Effects of Lumbar Sympathetic Blockade Renal Plasma Flow and Glomerular Filtration Rate.

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With this study we will investigate the effects of lumbar sympathetic blockade on ERPF and measured GFR and relative changes in non - invasive hemodynamics measured before and after continuous lumbar sympathetic blockade or splanchnic blockade in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Spinal cord and nerve root disorders
Study type	Observational invasive

Summary

ID

NL-OMON41932

Source
ToetsingOnline

Brief title
RELIEF study

Condition

- Spinal cord and nerve root disorders
- Renal disorders (excl nephropathies)
- Nervous system, skull and spine therapeutic procedures

Synonym
effects of nerve blockade on the kidney function

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: blockade, GFR, renal plasma flow (RPF), symphaticus

Outcome measures

Primary outcome

Primary Objective: to assess the effects of lumbar sympathetic blockade on glomerular filtration rate (GFR) and renal plasma flow (RPF) by studying the differences in measured GFR (in ml/min) and the difference in measured ERPF (in ml/min) before and after lumbar sympathetic blockade or splanchnic blockade in patients with a clinically assessed effective permanent blockade.

Secondary outcome

Secondary Objective(s):

to assess the differences before and after effective lumbar sympathetic blockade or splanchnic blockade in daytime office based blood pressure and systemic haemodynamics (non-invasive estimations of stroke volume, cardiac output, systemic vascular resistance and pulse wave velocity)

Study description

Background summary

With this study we will investigate the effects of lumbar sympathetic blockade on ERPF and measured GFR and relative changes in non - invasive hemodynamics measured before and after continuous lumbar sympathetic blockade or splanchnic blockade in patients with clinically evaluated successful permanent blockade

Blocking renal sympathetic innervation is a potential therapy for treatment-resistant hypertension. Renal sympathetic innervation regulates

sodium reabsorption and arterial resistance and thereby changes the effective renal plasma flow (ERPF), glomerular filtration rate (GFR) and systemic arterial blood pressure. Sympathetic innervation of the kidneys arise from spinal cord neurons in the ganglia T11 to L1. The postganglionic nerves enter the abdominal cavity and aortorenal ganglia and reach the kidneys through the walls of the extra - and intrarenal arteries. In animal studies it is shown that an increased sympathetic nerve activity causes a reduction in the ERPF and sodium excretion. This was the basis of a new therapy for treatment resistant hypertension: catheterbased renal sympathetic denervation, aiming to reduce sympathetic nerve activity by using radio -frequent ablation to interrupt the renal nerves that lie along the wall of the renal arteries. The intended effect of renal denervation is a lowering of systemic blood pressure, but a large variation in blood pressure response after renal denervation is shown. The effects of renal denervation on renal function (ERPF and GFR) in humans are unknown.
The renal effects of unilateral complete sympathetic blockade at the level L1 in humans have only been examined by a research group led by Solis Herruzo in 1987. Lumbar sympathetic blockade (LSB) is a technique to block postganglionic sympathetic innervation completely by local anesthetics at the level of L1. For the long- term effects (> 4 months) chemical neurolytic blockade with phenol or radiofrequency thermal ablation (splanchnic blockade SpB) is performed. This procedure is usually carried out one-sided, and usually at the level of L1 to L4.The study of Solis Herruzo examined the effects of LSB on creatinine clearance and measured ERPF in a small group of 8 patients with kidney failure due to hepatorenal syndrome. The patients showed a significant increase in ERPF and urinary sodium excretion after LSB. The effect was greatest in patients with an eGFR < 25ml/min at baseline.
Our study is based on these results: LSB seems to be a very suitable model to assess the renal effects of changes in renal sympathetic innervation of the human kidney.

An increased sympathetic nervous system causes vasoconstriction and increased arterial blood pressure. Sympathetic activity activates the renin - angiotensin - aldosterone - system, and leads to an increase in blood pressure. This also increases the cardiac output and GFR and ERPF. Therefore, we will explore the effects of LSB / SpB on ERPF and GFR and the relative changes in cardiac output, stroke volume, systemic vascular resistance and pulse wave velocity measured using non - invasive hemodynamic measurement with NexfinTM.

Study objective

With this study we will investigate the effects of lumbar sympathetic blockade on ERPF and measured GFR and relative changes in non - invasive hemodynamics measured before and after continuous lumbar sympathetic blockade or splanchnic blockade in patients with clinically evaluated successful permanent blockade

Study design

n=15 patients with an indication for lumbar sympathetic blockade or splanchnic blockade will be included in the study. Four to six weeks before the blockade the first measurement will be scheduled. On this day, ERPF measured with 131I Hippuran and GFR with 125I - Iothalamate will be measured. During these measurements, blood is collected. Prior to the study, all patients have had diet instructions and the patient has collected 24-hour urine samples. Systemic haemodynamics will be measured non-invasively with NexfinTM while standing and while in supine position breathing room air, 50% oxygen and 100% oxygen. The second measurement with identical measurements takes place 1-8 weeks after lumbar sympathetic blockade or splanchnic blockade, provided that it that the LSB or SpB has been successful (in LSB signs of vasodilation in the lower extremity, and pain reduction in case of splanchnic blockade) assessed by the clinician.

Study burden and risks

Radiation exposure due to the GFR measurement with 125I-iothalamate and ERPF measurement with 131I-hippuran is 0.8mSv, which is a minor risk class IIa of the ICRP. This is approximately 32% of the yearly background radiation in The Netherlands. Placement of an intravenous cannula causes the risk for infection and bleeding. The amount of blood drawn is 54 ml per measurement, amounting to 108 ml in total for two study days.
Patients receive air with different oxygen concentrations to breath over a non-rebreathing mask for 30 minutes. This has no negative effects. Only wearing the mask may give minimal discomfort.
The time spent is 13 hours in total. There are dietary restrictions for this study and two times 24hour-urine collections.
Patients do not have a benefit from participation nor 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

- age *18 years
- able to give informed consent
- no recent changes or expected changes in antihypertensive medications or psychopharmaca
- we aim at including at least 50% of the patients with an eGFR < 60ml/min. If the number of patients with eGFRs <60ml/min who are willing to participate in the study is more than patients with eGFR> 60ml/min: the patients with the lowest eGFRs will be selected for inclusion.

Exclusion criteria

- not willing to be informed about unexpected findings during the study
- neurologic disease
- Lung disease
- pregnancy
- renal replacement therapy (hemo- or peritoneal dialysis)
- iodine allergy
- allergy for shellfish
- not being able to resign from cigarette smoking/ nicotine use in any form, for >20 hours ;PLEASE NOTE: the second GFR and RPF measurements will only be performed in patients with a successful persistent blockade that has been clinically assessed by the pain specialist. In the case of LSB: treatment is regarded as successful upon vasodilatation and in the case of splanchnic blockade relief of pain.

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):	20-01-2015
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	08-08-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	11-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	10-03-2015
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
CCMO	NL48651.018.14

Study results

Date completed: 21-07-2017

Actual enrolment: 3