Catheterbased REnal SympatheCtomy for hypErteNsion after kidneyTranplantation

Published: 13-01-2012
Last updated: 28-04-2024

To test the efficacy of renal sympathetic denervation therapy with a special focus on preservation of renal allograft function.

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

Summary

ID

NL-OMON37896

Source
ToetsingOnline

Brief title
CRESCENT Trial

Condition

- Renal disorders (excl nephropathies)
- Renal and urinary tract therapeutic procedures
- Vascular hypertensive disorders

Synonym
therapy resistant hypertension in renal allograft recipients

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Nierstichting

Intervention

Keyword: hypertension, kidney transplantation, therapy

Outcome measures

Primary outcome

Primary endpoint is blood pressure reduction after 6 months (day time blood pressure assessed by 24-hours ambulatory measurement).

Secondary outcome

- Change in 123I-metaiodobenzylguanidine (123I-MIBG) uptake of native kidneys (i.e. effectiveness of denervation)

- Change in systemic sympathetic activity and plasma rennin and aldosterone activity

- Change in proteinuria after 6 months.

- Change in creatinine clearance after 6 months.

- Change in eGFR

- Change in number of antihypertensive drugs.

- Change in health related quality of life.

Study description

Background summary

In patients with a renal allograft, hypertension is a major etiological factor for cardiovascular morbidity, mortality and allograft nephropathy. Controlling hypertension in patients with a renal allograft is therefore crucial. There is a pressing, yet currently unmet clinical need for new blood pressure lowering strategies in renal allograft recipients.

The diseased native kidneys are major contributors to hypertension, through neuro-hormonal up-regulation that leads to high levels of renin and sympathetic

activity. Recently a catheter-based approach has been developed to disrupt renal sympathetic nerves. Currently this innovative technique has only been tested to lower blood pressure in therapy resistant hypertensive patients without significant renal disease.

We hypothesize that catheter based selective renal denervation of the native kidneys in renal transplant recipients will improve blood pressure control and diminish the number of antihypertensive drugs.

Study objective

To test the efficacy of renal sympathetic denervation therapy with a special focus on preservation of renal allograft function.

Study design

We propose a randomized controlled clinical trial (intervention group n=20; controls n=20). Intervention and control groups will receive standard protocolized antihypertensive treatment prior to, and during the trial. The interventiongroup will receive renal denervation in addition to standard treatment.

Intervention

Prior to study-inclusion all patients will receive standard protocolized hypertension treatment based on the National Kidney Foundation Kidney Disease Quality Outcomes Quality Initiative guidelines (2004). Renal sympathetic denervation is achieved by the interventional radiologist percutaneously entering the lumen of the main renal artery of each of the native kidneys, with a catheter connected to a radiofrequency generator. He applies 6-8 radiofrequency ablations within each renal artery. The procedure is performed in an outpatient clinic setting.

Study burden and risks

- The risks of femoral artery catheterisation are bleeding, infection and contrast-agent induced nephropathy.

- The risk of the venous canulation (for the 123I-MIBG scintigraphy, and for drawing blood) is haematoma formation, and infection.

- The direct burden of the ablation procedure is that it causes visceral pain (from the local heat of the radiofrequency probe) that will be treated with appropriate analgesics. The benefits of renal denervation are an expected lowering of blood pressure and thereby improved graft survival and cardiovascular co-morbidity risk and a reduction in the number of

anti-hypertensives needed.

- The total amount of radio-contrast agent administered during the catheterisation is < 100 ml. The risk of contrast induced (allograft) nephropathy is minimized by pre- and post-hydration.

- 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 2 (a 30 minutes) for the control group and 10 for the intervention group:
o 5 of 30 minutes: outpatient clinic visits and second day 123-I-MIBG scanning
o 2 of 4,5 hours: first day 123-I-MIBG scanning
o 2 of 2 hours: peroneal microneurography and
o 1 of 8 hours: for denervation procedure with pre and post-hydration.

- There are no known risks to the extra (ambulatory) blood pressure measurements.

- The total amount of blood taken in addition to standard care amounts to 20 ml for the patients in the control group and 70 ml for the patients in the intervention group.

- The total radiation exposure for patients in the intervention group due to 123I-MIBG amounts to 2 * 5,1 mSv and due to the ablation procedure to an estimated 0,7 mSv. The complete radiation exposure amounts to 11 mSv.

- The risk from the microneurography is the occurrence of temporary minor paresthesias at the site of probing in the weeks after the study [25]. This risk is thought to be very low (< 1 %). This risk is considered acceptable given the valuable data that this technique provides that can not be acquired otherwise.

From the introduction it is evident that the risks and burden for the patients are in proportion to the potential value of the research and the benefit that the patients in the intervention group may have. For the patients in the control group, there is a group related benefit.

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

- renal graft in situ since > 6 months, measured creatinine clearance > 35 ml/min, and
- diuresis of the native kidneys at transplant >200 ml/day or radiological evidence of residual flow in the renal arteries indicating that they are accessible for the intervention and
- day time blood pressure >140/90 mmHg (assessed by 24-hours ambulatory measurement within 3 month prior to inclusion in the study, as is regularly performed in the nephrology outpatient clinic) while
- treated according to National Kidney Foundation Kidney Disease Quality Outcomes Quality Initiative guidelines (2004), i.e. having been advised to minimize salt intake and using >3 antihypertensive medications in maximal tolerated dose, including a diuretic. Medications and their dosages should not have been changed since the measurement.

Exclusion criteria

- (planned) pregnancy, lactation
- life expectancy < 1 year
- non-functioning renal allograft in situ
- contraindications for (relative) hypotensive episodes i.e. haemodynamically significant valvular disease, documented transient ischemic attacks or angina pectoris during relative hypotension.

- heart failure, NYHA class III-IV; chronic Lung Disease Gold III-IV
- major complications during previous radiological interventions (i.e. allergy to contrast agent, cholesterol embolism)
- (reno) vascular abnormalities in any part of the catheter access (including the aortic-ileac tract) route that impede the procedure of renal denervation
- use of vitamine K antagonists or other (non-aspirin) form of anti-coagulatory therapy with an absolute indication (i.e. that cannot be temporarily stopped)
- implantable cardioverter defibrillator (ICD) in situ
- planned surgery within the next six months.
- Drugs- or alcohol abuse
- Inability to give informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-08-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	13-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	01-08-2012
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

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT:TC2998
CCMO	NL37711.018.11