Evaluating Myocardial Ischemia and Sympathetic Innervation in Patients with Chronic Kidney Disease before and during Renal Replacement Therapy using 99mTc-tetrofosmin and 123I-MIBG imaging

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Is sympathetic innervation and perfusion disturbed in patients with chronic kidney disease and will is change after HD?

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational non invasive

Summary

ID

NL-OMON37178

Source
ToetsingOnline

Brief title
Myocardial Ischemia Innervation imaging

Condition

- Cardiac arrhythmias
- Renal disorders (excl nephropathies)

Synonym
chronic kidney disease, dialysis

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Radiofarmaceutische industrie stelt de radiofarmaca beschikbaar.

Intervention

Keyword: Chronic Kidney Disease, dialysis, imaging

Outcome measures

Primary outcome

Cardiac ischemia and cardial neuropathy in patients with CKD (pre-dialysis) and

3 months after starting HD.

Secondary outcome

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Study description

Background summary

Cardiovascular diseases and autonomic dysfunction are the leading cause of death in patients with chronic kidney disease (CKD). Cardiac causes account for 40% to 50% of all deaths in dialysis patients. About 15% to 20% of these deaths occur suddenly and unexpectedly. Prevalence of coronary artery disease (CAD) in CKD patients varies from 24% in young nondiabetic hemodialysis patients to 85% in elderly diabetic uremic patients. However, there are a large, but as yet unknown number of totally asymptomatic individuals, especially those with diabetes who have myocardial ischemia. In diabetics, the lack of symptoms is attributed to the concomitant presence of diabetic autonomic neuropathy. Autonomic dysfunction is also commonly present in end-stage renal disease, but whether this results in lack of symptoms in cardiac ischemia is unknown.
Studies in patients on maintenance hemodialysis (HD) have shown that HD is an arrythmogenic process which can also induce myocardial ischemia6. HD patients with a reduced heart rate variability (HRV) on a 24-hour ambulatory Holter ECG monitoring seem to be at increased risk of all-cause mortality and sudden death as recently shown in a relatively small prospective study. Imaging showed

reduced sympathetic activity in the heart of hemodialysis patients, especially in diabetics. Another study has demonstrated electrocardiographic changes during HD, significant ST depression during HD was highly associated with CAD and it was an important prognosticator of subsequent cardiac events. Unknown is the extent of cardial ischemia and sympathetic dysfunction induced in patients receiving HD. It is known that in the normal population, cardiac ischemia and autonomic dysfunction is a good predictor for future cardiac events and it is also associated with increased long term mortality. Unclear is in which phase renal failure CAD and autonomic dysfunction will develop in HD patients. This may be during dialysis or even before starting dialysis.
Coronary angiography is the most effective method for detecting CAD, but its cost is high and the risk of complications is significant.

Thus, coronary angiography is unsuitable as a screening tool for CAD in asymptomatic patients. Further, coronary angiography can not evaluate ischemia of (non-) significant stenosis. Hence, non-invasive imaging techniques for the purpose of detecting myocardial ischemia has been used extensively in routine clinical practice and increasingly in hemodialysis patients. ECG-gated single-photon emission computed tomography (SPECT) myocardial perfusion scintigraphy using technetium-99m tetrofosmin (99mTc-tetrofosmin) is one of these modalities. Gated 99mTc-tetrofosmin SPECT assesses in one session myocardial ischemia, wall motion, left ventricular volumes and ejection fraction. Analysis of the autonomic function of the heart can also be performed by 123I-MIBG imaging, a well established additional method to evaluate the sympathetic innervation of the heart 15.
Thus far the presence and severity of CAD and autonomic dysfunction of the heart has never been studied in asymptomatic patients with stage 5 CKD who are not yet on dialysis (HD) using 99mTc-tetrofosmin and 123I-MIBG imaging. For that reason we want to evaluate myocardial ischemia and sympathetic innervation before starting HD with 99mTc-tetrofosmin and 123I-MIBG. The result of the pre-dialysis patients will be compared in the same patients 3 months after starting HD to evaluate the effect of hemodialysis on myocardial perfusion and innervation

Study objective

Is sympathetic innervation and perfusion disturbed in patients with chronic kidney disease and will is change after HD?

Study design

This study will include patients before starting dialysis (pre-dialysis). The design of the study will be longitudinal. Cardial ischemia and innervation will be assessed in the pre-dialysis period and 3 months after starting HD in the same patients. Cardiac ischemia will be visualized by using 99mTc-tetrofosmin rest and adenosine stress SPECT method and analyzed on a 4D-MSPECT-software

program. 123I-MIBG imaging will be performed 15 min and 3.5 hours after injection. Heart-to-the-mediatinum ratio and wash-out rate of 123I-MIBG will be calculated. Perfusion and innervation assessment of the heart is of evidenced clinical value. All scans in the pre-dialysis phase will therefore be performed in a clinical setting.
Also a normal database of the heart will be collected by 10 regular clinical patients with medullar thyroid carcinoma or paraganglioma that will receive a clinical 123I-MIBG scan. Only an extra image of 10 minutes will be performed in these patients. No extra 123I-MIBG will be injected and this image can be performed on the same day of injection of 123I-MIBG. A normal database is of importance for an accurate assessment of 123I-MIBG uptake in the heart.

Study burden and risks

Little pain during/after injection. Small radiation dose. Lay down quietly for 30 minutes in the gammacamera.

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

end-stage chronic kidney disease (stage 5)

Exclusion criteria

Patients with acute or previous myocardial infarction within 6 months prior to inclusion, angina pectoris within 6 months prior to inclusion, known coronary artery disease within 6 months prior to inclusion, or recent acute cardiac decompensation, as defined by sudden accumulation of pulmonary congestion or peripheral oedema, pregnancy, M. Parkinson, diabetes mellitus, Diffuse Lewy Body disease. Use of tricyclic antidepressant agents (interferes with 123I- MIBG uptake). Participation to a previous protocol involving radioactivity in the past year.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-05-2010
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO Date:	25-09-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-01-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL23343.042.08