Clock gene expression in hemodialysis patients

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This study aims at understanding the circadian disruption in chronic hemodialysis patients and provide a molecular basis for the etiology of sleep-wake cycle disturbances. The hypothesis that the circadian clock is disturbed in chronic hemodialysis...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Observational invasive

Summary

ID

NL-OMON37872

Source
ToetsingOnline

Brief title
CLEXID

Condition

- Nephropathies

Synonym
circadian rhythm, day-night rhythm

Research involving
Human

Sponsors and support

Primary sponsor: Meander Medisch Centrum
Source(s) of monetary or material Support: subsidie door Leo Fretz stichting Meander MC

Intervention

Keyword: circadian rhythm, clock genes, hemodialysis

Outcome measures

Primary outcome

Establish 24-hr peripheral clock gene and clock controlled output gene expression profiles in blood of chronic hemodialysis patients compared to control subjects to diagnose renal disease mediated circadian disruption.

Secondary outcome

1. Investigate the clock synchronization and phase-shifting potential of serum from chronic kidney disease patient and control groups. Renal patients are expected to have high levels of clock resetting compounds.

2. Determine the correlation between clock gene expression and a physiogical read-out (sleep).

Study description

Background summary

A disruption of the biological clock is presumed in chronic hemodialysis patients since they frequently suffer from sleep problems, frequently show a non-dipper blood pressure profile and lack a nocturnal melatonin surge, which is a reasonable readout for disturbed clock performance. The origin of these clinically observed disturbances is still unknown. Possibly, there is an underlying disturbed peripheral clock synchronization by constitutively high (rather than oscillating) amounts of humoral clock-resetting compounds.

Study objective

This study aims at understanding the circadian disruption in chronic hemodialysis patients and provide a molecular basis for the etiology of sleep-wake cycle disturbances. The hypothesis that the circadian clock is disturbed in chronic hemodialysis patients is tested. Two questions will be

addressed:

1. is renal failure associated to altered peripheral circadian expression of clock genes and clock-controlled genes in chronic hemodialysis patients compared to matched control subjects with normal kidney function and

2. is a constitutively increased level of clock resetting compounds in serum of chronic hemodialysis patients responsible for the disturbed circadian expression. Presumably certain compounds in HD-patients are continuously available exceeding threshold values, in comparison to lower and cyclically levels available in subjects with normal kidney function (including patients with and without disturbed sleep).

The outcome of these experiments will shed new light on treatment options, development of disease and optimizing chronopharmacology in patients with chronic kidney disease.

Study design

observational study

Study burden and risks

Hospitalized chronic hemodialysis patients with and without reported sleeping problems and their matched control subjects are asked to participate in the following:
- 7 blood samples taken in PAXgene tubes to collect blood and stabilize intracellular RNA (9.00, 13.00, 17.00, 21.00, 1.00, 5.00, 9.00) (HD patients and control subjects)
- 7 serum samples taken at 9.00, 13.00, 17.00, 21.00, 1.00, 5.00, 9.00 (HD patients and control subjects)
- 2 serum samples + hemodialysis bath water samples taken in standard collection tubes (before and after dialysis) (HD patients only)
- Epworth Sleepiness Scale (short sleepiness questionnaire) (HD and control patients)
- Chronotype questionnaire: Ochtend-/avondtype vragenlijst (HD patients and control subjects)
- Medication record (HD patients and control subjects)
- Registration of meal time + type of meal + coffee intake (HD patients and control subjects)
- 4 days of objective sleep measurements by actigraphy (HD patients and control subjects)

Participants don*t receive direct benefit from participation in the study. The collected data help to understand the circadian clock problems in chronic hemodialysis patients. In the future this can possibly be used to define

therapeutic targets, optimize dialysis schedules or develop chronopharmacotherapy.

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

Chronic hemodialysis patients:
- Hospitalized, stable chronic hemodialysis patients
- Written informed consent
- Age 18-85 years
- Good understanding of Dutch language;Control patients:
- Hospitalized, stable patients
- MDRD-GFR > 60 ml/min
- Age and gender matched with hemodialysis patient

- Written informed consent
- Age 18-85 years
- Good understanding of Dutch language

Exclusion criteria

- Blindness
- Fever
- CRP > 20 mg/L
- Diabetes
- Serious co-morbidity that prevents participation in this study according to the investigators (e.g. neurological, psychiatric, angina, heart failure NYHA class IV)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-07-2012
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO

Date:	27-04-2012

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL39856.100.12