PPI in secondary hemochromatosis.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25811

Source
Nationaal Trial Register

Brief title
PPI Shine Again

Health condition

Secondary hemochromatosis
Hereditary anemia
Proton pump inhibitor

Sponsors and support

Primary sponsor: University Medical Center Utrecht
Source(s) of monetary or material Support: ZonMW, Innovatiefonds Zorgverzekeraars

Intervention

Outcome measures

Primary outcome

The change in LIC measured by MRI of the liver expressed in milgram Fe/gram dry weight after one year of treatment with esomeprazole compared to one year treatment with placebo.

Secondary outcome

1. Tolerability of esomeprazole: the incidence of side effect / adverse events will be monitored every 3 months during study visits.

2. Quality of life: this will be assessed with EQ5D-forms, with time intervals of 3 months.

3. Cost-effectiveness analysis of esomeprazole in treatment of iron overload in hereditary anemia. This will be assessed by a prospective cost-effectiveness analysis. IMCQ and iPCQ questionnaires will be filled in with time intervals of 3 months.

4. Related changes in markers of iron metabolism: plasma hepcidin, serum ferritin.

5. Compliance to study drug.

6. Need for chelation therapy.

Study description

Background summary

Rationale: The number one cause of years lived with anemia in Western Europe is hereditary anemia. The major cause of morbidity and mortality in patients with hereditary anemia not requiring chronic blood transfusion is iron overload caused by increased uptake from the gut. Iron overload and hereditary anemia are a growing, underestimated emerging health care problem. Many patients on iron chelation therapy, including deferasirox (currently the most frequently used iron chelating agent) experience side effects such as gastro-intestinal problems and less frequently renal or hepatic failure. Not including the economic costs and loss of quality of life caused by side effects of iron chelation, the cost of prescription alone amounted about 5 million euros in 2014 in the Netherlands. Dietary uptake of iron can be reduced by gastric acid reduction. Observational studies suggest that PPIs reduce iron uptake. In a recent randomized controlled trial in hereditary hemochromatosis PPIs diminished the needed number of phlebotomies. Although, results of this trial cannot be extrapolated completely to patients with hereditary anemia, this is a strong suggestion for effectiveness in patients with hereditary anemia’s and secondary hemosiderosis. A safer alternative for the iron chelators would make it possible to intervene earlier in these patients at lower costs. Especially in low-income regions of the world, PPIs could be a life saving and affordable alternative to prevent and treat iron loading.

Objective: to show that PPIs are an effective and safe treatment of secondary hemochromatosis in patients with hereditary anemia and mild iron overload.

Study design: randomised placebo controlled cross-over trial.

Study population: 40 non-transfusion-dependent patients (adults) with a form of hereditary anemia with mild to moderate iron overload. Mild to moderate iron overload is defined as a baseline LIC (liver iron content) between 3 and 15 mg Fe/g dry weight (dw) without iron chelation therapy or on stable chelation therapy.

Intervention: 12 months treatment with esomeprazole 40 mg twice daily or 12 months treatment with placebo twice daily.

Primary endpoint: the change in LIC measured by MRI of the liver expressed in mg Fe/g dw after one year of treatment with esomeprazole compared to treatment with placebo.

Study objective

We hypothesize that proton pump inhibitors are an effective and safe treatment of secondary hemochromatosis in patients with hereditary anemia and mild iron overload.

Study design

MRI liver will be performed at baseline, T= 12 months and T= 24 months.

Intervention

12 months treatment with esomeprazole 40 mg twice daily or 12 months treatment with placebo twice daily.

Contacts

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Eligibility criteria

Inclusion criteria

o diagnosis of hereditary anemia: hemoglobinopathy (including all sickle cell syndromes and beta-thalassemia), sideroblastic anemia, congenital dyserythropoietic anemia or an erythrocyte enzyme deficiency.
o hemoglobin level before study inclusion <7.0 mmol/L.
o clinically stable and relevant iron overload defined as either one of:
o a baseline LIC measurement by MRI between 3 and 15 mg Fe/g without having received iron chelation 2 months prior to entering the study.
o OR a baseline LIC measurement by MRI between 3 and 15 mg Fe/g on stable chelation therapy (deferasirox, deferoxamine or deferiprone), with documented stable dosage the preceding 2 months and no expected dose reductions or increases the next two years.
o aged more than 18 years and able to sign informed consent.
o serum transferrin saturation higher than 0.40 once during the preceding 24 months.
o received less than 10 units of blood during the preceding 12 months.
o is expected to receive less than 4 units of blood during the following 12 months
o is not splenectomized during the preceding 24 months.

Exclusion criteria

o Pregnancy.
o Liver cirrhosis.
o Heart failure.
o Severe cardiac iron overload defined as MRI T2* < 20 ms.
o Severe liver iron overload defined as MRI LIC > 15 mg Fe/g dw.
o Expected poor compliance.
o Currently taking PPI and not able to stop for personal or medical reasons.
o Patients that are being phlebotomized as treatment for iron overload.
o Current peptic ulcer disease, gastro-intestinal bleeding or other causes of blood loss.
o Contra-indication for esomeprazole use.
o Concomitant use of clopidogrel.
o Contra-indication for MRI.
o Received more than 4 units blood during one of the treatment periods of 12 months.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2018
Enrollment:	30
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	08-11-2017
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 48585
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6659
NTR-old	NTR6836
CCMO	NL63198.041.17
OMON	NL-OMON48585

Study results