Development of chronic disease in newly diagnosed Idiopathic Thrombocytopenic Purpura of Childhood. A randomized controlled study on the influence of treatment with intravenous gammaglobulin on the course of the disease.

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To test the hypothesis that IVIG treatment diminish the risk of development of chronic disease, we designed a prospective clinical intervention study in children with newly diagnosed ITP.

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

Summary

ID

NL-OMON38126

Source
ToetsingOnline

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

Condition

- Platelet disorders

Synonym
idiopathic thrombocytopenic purpura, shortness of platelets due to increased destruction

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Sanquin Plasma Producten, echter alleen door kostenloze aanvulling van de voorraad Nanogam indien nanogam is gebruikt voor een studiepatiënt.,WKZ onderzoeksfonds;echter alleen via vergoeding voor parttime aanstelling onderzoeker.

Intervention

Keyword: chronic, immunoglobulin, ITP, quality of life

Outcome measures

Primary outcome

Primary outcome of the study is development of chronic disease, defined by

platelet count < 150 x10^9/L after six months.

Secondary outcome

- clinical parameters: bleeding tendency, time to recovery of platelet count

- quality of life of patients with ITP

- laboratory studies: genetic polymorphisms of IgG-Fc receptors and inhibiting

immune receptors, auto-antibody profile, glycosylation of auto-antibodies,

quantity and function of regulatory T cells.

Study description

Background summary

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 is about 5 in 100,000 children per year.
Management of acute ITP consists of carefull observation. Only in case of

severe bleeding treatment with corticosteroids or intravenous immunoglobulin has to be instituted. The advantage of IVIG over steroids is the lack of influence on diagnostic procedures in case of a wrong diagnosis, especially if malignancy is the cause of thrombocytopenia.
Most children with newly diagnosed ITP will not suffer from serious bleedings and will recover within 6 months. Nevertheless, thrombocytopenia has a major influence on daily life activities, because all activities which have a risk of causing severe bleeding have to be avoided. A group of about 25% of the patients will remain thrombocytopenic after 6 months and thus are diagnosed with chronic ITP. 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 confirmed by data of the international ITP registry, a recent meta-analysis and research in mice.

Study objective

To test the hypothesis that IVIG treatment diminish the risk of development of chronic disease, we designed a prospective clinical intervention study in children with newly diagnosed ITP.

Study design

The study comprises a randomised intervention study in which patients with newly diagnoses acute ITP will be randomised to receive standard treatment, namely carefull observation without medication, or intervention with IVIG treatment.

Intervention

Patients in the intervention arm will receive IVIG 0.8 g/kg once, within three days of diagnosis. 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 timepoints.

Study burden and risks

Patients in the intervention arm of the study will receive IVIG regardless of bleeding tendency. They will need an intravenous canule. There is a small risk of adverse reactions. The most important adverse reactions is an allergic reaction. The involved pediatricians will get proper instructions to recognize and treat these adverse reactions.
All parents and patients aged sveen years and older will be asked to fill out a short questionaire regarding quality of life.

Frequention of taking history, physical examination and blood samples is not different from regular management of acute ITP. The quantity of blood samples is more than during regular treatment. However, this quantity is limited, so adverse consequences for patients are not to be expected.
Because of the minimal risk of the research project and the limited burden for patients and parents, we have judged that the benefits of the project outweigh these risks. The benefits for patients in the intervention arm are: a temporary increase of platelet counts and therefore a decreased risk of severe bleeding. For patients in the control arm there will be extra attention for quality of life aspects.
If patients do not develop chronic ITP, benefits are evident: no limits in physical activities anymore and a strongly reduced risk of bleeding, which will significantly improve quality of life in patients as well of parents.

Contacts

Public
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584 EA
NL
Scientific
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584 EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Children (2-11 years)

Inclusion criteria

General inclusion criteria
- Children aged 3 months -16 years, presenting to a pediatrician with newly diagnosed acute ITP and
- Platelet count < 20 x 10 9 /L and
- Bleeding tendency < grade 4 (Buchanan) and
- no prior immunomodulating treatment within 4 weeks before diagnosis and
- signed informed consent by parents and/ or patients

Exclusion criteria

A patient presenting with any of the following criteria will not be included in the study:;General exclusion criteria
- 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
- immunomodulating treatment (IVIG, corticosteroids) within 4 weeks before diagnosis
- history of allergic reactions against human plasma, plasma products or intravenous immunoglobulin
- Severe or life threatening bleeding at presentation: grade 4 or 5 (Buchanan)
- No informed consent

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-05-2009
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nanogam
Generic name:	Human Normal immunoglobulin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-11-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-03-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-06-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-07-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-07-2009

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-07-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-02-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-08-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-08-2012

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2008-001597-33-NL
CCMO	NL18055.041.08
Other	TC 1563 (NTR)