Plasma oxalic acid level, renal oxalate deposition and renal transplant function

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Primary Objective: * Study the relationship between the pre-transplant plasma oxalic acid level and the risk of oxalate deposition in for cause renal transplant biopsies within 6 months after renal transplantation. Secondary Objective(s): * Track...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON46583

Source
ToetsingOnline

Brief title
Oxalic acid trial

Condition

- Other condition
- Appetite and general nutritional disorders
- Urolithiases

Synonym
secondary hyperoxaluria - renal stone disease

Health condition

nierinsufficiëntie, niertransplantatie

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting de Merel

Intervention

Keyword: kidney graft function, oxalate deposition, plasma oxalic acid level, Renal transplantation

Outcome measures

Primary outcome

Relationship between pre transplant oxalic acid levels and Oxalate deposition

in for cause renal allograft biopsies taken within 6 months after renal

transplantation

Secondary outcome

Renal graft and patient survival in patients divided in tertiles according to

pre transplant oxalic acid levels.

Relationship between oxalic acid in diet and type and intensity of renal

replacement therapy on one hand and pre transplant oxalic acid level and renal

graft survival on the other.

Study description

Background summary

Primary hyperoxaluria is an inborn metabolic disorder and is characterized by overproduction of oxalic acid, which precipitates as oxalate in various organs, especially in the kidney because this is the organ responsible for excretion of oxalix acid. It always leads to renal insufficiency. Secondary hyperoxaluria may be by caused by increased absorption as in gastro-intestinal disorders or by decreased excretion as in renal insufficiency. Hemodialysis patients may have very high oxalic acid levels: levels as high as those of patients with primary hyperoxaluria can be found. Dialysis can decrease the level but

normalization is not achieved. Moreover, within 48 hours after dialysis the level returns to pre-dialysis values. After renal transplantation the new kidney graft starts to excrete oxalic acid and very high concentrations of oxalic acid can be found in the urine. This may lead to oxalate deposition and renal graft function deterioration or even loss.
In patientes with secundary hyperoxaluria because of gastro-intestinal disease (besides their renal insufficiency), graft survival is known to be very bad and in many centres these patients are declined for transplantation. Ten of these patients have recently been transplanted in our centre with a protocol that aimed at lowering pre-transplant oxalic acid levels by intensive hemodialysis and low-oxalic acid diet. All were succesfull.
In a population of patients transplanted in the Erasmus MC in 2014-2015 we studied all for cause kidney biopsies for the presence of oxalate crystals within 3 months after kidney transplantation. 388 patients had been transplanted during that period of whom 149 had had a kidney biopsy. Oxalate crystals were present in 26 patients (17%) with a kidney biopsy. The patients without a biopsy had the best graft survival (1% had failed after 1 year), patients with a biopsy without oxalate functioned in between (8% of the kidneys had failed after 2 years). Patients with oxalate in their biopsy had the worst transplant survival (After 2 years, 30% of the kidneys had failed) (resp p=0.001 and p=0.018 compared to both other groups). The role of plasma and urine oxalic acid levels is unknown because they were not determined. Our present study aims at the relationship between oxalic acid levels before kidney transplantation and the occurrence of oxalate deposits in the kidney and decreased renal transplant survival. If high levels at transplantation play a role, measures to decrease these levels pre transplantation in order to prevent unnecessary loss of transplant kidneys may be indicated. This can easily be realized by re-institution of hemodialysis treatment shortly before transplantation to decrease levels. Over the years, the indications for dialysis shortly before transplantation have been liberated and it occurs that patients* last dialysis session was a few days before transplantation. In that period, the plasma oxalic acid could have risen considerably. Simple measures for improvement could consist of dialysis shortly before transplantation (a few hours) possibly combined with oxalic acid-restricted diet before transplantation.

Study objective

Primary Objective:
* Study the relationship between the pre-transplant plasma oxalic acid level and the risk of oxalate deposition in for cause renal transplant biopsies within 6 months after renal transplantation.
Secondary Objective(s):
* Track down the relationship between oxalic acid intake and dialysis status on the one hand and plasma oxalic acid levels on the other.
* Study the relationship between the pre-transplant plasma oxalic acid level and graft function and graft loss at 6 months and at 1 year after renal

transplantation.
Study the relationship between oxalate deposition in the graft and graft function and graft loss at 6 months and at 1 year after renal transplantation.
* The aim is therefore to evaluate the indication for oxalic acid lowering therapy shortly before transplantation.

Study design

This is an observational cohort study.
On the day of transplantation the patient will be asked to fill in a questionnaire on renal function replacement therapy and on food habits (oxalic acid content).
Shortly before transplantation (1-2 hours) 1 blood sample will be drawn to determine plasma oxalic acid value in a cohort of patients. In a small part of patients, where renal function is delayed and dialysis will be restarted after transplantation, another blood sample will be taken before start dialysis.
The relationship will be studied between the value of oxalic acid and post transplant oxalate deposition in the kidneys with for cause renal transplant biopsy within 6 months after transplantation. It will also be correlated to renal function and graft survival at 6 months and 1 year after transplantation.
A subsidy for determination of 400 samples was obtained. The number of patients that will be included depends on the number of patients that need 2 oxalic acid determinations (delayed graft function occurs in roughly 5% of patients). Between 275-325 patients can be included than.

Study burden and risks

Inclusion will be performed in the pre transplant outpatient setting.
The study actions will be performed during admission for transplantation. On the day of/before transplantation a questionnaire must be filled in (about 25 minutes)
One hour before transplantation 10 cc blood will be drawn while the patient is already in the operating room.
In patients in whom dialysis has to be re started during admission for transplantation another one-time 10 cc blood sample will be drawn for oxalic acid determination.

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

All patients that receive a renal transplant in our center are eligible

Exclusion criteria

Patients refuse to participate

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-08-2018
Enrollment:	375
Type:	Actual

Ethics review

Approved WMO Date:	30-03-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL64618.078.18