Glucose lowering by continuous tube feeding and Vildagliptin in addition to insulin in hyperglycemic acute stroke patients.

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To optimize glycemic control in acute ischemic stroke patients.

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

Summary

ID

NL-OMON33687

Source
ToetsingOnline

Brief title
GLUCOVAS

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Central nervous system vascular disorders

Synonym
cerebral infarction, glucose control, stroke; high glucose

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Novartis

Intervention

Keyword: acuut ischemic stroke, glucose regulation, hyperglycemia

Outcome measures

Primary outcome

The study has two primary endpoints

• 1) Glycemic control.

a) Mean glucose throughout protocol treatment

b) Percentage of time spent within target range.

• 2) Hypoglycemia

a) The total number of hypoglycemic events per group.

Hypoglycemia will be defined as any glucose value below 3.5 mmol/L.

b) Number of of serious hypoglycemic events (glucose value below 2.2

mmol/L)

c) Number of symptomatic confirmed events.

Secondary outcome

• Clinical outcome:

o Modified Rankin Score at three months follow-up (see appendix IV).

• Occurrence of pneumonia

• Treatment data:

o Total insulin dose U/dy en U/kg/dy

o Total amount of tube feeding administered

o Number of sensors inserted per patient

o Coefficient of Variation of CGMS derived glucose values

o Accuracy of FreeStyle Navigator, expressed as Mean Absolute Difference vs.

verification samples

Study description

Background summary

Post stroke hyperglycemia (HG) has been reported to negatively influence cerebral infarction size, and clinical outcome in several series. In non-stroke medical emergencies, prolonged treatment of HG with intensive insulin therapy greatly reduces mortality in patients with acute myocardial infarction, in intensive care patients and in patients undergoing coronary artery bypass grafting. One randomized control trial has investigated the use of intensive insulin therapy for HG in acute stroke, but no clinical effect was demonstrated. Glycemic control in this trial, however, was poor and glycemic control was continued for 24h only. We and others have reported previously that effective glycemic control in stroke patients is not easy to accomplish. Especially postprandial glucoses surges appeared difficult to control for. In a subsequent study, we subjected ischemic stroke patients to tight glycemic control (TGC) regime. This regime consisted in (i) continuous tube feeding; (ii) a more stringent insulin treatment algorithm with an increased number of glucose assessments, and (iii) a web-based program to assist nursing staff in the execution of the algorithm. With this regime, including ten patients, we were able to effectively maintain glucose values within a low physiological range (below 6.1 mmol/L) for five consecutive days on a regular stroke unit. This study had two drawbacks, however. First, TGC was accompanied by an increased number of hypoglycemic episodes compared to normoglycemic or hyperglycemic controls. Second, though inherent to the protocol design, patients were subjected to continuous tube feeding (irrespective of the ability to swallow) and to a high frequency of glucose assessments.
Continuous Glucose Monitoring Systems (CGM), which have recently become available for clinical use, has the potential to improve glycemic control as glucose levels out of target range (both high and low) can be anticipated much faster.
Another interesting option is the addition of the selective inhibitor of dipeptidyl peptidase-IV (DPP-4) vildagliptin (Galvus) to our treatment protocol. It has been shown that addition of vildagliptin to insulin therapy is associated with a reduction in HbA1c as well as a 30% reduction in hypoglycemia.

Study objective

To optimize glycemic control in acute ischemic stroke patients.

Study design

This is a multi centre factorial randomised one arm open and one arm placebo controlled trial.

Intervention

continuous tube feeding (vs. regular feeding)

Vildagliptin (vs. placebo)

IV insulin (all patients)

continuous glucose measurement (all patients)

Study burden and risks

Hypoglycemia
The main side effect of intensive insulin therapy is hypoglycemia. Mild hypoglycemia for a short period
does not cause any damage in healthy individuals. Prolonged severe hypoglycemia caused by excessive
insulin administration in normal individuals can cause neurological damage leading to convulsions, coma
and death. Convulsions and coma can be seen in normal human subjects with plasma glucose levels lower
than 1.5 mmol/l.
The first physiological response of the body during hypoglycemia is the inhibition of insulin release
followed by an increase in glucagon release and other counterregulatory hormones. Autonomic symptoms
such as anxiety, pallor, palpitations, restlessness, perspiration, tachycardia, tremor and warmth, emerge
at plasma glucose levels below 3.2 mmol/l. Neuroglycopenic symptoms such as confusion, drowsiness,
fatigue, inability to concentrate, irritability, lack of muscular coordination, lightheadedness, paresthesia,
personality change, slurred speech and weakness follow if plasma glucose drops below 2,8 mmol/l. These
symptoms and the autonomic symptoms are reversible.
Fingerprick:Periodic fingerpricks to control for glucsose values could be inconvenient. During first 24 hrs
patients will be monitored for viatal signs each our as in standard care. Fingerpricks will be intergrated in
these moments as much as possible.
Enteral tube feeding.
Patients can experience enteral tube feeding as incomfortable. Diarrhea and local skin infections have

been reported.

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

1) Supra-tentorial stroke with a time of onset within 24h before presentation.
2) An acute neurological deficit measurable with the National Institute of Health Stroke Score (NIHSS, see appendix I) >= 4 at presentation.
3) Venous plasma admission glucose > 7.0 mmol/l
4) Informed consent.

Exclusion criteria

1) Signs of cerebral hemorrhage on computed tomography scan
2) Previous history of diabetes mellitus treated with insulin
3) Patients in whom death appears imminent
4) Renal insufficiency defined as creatinine > 150 mmol/L
5) Patients under the age of 18
6) Pregnant patients
7) Expected transfer to a different hospital within 5 days.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2009
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Galvus
Generic name:	Vildagliptin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-04-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2008-007020-25-NL
CCMO	NL26099.018.08