Continuous, on-line determination of the plasma refill rate during combined hemodialysis and ultrafiltration

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Methodology (part A):(1) What is the intra-individual variation in refill? (2) Is the magnitude of the ultrafiltration rate of influence on refill? (3) Is the amount of the initial intended blood volume decline of influence on refill? Implementation...

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

Summary

ID

NL-OMON31569

Source
ToetsingOnline

Brief title
COPR

Condition

- Nephropathies

Synonym
chronic renal failure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Zie vraag G2a.

Intervention

Keyword: dry weight, hemodialysis, Plasma refill rate, ultrafiltration

Outcome measures

Primary outcome

Hydration status determined by: natriuretic peptides (BNP) before and after dialysis, blood volume monitoring, blood pressure and heart frequency during dialysis, non-invasive measuring of the extracellulair volume using bioimpedance analysis, ultrasonography of the vena cava one hour after dialysis, chest X-ray and 24-hour blood pressure measurement one day after dialysis (=part B, implementation).

Secondary outcome

Refill in the BV target range (=part A, methodology).

Study description

Background summary

Determining the correct dry weight and reaching a situation of true euvolemia in patients who are treated with hemodialyse is very difficult. A too high estimation of dry weight leads to chronic overvulling and hypertension, with an increase risk of cardiovascular events on the longer term. A too low estimation of dry weight not only leads to hypotension during the hemodialysis treatment itself, but also during the interdialytic interval. The accompanying symptoms and signs limit the quality of life.

There is no gold standard for determination of dry weight. The most used and accepted methods are bioimpedance analysis, ultrasonography of the vena cava and natriuretic peptides such as BNP. These methods are time-consuming and not very practical because of the need for specialized personnel.

Determination of the plasma refill rate (PRR) during dialysis is not possible without the use of radioactively labelled substances. We have developed a method that allows on-line determination of the PRR non-invasively and

continuously. During pilot research with hypotension prone patients, in which we investigated whether the PRR could be improved by means of two interventions, we saw that the refill during the second half of dialysis stopped in most of these hypotension prone patients. This led to the following hypothesis:

Hypothesis: the disappearing of refill indicates euvolemia of the interstitium.

Study objective

Methodology (part A):

(1) What is the intra-individual variation in refill?

(2) Is the magnitude of the ultrafiltration rate of influence on refill?

(3) Is the amount of the initial intended blood volume decline of influence on refill?

Implementation (part B):

(4) Is the moment that refill declines a good indication of reaching euvolemia of the interstitium?

Study design

Question 1: What is the intra-individual variation in refill?
Rationale: It is necessary to know the intraindividual variations in refill before refill changes can be used as a new method to determine dry weight.
-Protocol:
Dialysis 1: determination of lowest achievable blood volume (BV) change (=lowest achievable value during dialysis without hypotension or the value at which hypotension occurs) during dialysis with linear ultrafiltration (UF).
Dialysis 2: repeat dialysis 1.
Dialysis 3: With the same UF need as dialysis 1, UF is started at 3x linear UF rate until the BV target range is reached. This range is defined as the lowest achievable BV change, as found during dialysis 1, +2.5%. Start refill measurement: the UF rate is continuously adjusted by a software feedback algorithm to keep BV within the target range. I this situation UF rate equals refill.
Dialysis 4: repeat dialysis 3.

Question 2: Is the magnitude of the ultrafiltration rate of influence on refill?
-Rationale: it is possible that the speed at which the refill inducing factor (= BV reduction) is presented, is of influence on refill. A lower UF rate implies that the same reduction in BV will be achieved later, in other words

the refill inducing factor is presented slower.

-Protocol:
Dialysis 5: repeat dialysis 3, but with an initial speed of 2x instead of 3x linear UF rate.
Dialysis 6: repeat dialysis 6.

Question 3: Is the amount of the initial intended blood volume decline of influence on refill?
- Rationale: it is possible that the initial amount of BV decline is of influence on activating refill. This is investigated by setting the target BV range at a higher level with an unchanged initial UF rate. The refill mechanism is induced less in this way.

- Protocol:
Dialysis 7: repeat dialysis 3, but with BV target range set +2.5% higer than in dialkysis 2.
Dialysis 8: repeat dialysis 7.

Question 4: Is the moment that refill declines a good indication of reaching euvolemia of the interstitium?
- Rationale: Zie *Relevant Literature*.
- Protocol:
(A). Dry weight is determined by the usual clinical methods. Determine hydration status: BNP before and after dialysis, pattern of relative blood volume change, blood pressure and heart rate changes during dialysis, extracellular volume using bio-impedance analysis and vena cava ultrasonography one houd after dialysis, chest X-ray, 24 hour blood pressure measurement 1 day after dialysis.

Dialysis 1: determination of lowest achievable blood volume (BV) change (=lowest achievable value during dialysis without hypotension or the value at which hypotension occurs) during dialysis with linear ultrafiltration (UF).
Dialysis 2: With the same UF need as dialysis 1, UF is started at 3x linear UF rate until the BV target range is reached. This range is defined as the lowest achievable BV change, as found during dialysis 1, +2.5%. Start refill measurement: the UF rate is continuously adjusted by a software feedback algorithm to keep BV within the target range. I this situation UF rate equals refill.
When refill declines to 0, UF is stopped (=moment of *refill-euvolemia*). When this is before the target UF volume is reached, the target dry weight is increased by the amount that was not removed. When this is after target UF weight is reached, target dry weight is decreased by the extra amount that was removed. After this regular dialysis sessions are continued with the new target dry weight.

(B) After 2 weeks dialysis with the new target dry weight, the measurements

under (A) are repeated to determing the hydration status.
-Analysis: changes in parameters that determine volume status before and after changing target dry weight on the basis of *refill-euvolemia*.
- Power analysis: (a) adjusting target dry weight increases mean 24 hour blood pressure by 20 mmHg (SD 25 mmHg) in overhydrated patients and decreases it by 20 mmHg in underhydrated patients. Power 0.8, p <0.05: sample size 15 patients; (b) adjusting target dry weight changes BNP by 500 pg/ml (SD 400 pg/ml). Power 0.8, p <0.05: sample size 16 patients.

Taking into account loss to follow-up, a sample size of 20 patients is needed.

Intervention

The patients are compared under different ultrafiltration conditions (part A). Next, the target dry weight is determined (using primary study parameters), and the patients are ultrafiltrated according to the protocol. Then the volume status is determined again using primary study parameters and the hypothesis is tested (part B).

Study burden and risks

- Natriuretic peptides (BNP) befor and after dialysis: 2 extra blood samples taken from the arterial port of the dialysis tubing
- Non-invasive measurement of the extracellular volume using bioimpedance + ultrasonopgraphy of the vena cava one hour after dialysis: total time one hour
- Chest x-ray: 0.1 mSv
- 24-hour blood pressure measurement 1 day after dialysis: limits the patient in his freedom of movement
- Complete Quality of life-index form.

Risk:
- The risk of hypotension during hemodialysis is always present. We do not expect this risk to be higher when our intervention is applied.
- Chaning the dry weight on the basis of changes in refill patterns carries the risk of putting the patients in an overhydrated state.

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

Hemodialysis

Exclusion criteria

Onvermogen om informed consent te geven.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-03-2008
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	12-02-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL17913.041.07