Effect of mild diarrhea on tacrolimus exposure

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Primary objective: To assess the degree of tacrolimus over-exposure in renal transplant patients with mild diarrhea while on treatment with tacrolimus and mycophenolate mofetil.Secondary objective: To assess the intra-individual variability of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational non invasive

Summary

ID

NL-OMON32863

Source
ToetsingOnline

Brief title
Diarrhea and tacrolimus exposure

Condition

- Renal disorders (excl nephropathies)

Synonym
renal transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Een onderzoeksgrant van de firma Novartis; het betreft echter een investigator-driven studie

Intervention

Keyword: Diarrhea, Mycophenolate mofetil, Pharmacokinetics, Tacrolimus

Outcome measures

Primary outcome

Difference in the ratio AUC:trough level of tacrolimus between subjects with

mild diarrhea and controls.

Secondary outcome

Correlation between two measurements of ratio AUC:trough level of tacrolimus in

the same subject.

Study description

Background summary

Diarrhea is a frequent adverse event in patients treated with the combination of tacrolimus and mycophenolate mofetil and has an important impact on the pharmacokinetics of tacrolimus. In case of severe diarrhea, the exposure to tacrolimus can be increased several fold and is reflected in a substantial increase in trough levels. Mild diarrhea (2-3 stools per day) is more common and not always reported to the treating physician. In these cases, an increase in the total tacrolimus exposure may not be accompanied by a marked increase in tacrolimus trough levels. Consequently, ongoing mild diarrhea may result in unnoticed chronic tacrolimus overexposure leading to irreversible nephrotoxicity.

Study objective

Primary objective: To assess the degree of tacrolimus over-exposure in renal transplant patients with mild diarrhea while on treatment with tacrolimus and mycophenolate mofetil.
Secondary objective: To assess the intra-individual variability of tacrolimus pharmacokinetics.

Study design

Cross-sectional study with measurement of tacrolimus pharmacokinetics on two

occasions in subjects with mild diarrhea and in an equal number of controls with normal stools.

Study burden and risks

The pharmacokinetics of tacrolimus will be measured on two separate days. At each day blood samples will be collected just before and 1, 2, 4, 6 and 9 hours after oral intake. Participants will be asked to remain fasted until two hours after intake of tacrolimus. For blood sampling a dried blood spot method which includes finger pricks will be used. This method allows that participants take their own blood samples at home and send the dried blood spot samples to the hospital. Participants will receive training for using this method during a regular control visit to the hospital. During the training visit participants will also complete two questionnaires concerning gastro-intestinal symptoms, which will take about 20 minutes. The participation with this study does not require additional examinations or hospital visits. Adverse effects are not expected.

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. Recipient of a renal graft
2. Age: 18 years or older
3. Informed consent
4. At least 2 months after renal transplantation
5. Treatment with the combination of tacrolimus and MMF
6. Tacrolimus trough levels within the target range (5-10 ng/ml) at two subsequent occasions.
Cases: Average stool frequency 2-3 times/day OR unbound stools during last two weeks prior to inclusion.
Controls: Average stool frequency 1 time/day or less AND normal consistency of stools during last two weeks prior to inclusion.

Exclusion criteria

1. History of bowel resection
2. Severe diarrhea (> 3 stools per day)
3. Rectal blood loss
4. Signs of active CMV infection
5. Change in tacrolimus dosage within one week prior to inclusion

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-05-2010
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	08-09-2009
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	NL29414.091.09