Reproducibility of insulin injected by needle-free jet-injection for glycaemic management in healthy volunteers

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1. To compare the pharmacologic reproducibility of the rapid-acting insulin analogue aspart (Novorapid®) injected by jet-injection to that of the same insulin injected with a conventional pen. 2. To compare pharmacokinetic and -dynamic profile of...

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

Summary

ID

NL-OMON41800

Source
ToetsingOnline

Brief title
reproducibility of insulin by jet injection

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: European Pharma Group

Intervention

Keyword: aspart insulin, jet injection, pharmacology

Outcome measures

Primary outcome

Primary study in main study: the variability in glucose lowering effect as

reflected by the exogenous glucose requirement over four hours.

Primary study endpoint in sub-study: time to maximal glucose requirement.

Secondary outcome

Secondary study endpoints in main study include: variability of insulin

absorption over four hours; times to peak insulin level and to maximal glucose

requirement, safety and tolerability.

Secondary endpoints in sub-study include: time to peak insulin level, peak

insulin level, maximal glucose requirement, safety and tolerability.

Study description

Background summary

Using a specific jet injector for the administration of a rapid-acting insulin analogue has been shown to advance the absorption of insulin from the subcutaneous area into the bloodstream by 40-50%, when compared to conventional injection by insulin pens. The reproducibility of the jet stream method has not been previously determined in vivo. It is also unknown how the efficacy of injecting regular insulin by jet stream compares to that of rapid-acting analogues injected by conventional pen. We also hypothesize that the metabolic effect of soluble insulin administered by jet injection is similar to that of insulin aspart administered by conventional insulin pen. This is important because rapid acting insulin analogs are not worldwide available but are very important in maintaining stable blood glucose values and preventing diabetic complications.

Study objective

1. To compare the pharmacologic reproducibility of the rapid-acting insulin analogue aspart (Novorapid®) injected by jet-injection to that of the same insulin injected with a conventional pen.
2. To compare pharmacokinetic and -dynamic profile of regular insulin injected by jet injection to that of aspart insulin injected by conventional pen.

Study design

Double-blind double-dummy randomized controlled parallel/cross-over study

Intervention

All subjects will participate to two identical study days, after being randomized to the jet injector (J-I) study-arm or the conventional pen (C-P) study-arm. Subjects randomized to J-I will receive a standardized dose of aspart insulin subcutaneously by jet injection and a placebo administration (injection with a pen identical to a conventional pen but without actual contents) by conventional pen. Subsequently, glucose 20% will be given intravenously to maintain plasma glucose at fasting levels (normoglycemic clamp). Those randomized to C-P will receive the dose of aspart by conventional pen and the placebo administration by jet injection. The pharmacokinetic and pharmacodynamic profile of insulin aspart will be derived from the time-action profiles of plasma insulin levels and glucose requirements, respectively. Within-subject variability will be calculated for the pharmacokinetic and -dynamic profiles for both administration routes. All subjects will be asked to participate to one additional clamp study until 20 subjects have been enrolled, during which regular insulin will be administered by jet injection. The pharmacological profile will be compared to the profile obtained in patients randomized to C-P and obtained in a previous study.

Study burden and risks

All participants will undergo a standard physical examination to determine eligibility. For each experiment, two cannulae will be inserted intravenously, one for blood sampling, the other for glucose 20% as needed to maintain normoglycemia after insulin injection. A total of 148 ml of blood will be drawn during each experiment for laboratory measurements, i.e. 296 ml for two experiments or 444 ml for three experiments. The risk of hypoglycemia after insulin injection is negligible since plasma glucose levels will be measured at 5-10-min intervals and glucose will be infused should plasma glucose levels (tend to) fall below 4.8 mmol/l. Intravenous glucose may cause local irritation and occasionally phlebitis.

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

• Age 18-50 years
• Body-Mass Index 18-32 kg/m2
• Blood pressure <160/90 mmHg

Exclusion criteria

• Inability to provide informed consent
• Chronic use of medication other than oral contraceptives or thyroid hormone replacement therapy (with stable euthyroidism for at least 3 months)
• Treatment with systemic corticosteroids, immunosuppressive or cytostatic drugs
• Known allergy to aspart insulin

• History of a major cardiovascular disease event (myocardial infarction, stroke, symptomatic peripheral artery disease, coronary bypass surgery, percutaneous coronary or peripheral artery angioplasty) in the previous 6 months
• Presence of any other medical condition that might interfere with the study protocol
• Pregnancy or the intention to become pregnant
• Anemia, defined as an Hb of <8.1 mmol/l for male subjects and <7.5 for female subjects

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:	Recruitment stopped
Start date (anticipated):	23-01-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Insujet (jet injector)
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-01-2015
Application type:	First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL50999.091.14