Predicting Response to Iron Supplementation in Patients with active Inflammatory Bowel Disease

Published: 21-03-2022
Last updated: 30-01-2025

To evaluate if hepcidin levels can predict response to iron therapy with either ferrous fumarate, ferric maltol, and intravenous iron in patients with IBD.

Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON54041

Source
ToetsingOnline

Brief title
PRIme

Condition

- Gastrointestinal inflammatory conditions

Synonym
IBD, Inflammatory Bowel Disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Initiative on Crohn and Colitis,Norgine

Intervention

Keyword: hepcidin, IBD, iron deficiency

Outcome measures

Primary outcome

Whether hepcidin levels at baseline can predict response to iron therapy with either ferrous fumarate, ferric maltol, or intravenous iron (main parameters: hepcidin at baseline, binary response (yes / no) to iron therapy. The response to iron therapy is defined as an increase >1.2 mmol/l in hemoglobin or hemoglobin normalization at week 14 for patients with iron deficiency anemia; or an increase in ferritin >100 µg/l) and transferrin saturation >20% at week 14 for patients with iron deficiency without anemia)

Secondary outcome

- Changes in quality of life (SF-36)

- Changes in IBD disease activity (mHI)

- Changes in (work) activity impairment (WPAI)

- Changes in hypoxie- or inflammatiion-associated biomarkers, oxidative stress, microbiome

- Hypophosphatemia and other side effects

Study description

Background summary

Iron deficiency anemia is the most common systemic manifestation of Inflammatory Bowel Diseases (IBD)*Crohn's disease and ulcerative colitis. Iron deficiency with or without anemia poses a diagnostic and therapeutic challenge due to chronic gastrointestinal blood loss and the inflammatory nature of IBD.

Recent illumination of iron metabolism has brought attention to the systemic iron regulator*hepcidin, a peptide hormone that regulates intestinal iron absorption and systemic iron availability. Multiple factors regulate hepcidin synthesis: inflammation and iron overload upregulate hepcidin levels, while increased erythropoiesis, iron deficiency, and hypoxia downregulate hepcidin. Elevated hepcidin is associated with oral iron malabsorption in IBD. On the other hand, animal studies showed that iron deficiency could downregulate hepcidin even in inflammatory states, which leads to the question: which IBD patients should be treated with oral iron, and which patients should be treated with intravenous iron? Can we predict the response to iron therapy in patients with IBD?

Study objective

To evaluate if hepcidin levels can predict response to iron therapy with either ferrous fumarate, ferric maltol, and intravenous iron in patients with IBD.

Study design

Multicenter, prospective, and an exploratory study.

Intervention

A. Ferrous fumarate 2dd 100mg p.o. for 12 weeks
B. Ferric maltol 2dd 30mg p.o. for 12 weeks
C. Intravenous iron: dosage based on instructions on the national formulary 'Farmacotherapeutisch Kompas'

Study burden and risks

The risk for study subjects is negligible because patients do not run additional risk compared to standard care. Even outside the context of the study, patients would have to get their blood and stool samples tested as part of their IBD-care; in addition, they would need iron therapy for iron deficiency. Because patients need iron therapy, there is a risk of side effects or allergic reactions. These side effects are generally mild and reversible (e.g., constipation, tarry stool, or abdominal pain). Blood tests for study measurements will be done at the same time as tests for the standard care; hence, patients will not have an increased risk related to venipuncture. During 24 weeks, patients have to get tested four times, which yields an additional 40ml of blood for each blood withdrawal; however, the total amount of withdrawn blood volume is negligible and it will not increase patient's risk. In addition, delivering stool samples is not invasive and serves no risks to patients. Last but not least, patients will have to fill out three questionnaires over the course of the study. The questionnaires are short and not intrusive, it will take about 60 minutes to fill out all study

questionnaires.

It is known that iron deficiency and anemia are frequent and recurrent problems in patients with IBD. Given that this is a study with a negligible risk, we think it is justified to perform this study. The results may lead to personalized iron therapy in patients with IBD.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Established IBD diagnosis (Crohn's disease, ulcerative colitis, IBD-unclassified) - Adults (>=18 years of age) - Active IBD (defined as biochemical activity CRP >5 mg/L and/or FCP >150 mg/kg or as any endoscopic or radiologic disease activity) - Iron deficiency anemia (defined as ferritin <100 ug/l and hemoglobin <7.5 mmol/l for females or <8.5 mmol/l for males) or iron

deficiency (defined as ferritin <100 ug/l and transferrin saturation <20%) - Documented informed consent

Exclusion criteria

- Blood transfusion or therapy with oral and/or intravenous iron in the past eight weeks - Documented intolerance to oral or intravenous iron - Severe anemia (defined as hemoglobin <6.2 mmol/l for females and males) - Documented history of liver cirrhosis, heart failure, hemoglobinopathies, autoimmune hemolytic anemia, myelodysplastic syndrome, or chronic obstructive pulmonary disease (COPD) - Documented history of recent treatment for a malignancy (excluding dermatological malignancies such as basal cell carcinoma or squamous cell carcinoma). Patients can be included if the treatment for malignancy has been finalized >=6 months before the inclusion date. - Documented history of bariatric surgery or gastric/duodenal resections due to benign or malignant pathologies - End-stage renal disease (impaired renal function, defined as eGFR <30 ml/min/1.73m2) - Folic acid or vitamin B12 deficiency in combination with a macrocytic anemia (Mean Corpuscular Volume >100 fL + Hb <7.5 mmol/L for females or Hb <8.5 mmol/L for males) - Documented pregnancy or breastfeeding at the time of inclusion - Documented major operation (e.g., laparotomy) less than six weeks before inclusion - Unable to give informed consent due to inability to understand Dutch language or incapacitation (e.g., due to cognitive/psychological conditions or hospitalization in Intensive Care)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-06-2022
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CosmoFer
Generic name:	iron(III)-hydroxide dextran complex
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Feraccru
Generic name:	ferric maltol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ferinject
Generic name:	FERRIC CARBOXYMALTOSE
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ferrous fumarate TEVA
Generic name:	ferrous fumarate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Monofer
Generic name:	Ferric derisomaltose
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-03-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	04-05-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	24-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	01-07-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2022-000894-16-NL
CCMO	NL79105.058.22

Study results

Date completed: 20-12-2024

Summary results
Trial ended prematurely