Erythrocytapheresis versus Phlebotomy as maintenance therapy in patients with hereditairy hemochromatosis; a randomised, single blinded, sequential, cross-over trial

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The primary objective of the study is to determine the gain in effectiveness of TE compared with P when applied to remove excess iron during maintenance therapy of HH patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON33962

Source
ToetsingOnline

Brief title
Erythrocytapheresis versus Phlebotomy in HH patients

Condition

- Haematological disorders NEC

Synonym
Ironacumulation, Ironoverload

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Bloedbank
Source(s) of monetary or material Support: Sanquin stichting Bl;oedvoorziening

Intervention

Keyword: Erytrhocytapheresis, Hereditaire Hemochromatosis, Maintenance Treatment, Phlebotomy

Outcome measures

Primary outcome

Primary endpoint: The difference in number of required treatments and the

interval between treatments per year to keep the serum ferritine levels between

30 - 50 µg/L.

Secondary outcome

The potential preference of the patients for one of the techniques. To obtain

the answer to this secondary question, the patients are asked to fill in

validated questionares (SF 36, EQSD, NRS BASDAI)

Study description

Background summary

Hereditary Hemochromatosis (HH) is a genetic disorder of iron metabolism, resulting in excessive iron overload. Phlebotomy (P) is currently the standard therapy which consists of removal of 500 ml whole blood weekly. The aim is to reduce the serum ferritin levels to 50µg/L or lower and/or transferrin saturation <= 50%. Current therapy with phlebotomy requires, depending on the initial ferritin levels, between 20 to 100 procedures over a period of 6 to 24 months. Thereafter P procedures are reduced to 3 to 6 times as a lifelong maintenance therapy.
More recently Therapeutic Erythrocytapheresis (TE) has become a new therapeutic modality, which potentially offers a more efficient method to remove iron overload with fewer procedures in a shorter treatment period and with less side effects. The results from our pilot study showed a reduction in both total

number and duration of treatment of 69% by use of TE instead of P by newly diagnosed HH patients Preliminary results from our ongoing randomised controlled trial (NCT 00202436, MEC 04-150) presented during the AASLD single topic conference in Atlanta USA, on September 9th, 2007, indicated that TE seems to be an effective and safe method to remove iron overload in initial treatment of patients with HH. TE showed already a substantial reduction in the number of TE procedures necessary to bring the initial ferritine levels (at inclusion) to half their values, when compared to treatment by P.
In proposed clinical trial we will study whether TE can keep the ferritin levels in patients requiring maintenance therapy for HH < 50 µg/L, with minimally half the number of treatment procedures when compared to current standard therapy by P.

Study objective

The primary objective of the study is to determine the gain in effectiveness of TE compared with P when applied to remove excess iron during maintenance therapy of HH patients.

Study design

A randomized, single blinded, sequential, cross-over, clinical trial among patients currently receiving Phlebotomy as maintenance therapy for their iron overload due to HH.

Intervention

TE as a new therapeutic modality to reduce and/or prevent iron overload during maintenance therapy. This method will be compared with P, which is the current standard maintenance therapy. TE allows a more intense treatment since erythrocytes can be selectively removed from circulation. With TE up to 1000 ml erythrocytes per procedure can be removed, in comparison to 250 ml erythrocytes (500 ml whole blood) per Phlebotomy procedure.
The advantages of the TE treatment are multiple,
a TE is more patient friendly
b TE is more effective, given the intensity of iron removal per treatment procedure
c TE limits the number of required interventions per period of an entire treatment .

Study burden and risks

Possible side effects of both procedures are related to the risk of (hypo-volemic) collapse, which is slightly higher in the P, but lower in the TE. In the latter however mild citrate reactions may occur during some of the TE procedures. These episodes are basically self-limiting or can be remedied by

drinking a glass of milk.
Based on an ongoing clinical trial on the impact of TE as initial treatment of newly diagnosed patients with HH, the observed risks of TE (compared with P) seem lower.
We already observed a clear reduction in side effects in TE (1/81) versus P (9/294).
In both study arms bi-monthly blood will be collected to measure ferritin levels and Zinc Proto Porphyrine (ZPP) levels, the latter to safeguard against removing to much iron resulting in sub-clinical iron deficiency.

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

Patients with ironoverload, homozygous for C282Y, treated with Phlebotomy as maintenance

therapy for at least 6 month
Demonstrated therapy compliance with prescribed P so far
Ferritin level between 30-50 ug/L at start of the inclusion
Age 18 years an older
Weight > 50 kg
Signed informed consent
Willigness to fill out additional questionnaires at three points in time

Exclusion criteria

Patients recieving others therapies such as chelating therapy or forced dietary regimen
Patients younger than 18 years
Patients with excessive overweight (BMI>35)
Patients which are mentally incapacitade
Women being pregnant or expecting/planning to become pregnant during the two years period of the study
Patients with a malignancy
HH patients which are current blood donors

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2008
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO Date:	21-02-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-04-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-10-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL20814.068.07