INTRAVENOUS IRON TO TREAT POSTOPERATIVE ANEMIA IN OLDER CARDIAC SURGERY PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON56336

Source
ToetsingOnline

Brief title
AGE anemia

Condition

- Cardiac therapeutic procedures

Synonym
low red blood cell count after surgery, postoperative low hemoglobin

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis

Source(s) of monetary or material Support: Pharmacosmos,Sint Antonius onderzoeksfonds

Intervention

Keyword: anemia, cardiac surgery, elderly

Outcome measures

Primary outcome

Primary endpoint is disability as measured by the 12- item World Health Organization Disability Assessment score 2.0 (WHODAS-12 at POD 90 after elective cardiac surgery.

Secondary outcome

Secondary endpoints are change in patient reported outcome measures (PROMs) related to dyspnea (assessed with the Rose Dyspnea Score (RDS)) and to health-related quality of life (HRQL) (assessed with The Older Persons and Informal Caregivers-Short Form (TOPICS-SF) questionnaire) at POD 90, the number of postoperative red blood cell (RBC) transfusions, change in reticulocyte hemoglobin content (pg) from randomization to hospital discharge, Hb levels at discharge, hospital complications and days alive and out of hospital at 90 days. Lastly, the difference in functional outcomes (e.g. steep ramp or 6-minute walk test) and Hb value at POD 90 will be assessed as an exploratory endpoint.

Study description

Background summary

Postoperative anemia is common in cardiac surgery with cardiopulmonary bypass.

Iron deficiency delays the recovery from postoperative anemia and may negatively affect the postoperative trajectory of cardiac surgery patients.

Study objective

This study has been transitioned to CTIS with ID 2024-515920-35-01 check the CTIS register for the current data.

To determine the effect of treatment of postoperative iron deficiency anemia (IDA) with intravenous iron (IVI) on disability 90 days after cardiac surgery.

Study design

Randomized placebo-controlled double blind multicenter trial.

Intervention

Postoperative treatment with a single dose IVI (ferric derisomaltose, Monofer®, N = 155) compared to postoperative treatment with sodium chloride 0.9% (placebo, N = 155).

Study burden and risks

Study related benefits:
Anemia after cardiac surgery is very common and causes fatigue and lethargy, which impairs recovery. Treatment of anemia with oral iron tablets takes several months to increase RBC counts and is often not well tolerated due to side effects, such as stomach pain and constipation. IVI has minimal side effects and treatment consists of a single gift (which takes approximately 60 minutes). IVI has a proven positive effect on Hb values in the postoperative trajectory, and so it is our expectation that patients who receive IVI will have a faster recovery and experience less postoperative disability.

Study related risks: Ferric derisomaltose is an IV therapy approved by the European Medicines Agency (EMA) for treatment of iron deficiency where oral iron cannot be used or there is a need for rapid delivery of iron. Ferric derisomaltose was originally approved in the European Union (EU) in 2009, and it has been available in the Netherlands since 2009 with the trade name Monofer. All IVI preparations carry a small risk for acute severe hypersensitivity reactions. Other less severe manifestations of immediate hypersensitivity, such as urticaria and itching may also occur. In a review of the safety of IV iron preparations that included ferric derisomaltose, the EMA concluded that the benefit-risk balance of intravenous iron containing medicinal products is favorable as the benefits outweigh the risks in the treatment of iron deficiency when used under their current indications. Ferric derisomaltose will be used within its approved indication in the study, and

subsequently the risks associated with the treatment are considered low. Furthermore, for this study an additional blood sample is required. Risks of venepuncture are minimal and limited to blood loss, fainting, infection and multiple attempts to locate a vein.

Extent of the burden
Control group: standard preoperative care, additional assessment of questionnaires for disability (12-item WHODAS 2.0), HRQL (TOPICS-SF) and cardiac symptoms (RDS), standard ICU admission after cardiac surgery, screening for postoperative IDA on POD1 (i.e. assessment of iron status), intravenous treatment with placebo on POD1 in the ICU (total duration of administration and monitoring approximately 90 minutes. Note: this will not prolong routine ICU admission), standard hospital follow-up for complications, venepuncture for study related blood sample at hospital discharge, additional follow-up with questionnaires for disability (12-item WHODAS 2.0), HRQL (TOPICS-SF) and cardiac symptoms (RDS) at POD 90. At 90 days, the results from the functional tests (e.g. steep ramp test or 6-minute walk test) that are routinely performed during standardized cardiac rehabilitation programs in both hospitals are requested through the treating physical therapist. Furthermore, laboratory results (i.e. Hb values) will be requested (if available) from treating cardiologists when patients have visited the out-patient clinic for follow-up.
Intervention group: standard preoperative care, additional assessment of questionnaires for disability (12-item WHODAS 2.0), HRQL (TOPICS-SF) and cardiac symptoms (RDS), standard ICU admission after cardiac surgery, screening for postoperative IDA on POD1 (i.e. assessment of iron status), intravenous treatment with IVI (ferric derisomaltose) on POD1 in the ICU (total duration of administration and monitoring approximately 90 minutes. Note: this will not prolong routine ICU admission), standard hospital follow-up for complications, venepuncture for study related blood sample at hospital discharge, additional follow-up with questionnaires for disability (12-item WHODAS 2.0), HRQL (TOPICS-SF) and cardiacsymptoms (RDS) at POD 90. At 90 days, the results from the functional tests (e.g. steep ramp test or 6-minute walk test) that are routinely performed during standardized cardiac rehabilitation programs in both hospitals are requested through the treating physical therapist. Furthermore, laboratory results (i.e. Hb values) will be requested (if available) from treating cardiologists when patients have visited the out-patient clinic for follow-up

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

• Mentally competent with age >= 70 years
• Elective aortic valve replacement or coronary artery surgery
• Expected uncomplicated postoperative trajectory, defined as:
- No inotropic agents or ventilation at time of final inclusion (day 1)
- Expected discharge to general ward at day 1
• Moderate postoperative iron deficiency anemia, defined as:
- Hb between 85 and 110 g/L and
- Ferritin <100 µg/L or
- Iron saturation < 20%

Exclusion criteria

• Medical history of iron overload/haemochromatosis
• Medical history of liver cirrhosis or ALT/AST value in blood serum triple of normal value (female patients: ALT >120, AST >105 U/L. Male patients: ALT>150, AST>135 U/L)
• Severe renal failure (eGFR<15ml/min/1.73m2)
• Recent treatment with IVI (<12 weeks prior)
• Serious or severe allergic reaction to IVI in medical history

• Severe asthma or eczema in medical history (atopic constitution)

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:	Recruiting
Start date (anticipated):	08-12-2021
Enrollment:	310
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Monofer
Generic name:	ferric derisomaltose
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	26-07-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	30-03-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EU-CTR	CTIS2024-515920-35-01
EudraCT	EUCTR2021-001949-12-NL
ClinicalTrials.gov	NCT04913649
CCMO	NL77442.100.21