Proton pump inhibitors in the prevention of iron reaccumulation in patients with hereditary hemochromatosis

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The effectiveness an cost effectiveness of PPIs compared to standard phlebotomy therapy in the prevention of iron overload in patients with hereditary hemochromatosis.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Iron and trace metal metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON38058

Source
ToetsingOnline

Brief title
He-ppi

Condition

- Iron and trace metal metabolism disorders

Synonym
hereditary hemochromatosis/ ironreaccumulation disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Annadal Stichting

Intervention

Keyword: hemochromatosis, ironreaccumulation, Phlebotomy, PPI

Outcome measures

Primary outcome

The total number of phlebotomies for the group taking PPI treatment compared to

the group taking placebo

Secondary outcome

Quality of life

Cost-effectiveness

Patient satisfaction

Side effects of treatment (PPI)

Study description

Background summary

Hereditary Hemochromatosis (HH) is a genetic disorder of iron metabolism, resulting in excessive iron overload causing damage of different important organs like heart, liver, pancreas and joints. Complications and symptoms can regress by intensive treatment reducing the iron overload stores(Adams et al, Pietrangelo et al, van der Plas et al).
Different genes have been identified playing a role in the pathofysiology of iron overload. A clinically important HFE gene mutation is the C282Y, located on chromosome 6. The homozygous mutation is found in 1 out of 200-400 people in the Netherlands with a variable penetrance for clinical HH of 10%, estimating that about 4.000 * 8.000 individuals in the Netherlands are at risk and require therapy (Swinkels et al, Jacobs et al).
Phlebotomy is currently the standard therapy which consists of removal of 500 ml whole blood weekly, representing a loss of 250 mg iron. In naive patients between 20 to 100 phlebotomies are required to reduce the serum ferritine levels to 50 *g/L. Thereafter, a lifelong maintenance therapy of 3 to 6 phlebotomies yearly is needed.
For absorption, dietary iron (70%) is reduced by gastric acid form the ferric (Fe3+) to the ferrous form (Fe2+). Recently, in an observational open study,

Hutchinson et al. found that HH patients treated with proton pump inhibitors (PPI) needed fewer phlebotomies, resulting in a drop of 2.5 (SEM 0.25) to 0.5 (SEM 0.25) liter per year (Hutchinson et al).
Since PPI therapy is very common, we foresee within short notice an expansion of PPI prescription in HH patients. Thus, structured evaluation of efficacy, costs and patients compliance, acceptance and therapy preference is now mandatory.
Research question: The primary objective is to determine the effectiveness and cost effectiveness of PPI*s compared to standard phlebotomy therapy in the prevention of iron overload in HH patients.

Study objective

The effectiveness an cost effectiveness of PPIs compared to standard phlebotomy therapy in the prevention of iron overload in patients with hereditary hemochromatosis.

Study design

Multi-center trial in two hospitals in the South of Limburg (Atrium medical Center, Maastricht university medical center) and hospital in Belgium (University Hospital Gasthuisberg). The study will be conducted in randomised double blind manner. The follow up will be one year.

Intervention

patients are randomized either for the group receiving a PPI or a placebo. Every 2 month the ferritin level is measured and decided if the patient need a phlebotomy (Ferritin >50 µg/L).

Study burden and risks

The patient should take on tablet a day (placebo/PPI). Two times a year an outpatient clinic visit is planned, which is normal for the patient. Every two months a blood sample is taken. When the ferritin is > 100 ug/l a phlebotomy is planned. We asked the patient to fill in questionnaires every two months (BASDAI/ SF-36/EQ-5D). At inclusion the patient will be physical examined.

Side effects of PPIs are rare. The most often mentioned (1-10%) are pain in upper abdomen, diarrhoea, constipation, flatulence and headache. Data of long term complications are sparse. Elevation of hormone Gastrin is found and can lead to expansion of enterochromafinlike cells (ECL)7-14 without risk of carcinoma 15. In small studies bacterial overgrowth has been observed as a consequence of strong acid suppression 16-18. The patients have a slight elevated change of bacterial gastrointestinal infections 19 and pneumonia 20.

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

Patient with hereditairy hemochromatosis, homozygous for c282Y currently treated with phlebotomy as maintenance therapy for at least 12 months with >/<= phlebotomies per year.;Ferritin level between 50-100 ug/l at start of inclusion.;Age 18-75 years;Weight > 50kg

Exclusion criteria

Patients receiving other therapies such as chelating therapy or forced diet;Obesitas (BMI > 35);Patients who are mentally incapacitated;pregnancy; women expecting / planning to become pregnant during the study period.;Patients with a malignancy;Patients already on ppi treatment;patients experienced side effects ppi.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2013
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pantomed
Generic name:	Pantoprazol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-08-2012
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	27-08-2012
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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
EudraCT	EUCTR2012-000603-32-NL
ClinicalTrials.gov	NCT01524757
CCMO	NL33644.096.12