The sequestration pattern of thrombocytes in healthy adults: results of the ITP liver and spleen scan.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Platelet disorders
Study type	Observational invasive

Summary

ID

NL-OMON54593

Source
ToetsingOnline

Brief title
Sequestration Pattern Of Thrombocytes in healthy adults (SPOT)

Condition

- Platelet disorders
- Autoimmune disorders

Synonym
Immune Trombocytopenia (ITP)

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: HagaZiekenhuis

Intervention

Keyword: Healthy adults, ITP, ITP liver/spleen scan, Sequestration pattern

Outcome measures

Primary outcome

The platelet sequestration pattern (% splenic, % hepatic, %mixed) in healthy subjects.

Secondary outcome

Platelet counts before and after scan (x10^9/ L)

Platelet half life (in hours)

Mean platelet life span (in hours)

Mean platelet turnover (in hours)

Labelling percentage (in %)

Percentage of platelets remaining in the circulation after 48 hours (in %)

Differences between sequestration patterns in healthy adults an ITP patients (in S:L ratio)

Differences between sequestration patterns in heathy individuals over time (in S:L ratio)

Study description

Background summary

Splenectomy is a commonly used second line therapy for Immune Thrombocytopenia (ITP). Several studies have shown that outcome of spleen-liver scans are associated with treatment success after splenectomy. These spleen-liver scans analyze the sequestration pattern of labeled thrombocytes. The limited evidence available shows that a splenic sequestration pattern is associated with a high rate of treatment success (88%), a mixed splenic/hepatic pattern with an

intermediate rate of treatment success (55%) and a hepatic pattern with a low (16%) rate of treatment success after a splenectomy. The pathophysiology is still unknown. Furthermore, these studies only investigated sequestration patterns in patients with ITP. To the best of our knowledge, no studies on platelet sequestration pattern has been conducted in healthy adults. To gain insight in the mechanisms of platelet destruction and the pathophysiology of treatment success it is important to compare healthy adults with ITP patients. Until now, no studies have been performed concerning the pattern of platelet destruction in healthy subjects and the role of the spleen and liver in this process. Gaining insight into the platelet sequestration patterns in healthy adults allows us to compare these results with those of ITP patients and be able to classify the pattern as *normal* or *deviant*, which might give more insight into platelet destruction characteristics of ITP patients. Moreover, there are currently insufficient data available to evaluate whether these platelet sequestration patterns could change over time spontaneously. This information could shine a new light on the physiology of the lifespan of platelets as well as the use of the ITP liver/ spleen scan as a diagnostic tool in management of ITP.

Study objective

The main objective of this study is to describe the sequestration pattern of platelets in healthy adult volunteers. The secondary objective is to make a comparison between the sequestration patterns in healthy volunteers, and the patterns in ITP patients (as found in previous studies). Moreover, we aim to compare the sequestration pattern of platelets in healthy adults between two different time points.

Study design

This is a prospective cohort study. Ten healthy volunteers will be included in this study. The Participants will undergo an ITP liver/spleen scan. Participants have a follow-up of two months.A screening assessment will be performed to asses the eligibilty of each volunteer for this study. Potential study participants will be interviewed about their clinical history and a blood sample will be taken. If a volunteer is included in the study, they will undergo the ITP liver and spleen scan. The 111-indium scan will be performed at the Haga Teaching Hospital in the Netherlands. Sixty-two ml whole blood will be derived from the study participants (t= 0). In the lab of GE-Health the platelets within this blood sample will be labelled with 111-indium tropolone. Moreover, platelet counts will be determined. Three to four hours after the blood samples are taken the platelets will be reinfused in the patient (t=1). During the first 30 minutes after infusion, dynamic series (both anterior and posterior) and static series will be made (t=2). At 3 hours (t=3), 24 hours (t=4) and 48 hours (t=5) a static study will be made and blood samples of 10 ml will be taken at each time point. Platelet counts (PC) are determined from

these blood samples. After two months, all study participants will be called and asked some follow-up questions.

The procedure for the 2nd ITP liver spleen scan will be largely the same, except for the following:
1) Four additional scans at t= 72 hr, t = 96 hr, t= 120 hr and t = 144 hr will be performed. The scan at t =120 hr and t = 144 hr will take 5 minutes longer than the other scans.
2) A total body scan will be made instead of a scan of only the abdomen.

Patients will again be screened for their eligibility (t=6). During the first day of the ITP liver/ spleen scan blood samples will be taken, platelets will be labelled with 111-indium tropolone, platelets will be reinfused in the study participant and during the first 30 minutes dynamic and static series will be made (t =7,8). At 3 hours (t=9), 24 hours (t=10), 48 hours (t=11), 72 hours (t=12), 96 hours (t=13), 120 hours (t=14) and 144 hours (t=15) a static study will be made and blood samples of 10 ml will be taken at each time point. After 2 months, the study participants will be called and asked some follow-up questions (t=16).

Study burden and risks

This study investigates the platelet sequestration pattern in healthy subjects. In this study the subjects will be exposed to a radiation of 1.56 mSV during the ITP liver/ spleen scan. However, we do not expect that this dose of radiation will cause any immediate or long term risks. The radiation dose is safe and relatively low compared to the dose of a CT-scan of the abdomen and pelvis is 10 mSv. Furthermore, the background radiation in the Netherlands is about 2.5 mSv per year. No (severe) adverse events have been seen in ITP patients who underwent the scan for diagnostic purposes. Besides the extra radiation, blood samples will be taken from the study participants. The required vena punction is commonly performed in general practice and almost no adverse events are seen in healthy subjects. Hence, to our best knowledge, we expect patients not to be exposed to any (serious) hazard in this protocol.

For the 2nd phase of the study the exposure to radioactive isotopes will be the same as the first indium-111 scan, as the same dose of indium-111 labelled platelets will be administered. Hence, there is no additional radiation exposure compared to the standard scan protocol (1st ITP Liver/ Spleen scan). Even though the study participants will undergo the ITP liver/spleen scan for the 2nd time after 2 years, the total doses will be relatively low (1.56 mSv) compared the standard CT thorax/ abdomen (10 mSv). Hence, we do not expect the 2nd dose of radiation will cause immediate or long-term risk for the study participants.

Except gathering knowledge about their own sequestration pattern, there is no direct benefit for the healthy subjects participating in this trial. However,

this study will be of great value to extend the knowledge about the normal platelet sequestration pattern in healthy subjects. This information can be of importance for the research to ITP and its pathogenesis. Moreover, this study can potentially contribute in the development and improvement of diagnostics and clinical decision making for patients with ITP.

Contacts

Public
HagaZiekenhuis

Els Borst-Eilersplein 275
Den Haag 2545 AA
NL
Scientific
HagaZiekenhuis

Els Borst-Eilersplein 275
Den Haag 2545 AA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy, as determined by screening assessments and judgement of researchers
>18 years old
Informed consent

Exclusion criteria

Pregnancy or planning to become pregnant during the study period
Liver disease (Child Pugh >7)
Hematological/ platelet/ bone marrow disease in history or in co-existence
Autoimmune disease in history or in co-existence
Transplantation in history
(Partial) splenectomy in history
Any other clinically relevant history as determined by screening assessments and the judgement of the researchers , •(Suspected) allergy to one of the isotopes or contents used for platelet scintigraphy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-04-2021
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
Approved WMO Date:	16-07-2020

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
Approved WMO Date:	23-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
Approved WMO Date:	26-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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
CCMO	NL69208.098.19

Study results

Date completed:	30-01-2024
Actual enrolment:	10