The TIKI study: Treatment with or without IVIG in Kids with acute ITP.

No registrations found.

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

Summary

ID

NL-OMON19894

Source
NTR

Brief title
TIKI

Health condition

English: acute immune thrombocytopenic purpura, ITP.
Nederlands: acute idiopathische thrombocytopenische purpura, ITP.

Sponsors and support

Primary sponsor: University Medical Center Utrecht (UMCU), Wilhelmina Children's Hospital (WKZ)
Source(s) of monetary or material Support: WKZ fonds, Landsteiner Foundation

Intervention

Outcome measures

Primary outcome

- Main study parameter is the percentage of patients developing chronic ITP, defined by a

platelet count of < 150 x 10^9/l six months after diagnosis.

Secondary outcome

- Clinical parameters during the course of the disease, eg: bleeding score graded according to the revised grading system developed by Buchanan, and time between onset of symptoms and recovery of platelet numbers.

- Comparing the HRQoL in parents and patients with acute ITP who did and did not have IVIG and in those that do and do not develop chronic ITP.

- Estimation of variability of biological parameters of the immune system of the patient that are supposed to be involved in the differences in outcome between acute vs. chronic disease as well as between response on IVIG treatment vs. non response. These include:

A) the genetic polymorphisms of the activating and inhibiting IgG-Fc receptor and other inhibiting immune receptors.

B) Immunoglobulin glycosylation variability within the platelet auto antibodies and its changes during time, as well as the changes due to IVIG treatment.
C) Quantity and function of regulatory T cells.

Study description

Background summary

Rationale:
Acute idiopathic thrombocytopenic purpura (ITP) in childhood is characterized by auto-immune destruction of platelets and a typical history of acute development of purpura and bruising in an otherwise healthy child. The incidence in The Netherlands is approximately 120-150 newly diagnosed children per year.

In The Netherlands, according to the current guidelines, the management of acute ITP in children consists mainly of careful observation. Only in case of severe bleeding, occurring in about 2-3% of all patients, treatment with corticosteroids or intravenous immunoglobulin (IVIG) has to be instituted. Most children with newly diagnosed ITP will recover within 6 months. Nevertheless, thrombocytopenia has a major influence on daily life activities, because all activities which carry a risk of causing severe bleeding have to be avoided. About 25% of the patients will remain thrombocytopenic after 6 months and thus are diagnosed with chronic ITP.

The incidence of bleeding correlates well with the duration of the thrombocytopenia and thus with chronic disease.

In a previous prospective observational study we found a significant reduction of relative risk of developing chronic disease in children treated with IVIG in the acute phase. These results are supported by data of the international ITP registry, a recent meta-analysis and research in mice.

Objective:
The primary objective is to investigate to what extent early IVIG treatment in children with newly diagnosed acute ITP reduces the risk of development of chronic disease. Secondary objectives are:
1) To estimate the alteration in the clinical parameters during the course of the disease, eg: bleeding score and time between onset of symptoms and recovery of platelet numbers.
2) To measure the difference between the health-related quality of life (HRQoL) in parents and patients with acute ITP who did and did not have IVIG and in those that do and do not develop chronic ITP.
3) To study biological parameters to learn more about the pathogenesis of ITP and of the working mechanism of IVIG.

Study design:
The study comprises a randomized controlled intervention study in which patients with newly diagnosed acute ITP will be randomized to receive either standard treatment, namely careful observation without medication, or intervention with IVIG treatment.

Study population:
Children aged 3 months-16 years (according to the International ITP registry (ICIS) criteria) with newly diagnosed ITP presenting to a pediatrician without severe bleeding, and with platelets < 20 x 10^9/l and no prior immunomodulating treatment within 4 weeks before diagnosis.

Intervention:
Patients in the intervention arm will receive IVIG 0.8 g/kg once, within three days of diagnosis. Patients in the control arm will have careful observation and will only receive medication (IVIG, prednisone) in case of severe bleeding. In all patients clinical data and blood samples will be collected at diagnosis, 1 and 4 weeks and 3, 6 and 12 months after diagnosis. Questionnaires regarding quality of life will be obtained at the same time points.

Main study parameters/endpoints:
Primary outcome of the study is the development of chronic ITP, defined by a platelet count < 150 x10^9/L six months after presentation with thrombocytopenia. Secondary parameters are

1) bleeding score according to Buchanan,
2) time in weeks to reach recovery of platelets;
3) HRQoL in children with acute ITP and their parents
4) genetic polymorphisms of FcãR's and other inhibiting immune-receptors;
5) Glycosylation patterns of anti-platelet-antibodies and the changes in these patterns during time;
6) Quantity and function of regulatory T cells.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients in the intervention arm of the study will receive IVIG. They will need an intravenous canule. The administration of IVIG carries only a minor risk of adverse reactions, of which headache is the most common. Secondly, IVIG is a human blood product, of which a minor risk of transmission of viruses that are not yet known to us cannot be excluded.

At time points 0, 1 week, 4 weeks, 3, 6 and 12 months all parents, and, from the age of seven years also patients, will be asked to fill out a questionnaire regarding HRQoL. At the same time points also a history and physical examination will be done and blood samples will be taken. This frequency of blood sampling and physical examination is not different from regular management of acute ITP. The volume of the blood samples for the study involves a total of 60-100 ml over a period of one year. This amount is so limited that adverse consequences for patients are not to be expected.

Acute ITP in children is a different disease than ITP in adults with regard to clinical course, as well as presumed etiology. The response to immunomodulating treatment also differs between children and adults with ITP. Therefore, to answer our questions, this study cannot be performed in an adult population.

Study objective

The primary objective is to investigate to what extent early IVIG treatment in children with newly diagnosed acute ITP reduces the risk of development of chronic disease.

Secondary objectives are:

1. To estimate the alteration in the clinical parameters during the course of the disease, eg: bleeding score and time between onset of symptoms and recovery of platelet numbers.

2. To measure the difference between the health-related quality of life (HRQoL) in parents and patients with acute ITP who did and did not have IVIG and in those that do and do not develop chronic ITP.
3. To study biological parameters to learn more about the pathogenesis of ITP and of the working mechanism of IVIG.

Study design

At diagnosis, after 1 week, 1 month, 3 months, 6 months and 12 months.

Intervention

The intervention consists of one dose of 0.8 g/kg bodyweight Nanogam ®, a liquid intravenous immunoglobulin, manufactured by Sanquin.

Besides the primary intervention, quality of life questionnaires and laboratory studies will be performed.

Contacts

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Eligibility criteria

Inclusion criteria

General inclusion criteria:

1. Children aged 3 months -16 years, presenting to a pediatrician with newly diagnosed acute ITP

2. Platelet count < 20 x 10 9 /L

3. Bleeding tendency < grade 4 (Buchanan)

4. No prior immunomodulating treatment within 4 weeks before diagnosis

5. Sufficient comprehension of the Dutch language

6. Signed informed consent by parents and/ or patients

Exclusion criteria

General exclusion criteria:

1. Clinical features that are not compatible with the diagnosis of acute ITP, for example: presence of other auto-immune phenomena, organomegaly, other cytopenias besides thrombocytopenia or features susceptible for infectious disease like hepatitis, Epstein-Barr virus or HIV

2. Immunomodulating treatment (IVIG, corticosteroids) within 4 weeks before diagnosis

3. History of allergic reactions against human plasma, plasma products or intravenous immunoglobulin

4. Severe or life threatening bleeding at presentation: grade 4 or 5 (Buchanan)

5. A patient known with IgA deficiency with IgA antibodies

6. A patient known with renal insufficiency

7. Insufficient comprehension of the Dutch language

8. No informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2009
Enrollment:	200
Type:	Actual

Ethics review

Positive opinion

Date:	26-11-2008
Application type:	First submission

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
NTR-new	NL1493
NTR-old	NTR1563
Other	METC UMCU : 08-162
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results

Blood. 2018 Jun 26. pii: blood-2018-02-830844. doi: 10.1182/blood-2018-02-830844. [Epub ahead of print]
Intravenous immunoglobulin versus observation in childhood immune thrombocytopenia: a randomized controlled trial.
Heitink-Pollé KMJ1, Uiterwaal CSPM2, Porcelijn L3, Tamminga RYJ4, Smiers FJ5, van Woerden NL6, Wesseling J7, Vidarsson G8, Laarhoven AG8, de Haas M9, Bruin MCA10.