Assessment of sympathetic reinnervation of the kidney allograft with 123I-MIBG scintigraphy. (RENnervate study).

Published: 15-05-2013
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To assess renal sympathetic reinnervation in the kidney allograft by 123-I-MIBG scintigraphy.

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

Summary

ID

NL-OMON39698

Source
ToetsingOnline

Brief title
RENnervate study

Condition

- Renal disorders (excl nephropathies)

Synonym
Regrowth of sympathetic nerves in the transplanted kidney

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 123-MIBG scintigraphy, kidney transplantation, reinnervation

Outcome measures

Primary outcome

To compare allograft sympathetic reinnervation by 123I-MIBG washout rates

between patients with a recent transplantation (6-18 months), patients with an

allograft in situ for > 4* and <7 years and patients who have a kidney

transplantant >10 years.

Secondary outcome

not applicable

Study description

Background summary

A number of renal transplant recipients have excellent functioning grafts for many years after transplantation. Most obvious this is due to immunological factors, infection rates and comorbidity. However, it is unclear whether renal nerve regrowth in the allograft might influence graft survival. Due to the explantation process, the renal allograft is entirely denervated at time of transplantation.
In years after transplantation, it is unknown to what extend and when regeneration of renal sympathetic nerves after transplantation occurs.

Assessment of the sympathetic nerve activity (SNA) can be determined by peroneus microneurography or catecholamine levels in plasma. However, these methods are indirect, invasive and impractical and do not supply information about regional sympathetic nerve activity.
123I-metaiodobenzylguanidine (123I-MIBG) is a radio-labeled analogue of noradrenaline and is taken up by presynaptic nor-adrenaline transporters and thereby it can provide an estimate of sympathetic activity. 123I-MIBG scintigraphy has shown to offer prognostic information in patients with heart failure.
Since kidney transplantation is the only durable therapy for end stage renal disease, allograft nephropathy remains an important clinical problem. Various

lines of evidence suggest that sympathetic denervation of the allograft plays a role in the pathogenesis of allograft nephropathy.
Due to the explantation process, the renal allograft is entirely denervated at time of transplantation. There is histological evidence that after transplantation there is re-innervation of the allograft. However, up to 2,5 years after transplantation such reinnervation has been shown not to be of functional significance. Reinnervation is a potential therapeutic aim to prevent allograft nephropathy.
We hypothesize that allograft sympathetic reinnervation is a slow process which takes >10 years to reach functional capacity.

If there is a >7.5% difference in washout-rate n the kidney graft compared to the mediastinum, we assume that this implicates reinnervation of the graft. We assume that if renal re-innervation occurs, 123I-MIBG uptake will be higher in patients with an older renal allograft compared to recent transplanted allografts that show decreased or lack of 123I-MIBG uptake.Therefore, patients with a graft in situ for > 10 years will be studied initially.A negative control group is studied, consisting of n=6 oliguric/anuric patients 0-6 weeks after kidney transplantation with one or both native kidneys in situ.

Study objective

To assess renal sympathetic reinnervation in the kidney allograft by 123-I-MIBG scintigraphy.

Study design

We propose an observational pilot study with n=6 renal transplant patients with a functioning allograft in situ for 6-18 months, n=6 kidney transplant patients with an allograft for > 4* but <7 years in situ and n=6 with their allograft in situ >10 years and a negative control group is studied consisting of n=6 oliguric/anuric patients 0-6 weeks after kidney transplantation with one or both native kidneys in situ.

All patients will undergo 123I-MIBG scintigraphy. They will receive 185 MBq of 123I-MIBG intravenously.
Subsequently at 15 min and 4 hrs and 24 hours post injection planar images are made in combination with SPECT at 4 an 24 hours post injection. The SPECT acquisition is combined with a low dose CT-scan of the abdomen (without intravenous contrast) to relate the 123I-MIBG uptake to anatomical structures.
All six patients with a graft in situ for > 10 years will be studied initially.

Study burden and risks

- The risk of the venous canulation (for the 123I-MIBG scintigraphy) is

haematoma formation, and infection.
- Time burden: patients with a kidney transplant attend their nephrologist on average 4 times a year. The number of extra (outpatient) clinic visits for participation in this study is approximately 3.5hours.
- There are no known risks to the extra blood pressure measurements.
- The complete radiation exposure due to 123I-MIBG amounts to 8.0 mSv which is an intermediate risk according to the category IIb of the ICRP (rapport ICRP62).

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

Negative control group: recently transplanted patients (n<=6)
- renal graft in situ for 0-6 weeks

- a measured creatinine clearance *50 ml/min
- having at least one native kidney in situ;When the negative control group with normal kidney function will show 123I-MIBG activity, an additional negative control group is studied, consisting of n<=6 recently transplanted anuric patients
- renal graft in situ for 0-6 weeks
- anuria due to delayed graft function or non-functioning graft (diuresis of maximum 150ml/day)
- having at least one native kidney in situ;Recently transplanted patients (n<=6)
- renal graft in situ for 6-18 months at time of measurement
- a measured creatinine clearance *50 ml/min
- having at least one native kidney in situ;Approximately 5 year renal transplant survivors (n<=6)
- renal graft in situ for > 4* < 7 years at time of measurement
- a measured creatinine clearance *50 ml/min
- having at least one native kidney in situ;Long term graft survivors (n<=6)
- renal graft in situ for >10 years at time of measurement
- a measured creatinine clearance *50 ml/min
- having at least one native kidney in situ

Exclusion criteria

- pregnancy
- unable to give informed consent
- absolute indication for alpha and beta-blocking agents
- allergy for iodine

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-07-2013

Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	15-05-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2014
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

ID: 26074
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL42557.018.13
OMON	NL-OMON26074