Pharmacokinetics and Pharmacodynamics of metformin in patients with type 2 diabetes and renal impairment

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON38577

Source
ToetsingOnline

Brief title
Metformin in diabetic nephropathy

Condition

- Diabetic complications

Synonym
Diabetic Nephropathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Diabetic Nephropathy, Metformin, Pharmacodynamics, Pharmacokinetics

Outcome measures

Primary outcome

Main study parameters/endpoints: The main study parameter is the correlation between the plasma concentration and pharmacokinetic parameters of metformin with Hba1c% in patients with type 2 diabetes and eGFR<60 ml/min/1.73m2.

Secondary outcome

• Correlation of pharmacokinetic parameters and plasma concentration of metformin with lactic acid

• Correlate plasma concentrations of metformin with renal function (eGFR) in patients with type 2 diabetes and eGFR < 60 ml/min/1.73m2

• Correlate red blood cell concentrations of metformin with renal function (eGFR) in patients with type 2 diabetes and eGFR < 60 ml/min/1.73m2

• within-person day-to-day variability in plasma metformin concentration and pharmacokinetic parameters

• Correlate pharmacogenetic polymorphisms with metformin pharmacokinetics and pharmacodynamics in patients with type 2 diabetes and eGFR <60 ml/min/1.73m2

Study description

Background summary

Metformin is largely excreted unchanged in the urine and, consequently, its dosage should be reduced in renal impairment or metformin should be

discontinued in order to avoid metformin toxicity with possible life-threatening lactic acidosis. In clinical practice, metformin is prescribed in many patients with diabetic nephropathy. Current clinical practice guidelines recommend discontinuation of metformin when kidney function falls below 60 ml/min/1.73m2. The basis for this guideline is poorly developed and well conducted studies on the balance of benefits and risks in this population are lacking.

Study objective

The objective of the proposed study is to develop techniques for optimizing the dosage of metformin through measurement of the concentrations of the drug in plasma or red blood cells and the concentration of haemoglobin A1c in patients with diabetes and nephropathy and to correlate plasma metformin concentrations and pharmacokinetic parameters with Hba1c and lactic acid levels. The ultimate objective is to develop a dosage table which provides a reasonable initial guide to prescribe metformin.

Study design

Observational study

Study burden and risks

Results of this study can contribute to practical decision rules and dosing schedules for metformin in patients with diabetic nephropathy. The first blood sample will be collected at the regular visit of the patient when blood is already drawn for clinical laboratory parameters. The extra blood sample and 24-hour urine that is needed for this pharmacokinetic study outweigh the potential benefits of improving dosing schedules for metformin.

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 years
•Patients prescribed metformin for at least 2 days
•eGFR > 15 ml/min/1.73m2
•Willing to provide informed consent

Exclusion criteria

•Need for chronic hemodialysis
•Presence of severe debilitating illness at the discretion of the treating physician
•Donation of blood to the blood bank in prior 3 months
•Veins not suitable for venepuncture

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-11-2013
Enrollment:	110
Type:	Actual

Ethics review

Approved WMO

Date:	18-11-2013
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
CCMO	NL43847.042.13