Actual enrolment:	26

First publication
01-01-1900