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Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome: the PREDNOS 2 study

Submission date
25/10/2012

Recruitment status
No longer recruiting

Registration date
26/10/2012

Overall study status
Completed

Last Edited
24/01/2022

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary:
Background and study aims
Steroid-sensitive nephrotic syndrome (SSNS) is the most common kidney disease of childhood. Large amounts of protein are leaked into the urine resulting in generalised oedema (swelling). It is treated with high-dose oral prednisolone, a steroid drug which is effective, though associated with a number of serious side effects. Following successful initial treatment, 70-80% of children develop relapses where leakage of protein into the urine recurs. These are associated with a risk of significant complications. Relapse of nephrotic syndrome is treated with a further course of high-dose prednisolone, further increasing the risk of side effects. Children are kept off school, resulting in educational impairment and parental absence from work. Around 50% of children suffer frequent relapses (four or more per year). In this situation, attempts are made to reduce prednisolone exposure using other more potent drugs such as ciclosporin and cyclophosphamide, which are associated with other significant side effects. It is therefore logical to attempt to reduce the frequency of relapses. There is known to be a strong link between viral upper respiratory tract infection (URTI, the common cold) and the development of relapse of nephrotic syndrome. Three previous small studies have suggested that the use of a short course of daily prednisolone at the time of URTI reduces the rate of disease relapse. This study aims to find out whether the use of such therapy effectively and safely reduces the rate of relapse in a large population of UK children.

Who can participate?
Participants aged over 1 year and less than 19 years will be eligible if they have relapsing SSNS, defined as having experienced two or more relapses in the previous 12 months.

What does the study involve?
We will randomly allocate 300 children with relapsing SSNS to receive either 6 days of daily prednisolone or continue unchanged on their existing therapy (the current standard of care) each time they develop a URTI over a 12-month period. We will assess the frequency of URTI-

related relapse of nephrotic syndrome in both groups and look carefully for side effects of treatment. The 300 participants will be recruited from over 100 UK hospitals.

What are the possible benefits and risks of participating?
Participants will receive a 6-day course of prednisolone each and every time they develop an URTI over the 12-month study period. There is the risk that this course of action will increase overall steroid exposure without reducing relapse rate. We will be monitoring patients every 3 months and will carefully document side effects, including impact on behaviour. Those children who experience steroid toxicity during the course of the study will have their background immunosuppressive treatment enhanced in an attempt to reduce relapse frequency. There will be no additional study visits for the purposes of the study alone. The three monthly visits are in keeping with routine care in children with relapsing nephrotic syndrome.

Where is the study run from?
Birmingham Clinical Trials Unit (UK). A list of over 100 sites can be found at https://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/renal/prednos2/investigators/recruitment.aspx

When is the study starting and how long is it expected to run for?
Recruitment will begin in early 2013 and continue for a 2-year period. Each subject will be followed-up every 3 months over a period of 1 year which is in keeping with routine clinical practice. The study will run for a total of 4 years.

Who is funding the study?
The National Institute for Health Research (NIHR) Health Technology Assessment programme.

Who is the main contact?
Dr Martin Christian (Chief Investigator)
Martin.Christian@nuh.nhs.uk)

Previous plain English summary:
Background and study aims
Steroid-sensitive nephrotic syndrome (SSNS) is the most common kidney disease of childhood. Large amounts of protein are leaked into the urine resulting in generalised oedema (swelling). It is treated with high-dose oral prednisolone, a steroid drug which is effective, though associated with a number of serious side effects. Following successful initial treatment, 70-80% of children develop relapses where leakage of protein into the urine recurs. These are associated with a risk of significant complications. Relapse of nephrotic syndrome is treated with a further course of high-dose prednisolone, further increasing the risk of side effects. Children are kept off school, resulting in educational impairment and parental absence from work. Around 50% of children suffer frequent relapses (four or more per year). In this situation, attempts are made to reduce prednisolone exposure using other more potent drugs such as ciclosporin and cyclophosphamide, which are associated with other significant side effects. It is therefore logical to attempt to reduce the frequency of relapses. There is known to be a strong link between viral upper respiratory tract infection (URTI, the common cold) and the development of relapse of nephrotic syndrome. Three previous small studies have suggested that the use of a short course of daily prednisolone at the time of URTI reduces the rate of disease relapse. This study aims to find out whether the use of such therapy effectively and safely reduces the rate of relapse in a large population of UK children.

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Who is funding the study?
The National Institute for Health Research (NIHR) Health Technology Assessment programme.

Who is the main contact?
Dr Nicholas Webb (Chief Investigator)
Nicholas.Webb@cmft.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Mr Adam Khan

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-003476-39

Protocol serial number
13410

Study information

Scientific Title
Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome: the PREDNOS 2 study

Acronym
PREDNOS 2

Study objectives
Steroid sensitive nephrotic syndrome (SSNS) is the commonest kidney disease of childhood. Large amounts of protein are leaked into the urine resulting in generalised oedema (swelling). Treatment is with high dose oral prednisolone, a steroid drug which is effective, though associated with a number of serious side effects. Following successful initial treatment, 70-80% of children develop relapses where leakage of protein into the urine recurs. These are associated with a risk of significant complications. Treatment of relapse of nephrotic syndrome is with a further course of high dose prednisolone, further increasing the risk of sideeffects. Children are kept off school, resulting in educational impairment and parental absence from work. Around 50% of children suffer frequent relapses (4 or more per year). In this situation, attempts are made to reduce prednisolone exposure using other more potent drugs e.g. ciclosporin and cyclophosphamide, which are associated with other significant side effects. It is therefore logical to attempt to reduce the frequency of relapses.

There is known to be a strong link between viral upper respiratory tract infection (URTI the common cold) and the development of relapse of nephrotic syndrome. Three previous smalll studies have suggested that the use of a short course of daily prednisolone at the time of URTI reduces the rate of disease relapse. The PREDNOS 2 study aims to determine whether the use of such therapy effectively and safely reduces the rate of relapse in a large population of UKchildren. We will randomise 300 children with relapsing SSNS to receive either 6 days of daily prednisolone or continue unchanged on their existing therapy (the current standard of care) each time they develop a URTI over a 12 month period. We will assess the incidence of URTI related relapse of nephrotic syndrome in both study arms and look carefully for side effects of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West GM Central Research Ethics Committee (REC), Ref. No: 12/NW/0766 - approval pending

Study design
Double blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Steroid sensitive nephrotic syndrome

Interventions
Randomised to receive either 6 days of daily prednisolone or continue unchanged on their existing therapy (the current standard of care) each time they develop a URTI over a 12 month period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Prednisolone

Primary outcome(s)
Current primary outcome measure as of 17/10/2019:
First URTI-related relapse of nephrotic syndrome during the 12-month follow-up period.

Relapse is defined as Albustix positive proteinuria (+++ or greater) for three consecutive days or the presence of generalised oedema plus 3+ proteinuria. URTI-related relapse is defined as a relapse occurring within 14 days of the development of an URTI. First URTI-related relapse refers to the first URTI-related relapse which occurs within the 12-month study follow-up period.

Previous primary outcome measure:
URTI-related relapse of nephrotic syndrome following first URTI during 12 month follow-up period. Relapse is defined as Albustix positive proteinuria (+++ or greater) for 3 consecutive days or the presence of generalised oedema plus 3+ proteinuria. URTI-related relapse is defined as a relapse occurring within 14 days of the development of an URTI. First URTI refers to the first URTI which occurs within the 12 month study follow up period. Relapse will be assessed at each clinic visit which will be every three months for a period of one year in keeping with routine clinical practice.

Key secondary outcome(s))

1. Rate of URTI-related relapse of nephrotic syndrome (relapses per year)
2. Rate of relapse (URTI-related and non URTI-related) of nephrotic syndrome (relapses per year)
3. Cumulative dose of prednisolone (mg/kg and mg/m2) received over the 12 month study period
4. Incidence of SAEs
5. Incidence of adverse effects of prednisolone including assessment of behaviour using the Achenbach Child Behaviour Checklist
6. Incidence of escalation of background immunosuppressive therapy (e.g. addition of ciclosporin, tacrolimus, cyclophosphamide etc.)
7. Incidence of reduction of background immunosuppressive therapy (i.e. cessation of long term maintenance prednisolone therapy)
8. Quality of life using the CHU-9D, EQ-5D and PedsQL
9. Cost per relapse of nephrotic syndrome
10. Cost per QALY gained

Completion date
31/07/2020

Eligibility

Key inclusion criteria
Subjects aged over 1 year and less than 19 years will be eligible for inclusion if they have relapsing SSNS, defined as having experienced 2 or more relapses in the preceding 12 months. This will include the following groups:
1. Subjects on no longterm immunosuppressive therapy
2. Subjects receiving long term maintenance prednisolone therapy at a dose of up to and including 15mg/m2 on alternate days. Note that this is the maximum dose at the time of recruitment. If children subsequently receive a higher dose e.g. after relapse, they can remain in the study.
3. Subjects receiving long term maintenance prednisolone therapy at a dose of up to and including 15mg/m2 on alternate days in conjunction with other immunosuppressive therapies, including levamisole, ciclosporin, tacrolimus, MMF, mycophenolate sodium and azathioprine
4. Subjects receiving longterm immunosuppressive therapies, including levamisole, ciclosporin, tacrolimus, MMF, mycophenolate sodium and azathioprine without long term maintenance prednisolone therapy.
5. Subjects who have previously received a course of oral or intravenous cyclophosphamide:
5.1. Must have experienced two relapses in the 12 months prior to randomisation (in keeping with all other subjects)
5.2. Must have experienced at least one of these relapses following completion of cyclophosphamide therapy
5.3. Must be at least 3 months post completion of oral or intravenous cyclophosphamide therapy
6. Subjects who have previously received a single dose or course of intravenous rituximab:
6.1. Must have experienced two relapses in the 12 months prior to randomisation (in keeping with all other subjects)
6.2. Must have experienced at least one of these relapses following completion of rituximab therapy
6.3. Must be at least 3 months post completion of intravenous rituximab therapy
7. Parents and (where age appropriate) subject understand the definition of URTI and the need to commence study drug once this definition has been met

8. Written informed consent obtained from the subjects parents/guardians and written assent obtained from subject (where age appropriate). Subjects aged 16 years and above will provide their own written informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
1 years

Upper age limit
19 years

Sex
All

Total final enrolment
365

Key exclusion criteria
1. Subjects with steroid resistant nephrotic syndrome
2. Subjects receiving, or within 3 months of completing a course of oral or intravenous cyclophosphamide
3. Subjects receiving, or within 3 months of receiving a course of rituximab
4. Subjects on daily prednisolone therapy at time of recruitment
5. Subjects on a long term maintenance prednisolone dose of greater than 15mg/m2 on alternate days at time of recruitment
6. Subjects with a documented history of significant nonadherence with medical therapy
7. Subjects who will be transferred from paediatric to adult services during the 12 month study period
8. Subjects unable to take prednisolone tablets, even in crushed form
9. Known allergy to prednisolone

Date of first enrolment
01/11/2012

Date of final enrolment
31/01/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Birmingham Clinical Trials Unit
Birmingham
United Kingdom
B15 2TT

Study participating centre
A list of over 100 sites can be found at https://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/renal/prednos2/investigators/recruitment.aspx
United Kingdom
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Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme 11/129/261

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/12/2021	21/12/2021	Yes	No
Results article		01/01/2022	24/01/2022	Yes	No
Protocol article	protocol	27/04/2014		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes