The immunomodulatory effects of phlebotomy

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To assess the ex vivo cytokine production of whole blood during 28 days after phlebotomy (routine withdrawal of 500 ml of blood).

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

Summary

ID

NL-OMON41161

Source
ToetsingOnline

Brief title
The immunomodulatory effects of phlebotomy

Condition

- Haematological disorders NEC
- Immunodeficiency syndromes

Synonym
blood loss, hemorraghe

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cytokines, Innate immunity, Iron homeostasis, Phlebotomy

Outcome measures

Primary outcome

Change in ex vivo TNF-* production of whole blood, induced by incubation with LPS, on day -1, 0, 1, 3, 5, 7, 14, 21 and 28 following the withdrawal of 500 ml of blood at the blood bank.

Secondary outcome

- the change in ex vivo production of other cytokines (IL-6, IL10) of whole blood elicited by incubation with LPS, on day -1, 0, 1, 3, 5, 7, 14, 21 and 28 following the withdrawal of 500 ml of blood at the blood bank.

- Changes in hemoglobin, hematocrit, white blood cell count and differential on day -1, 0, 1, 3, 5, 7, 14, 21 and 28 following the withdrawal of 500 ml of blood at the blood bank.

- Changes in plasma hepcidin concentration in the 28 days following the withdrawal of 500 ml of blood at the blood bank

- Changes in other markers of iron homeostasis (serum iron, transferrin saturation, ferritin) in the 28 days following the withdrawal of 500 ml of blood at the blood bank

Study description

Background summary

The loss of blood by haemorrhage or routine phlebotomy as performed during blood donation by healthy volunteers, has large effects on systemic iron

homeostasis. The relative shortage of erythrocytes after blood loss is compensated for by increasing the production of new red cells by the bone marrow. As iron is needed for effective haemoglobin synthesis, the transport of iron to the bone marrow needs to be increased. This is accomplished by the suppression of hepcidin production in the liver. Hepcidin is the central regulator of iron homeostasis. It can regulate serum iron levels effectively by downregulating iron channel ferroportin on iron exporting cells. Hepcidin production is increased in response to inflammation en high systemic iron content, and is suppressed by increased erythrocyte production, hypoxia, anemia, and low systemic iron content. Therefore, blood loss leads to hepcidin suppression, increased release of iron into the circulation and decrease of iron stores.
Alterations in iron metabolism can have immunomodulatory effects. The intra cellular iron content in macropahges and monocytes, has shown pro-inflammatory effects in several investigations. Hepcidin is reported to have pro-inflammatory effects in some reports, and anti-inflammatory effects in others.
Although phlebotomy is routinely performed in blood donors, and seemingly does not have significant health risks, it is highly relevant to know what the effect of phlebotomy is on immunity. Alterations in immunity due to phlebotomy could have beneficial effects, like the suppression of the low grade inflammatory process that contributes to atherosclerosis, but in theory could also contribute to a suppressed innate immune response that could increase the risk of infection. This is not only relevant for blood donors, but also for patients suffering from blood loss and for daily clinical practice in which blood is routinely drawn of patients for laboratory determinations.

Study objective

To assess the ex vivo cytokine production of whole blood during 28 days after phlebotomy (routine withdrawal of 500 ml of blood).

Study design

Prospective intervention study in 10 healthy male volunteers.

10 healthy volunteers will donate 500 mL at the blood bank, according to normal procedures (day 0).

On day -1, 0, 1, 3, 5, 7, 14, 21 and 28 blood will be drawn for the determination of:
- ex vivo cytokine production (TNF-alfa, IL-6, IL-10).
- hemoglobin, hematocrit and leucocyte differentiation.
- hepcidin.
- Iron parameters (serum iron, transferrin saturation, ferritin).

Intervention

Phlebotomy (withdrawal of 500 mL volbloed)

Study burden and risks

The study consists of 11 visits:
- 1 screening visit
- 1 phlebotomy visit
- 9 follow-up visits

At the screening, a questionaire will be filled out by the subject, and a short physical examination will be performed.

At the visit for phlebotomy at the blood bank, another questionaire will be filled out for registration purposes at the blood bank. Also, the hemoglobin level will be checked. Then, a vene in the elbow will be puntured and 500 mL of blood will be withdrawn.

At the follow-up visits, each time 2 tube of blood will be drawn (7 mL total). Also, subjects will be questioned for the occurence of adverse events, especially regarding intercurrent infections.

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

- Male
- Age >18 and <36 years
- Healthy as concluded from medical history

Exclusion criteria

- Having donated blood to the blood bank within one year preceding phlebotomy
- Significant blood loss from trauma within one year preceding phlebotomy
- Having lost > 100 ml of blood due to any cause, within 3 months preceding phlebotomy (not counting blood withdrawn during screening visit)
- Having lost > 50 ml of blood due to any cause, within 1 month preceding phlebotomy (not counting blood withdrawn during screening visit)
- Having lost >20 ml blood due to any cause, within 1 week preceding phlebotomy (not counting blood withdrawn during screening visit)
- Family history of thallasemia, sickle cell disease, hereditary hemochromatosis, or iron refractory iron deficiency anemia
- Signs of history of infection within 2 weeks preceding phlebotomy
- History of frequent vasovagal response

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-03-2014
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	17-03-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
ClinicalTrials.gov	NCTnummervolgt
CCMO	NL47674.091.14