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Multi-centre randomised placebo-controlled trial of corticosteroids in the prevention of coronary artery abnormalities in acute Kawasaki Disease (KD)

Submission date
15/06/2005

Recruitment status
Stopped

Registration date
15/11/2005

Overall study status
Stopped

Last Edited
06/02/2009

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Acronym
CORT-KD

Study objectives
We hypothesise that systemic corticosteroids, when administered early in the course of Kawasaki disease, will reduce the prevalence of Coronary Artery Abnormalities (CAA) at two months (eight to ten weeks) after its onset.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Kawasaki disease (mucocutaneous lymph node syndrome)

Interventions
Patients in the treatment group will receive:
1. Pulsed-dose IntraVenous MethylPrednisolone (IVMP) therapy: Methylprednisolone 30 milligrams (mg) per kilogram (kg) of body weight (maximum, 1.5 g) intravenously in a single dose over one hour on the day of randomisation (day one), followed by
2. Oral Prednisolone (OP) course: Prednisolone 2 mg per kg of body weight per day (maximum dose, 60 mg per day) in two divided doses orally for seven days, starting on the second study day (day two)

Control: Placebo for both intravenous and oral treatments

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Methylprednisolone, immunoglobulin, prednisolone

Primary outcome(s)
The major outcome of the study is the incidence of predefined abnormality of one or more coronary arteries at 8 weeks after fever onset.

Coronary artery abnormality is defined fully in the trial protocol and includes both coronary artery dilatation and aneurysm. Coronary artery dilatation is defined as an intraluminal CA diameter of ≥3 mm but <4 mm in a child <5 years and ≥4 mm but <5 mm in a child ≥5 years.

Key secondary outcome(s))
1. Death any cause, cardiac cause
2. Other morbidity in first year:
a. Myocardial infarction
b. Congestive heart failure (by clinical assessment)
c. Adverse effects (corticosteroids):
i. Gastrointestinal (GI) bleeding
ii. Elevated Blood Pressure (BP) (systolic or diastolic BP more than 95th percentile for age, height and gender)
iii. Serious infection within first three weeks (study day less than or equal to 21)
iv. Glycosuria
3. Coronary artery z scores
4. Aneurysm size (largest)
5. Number of aneurysms
6. Other singular echocardiographic abnormalities:
a. Pericardial effusion
b. Left ventricular dysfunction
c. Aortic arch abnormality
d. Carotid artery abnormality
e. Abnormality of other great vessels
7. Days to defervescence (cumulative days of continuous fever), calculated as: Number of consecutive days on which child has at least one temperature more than or equal to 38.0 °C, beginning with study day one (day of initiation of IVMP or IV placebo)
8. Fever recrudescence within two weeks, defined as: recurrence of fever following defervesence (no temperature more than or equal to 38.0 °C for more than or equal to 24 hours) occurring more than or equal to 48 hours after cessation of the first IVIG infusion
9. Treatment non-responsiveness, defined as: Fever (more than or equal to 38.0°C) persisting for more than or equal to six days after start of first IVIG infusion
10. Number of doses of IVIG required (one or two) for treatment responsiveness
11. Echocardiographic CAA at one year after treatment

Completion date
01/09/2012

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
Patients aged one month to 16 years, inclusively, who present with either of the following (1. OR 2.):

1. A history of fever for at least four days, but not more than ten days, in addition to more than or equal to four of the five following features, identified by history and/or at presentation:
a. Oral mucosal changes any one of:
i. Redness, dryness, cracking, fissuring, peeling or bleeding of lips, or
ii. Diffuse redness of oral and pharyngeal mucosae, or
iii. Strawberry tongue (e.g. deep redness, prominent fungiform papillae)
b. Extremity changes redness of palms and soles, and/or induration (swelling) of hands and feet
c. Skin rash any rash that is non-vesicular and non-bullous
d. Conjunctivitis bilateral and non-purulent
e. Anterior cervical lymphadenopathy (any)

OR

2. A history of fever for at least five days, but not more than ten days, in addition to three of the five features listed above AND any one of:
a. Serum C-Reactive Protein (CRP) more than or equal to 30 mg/l, or
b. Serum Erythrocyte Sedimentation Rate (ESR) more than or equal to 40 mm/hour, or
c. Plasma viscosity more than or equal to 1.7 mPa/s

Not all of these clinical features need be present at enrolment or at a single point in time.

'Fever' is considered to be pyrexia by history (e.g. tactile assessment by parent) OR by direct measurement. Whenever measured, fever is defined as a temperature of more than or equal to 38.0 °C (100.4 °F), determined by any method (e.g. oral, rectal, tympanic or axillary). A parental impression of pyrexia by tactile assessment alone can be taken as a day of fever, regardless of any measured temperature. The first day of fever is taken as the day on which the parent or guardian reports that the child first had a fever, either by history or recorded measurement.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
1 months

Upper age limit
16 years

Sex
All

Key exclusion criteria
1. Fever for more than or equal to 11 days
2. Previous diagnosis of KD (e.g. recurrent disease or a second discrete symptomatic presentation of KD)
3. Clinical features suggesting disease other than KD, including any of:

a. Exudative conjunctivitis
b. Exudative pharyngitis
c. Exudative tonsillitis
d. Discrete intra-oral ulcerations or lesions
e. Bullous or vesicular rash
f. Hepatosplenomegaly and generalized adenopathy (e.g. inguinal and cervical)
4. Known or suspected acute diagnosis of:
a. Viral infection adenovirus, enteroviruses, Epstein-Barr Virus (EBV, infectious mononucleosis), CytoMegaloVirus (CMV), measles
b. Bacterial infection bacterial cervical adenitis, scarlet fever, staphylococcal scalded skin syndrome, toxic shock syndrome (S. aureus or group A streptococcus)
c. Rickettsial infection - leptospirosis, Rocky Mountain spotted fever
d. Drug hypersensitivity reaction
e. Stevens-Johnson Syndrome (SJS)
f. Juvenile Idiopathic Arthritis (JIA)
g. Leukaemia, lymphoma or other malignancy
h. Mercury hypersensitivity reaction (acrodynia)
5. Significant positive blood culture (single, non-contaminant organism)
6. Throat swab culture positive for group A streptococcus (Streptococcus pyogenes)
7. Positive Anti-Streptolysin-O titer (ASO titer)
8. Severe Congestive Heart Failure (CHF), with signs/symptoms present
9. Chronic renal failure
10. Liver failure
11. Severe systemic infection
12. Contraindication to systemic corticosteroid therapy:
a. History of allergic reaction (hypersensitivity) to intravenous methylprednisolone or one of its components
b. Severe allergy to an oral or intramuscular corticosteroid
c. Current treatment with any of: amphotericin, carbamazepine, cyclosporine, methotrexate
d. Active varicella infection
e. Exposure to case of varicella within the previous 21 days
13. Current oral, intravenous or intramuscular corticosteroid treatment
14. History of allergic reaction or severe systemic response to any human immune globulin preparation
15. Known Immunoglobulin A (IgA) deficiency or agammaglobulinaemia (antibody immune deficiency)
16. Lack of written informed parental consent
17. Enrolment in another study that might affect treatment delivery or efficacy or clinical follow-up

Administration of IVIG prior to enrolment does not necessarily exclude the child from enrolment in the trial. The presence of CA aneurysms on baseline echocardiogram is also not an exclusion criterion. However, any aneurysm must be documented by a study cardiologist.

Date of first enrolment
01/09/2006

Date of final enrolment
01/09/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Academic Unit of General Paediatrics and Child Health
Leeds
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Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Not defined

Funder Name
Non-commerical independent funding

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration