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A pilot study to investigate the effects of short course oral corticosteroid therapy in early dengue infection in Vietnamese patients

Submission date
24/07/2008

Recruitment status
No longer recruiting

Registration date
21/10/2008

Overall study status
Completed

Last Edited
15/01/2014

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Patients with dengue can experience a variety of serious complications including shock, low blood platelets, and bleeding. Since these problems occur at a time when the virus is disappearing from the body, they are thought to caused partly by the bodys own natural defence mechanisms. Corticosteroids are a type of treatment that suppresses the natural defence mechanisms and therefore might prevent the development of such complications. However, it is also possible that this treatment could slow the clearance of the virus from the body, which might in turn cause more serious disease. Therefore, we performed this study the first of its kind to look at the safety of an early short course of oral prednisolone therapy (a kind of steroid) in patients with dengue. We investigated the effect of both low and high dose steroid treatments.

Who can participate?
Ethnic Vietnamese participants aged between 6 and 20 years and weighing at least 20 kg, who presented with a clinical diagnosis of dengue and fever for <=72 hours, but who had no signs of serious illness.

What does the study involve?
Suitable patients admitted to hospital within the first 3 days of fever were randomly allocated to receive either low or high dose oral prednisolone daily for 3 days, or a sham tablet containing no active drug. The treatments looked identical and none of the staff or patients involved knew which kind of treatment the participants received. All participants were reviewed daily until they had recovered fully, with careful documentation of a number of clinical factors and laboratory values related to their health and also to the level of virus in their body. They were then followed up several weeks after discharge to make sure that they had recovered fully.

What are the possible benefits and risks of participating?
Possible benefits included the fact that oral steroids might reduce the risk of developing the major complications of dengue described above. Adverse effects are rare in association with short courses of oral steroids given for other conditions such as asthma. Behaviour disturbance

is occasionally reported among children receiving high doses but this usually improves when the drug is stopped. Other possible risks included the potential for making bleeding more severe than it might otherwise be, and for upsetting the regulation of blood sugar control and other systems related to the bodys metabolism. In addition, there might have been an increase in the amount or persistence of dengue virus in the body, due to suppression of the normal mechanisms that clear the virus during an infection.

Where is the study run from?
The study was conducted by researchers at the Oxford University Clinical Research Unit in Ho Chi Minh City, Viet Nam, in collaboration staff at the Hospital for Tropical Diseases of Ho Chi Minh City.

When is the study starting and how long is it expected to run for?
The study ran from August 2009 to January 2011.

Who is funding the study?
The Wellcome Trust (UK).

Who is the main contact?
The Clinical Trials Unit at the Oxford University Clinical Research Unit Viet Nam
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CTU06DXJUN08

Study information

Scientific Title
A randomized, placebo-controlled, partially blinded (drug versus placebo) trial of early corticosteroid therapy in Vietnamese children and young adults with suspected dengue infection

Study objectives

The primary objective is to assess the safety of a short course of oral corticosteroids versus placebo used early in the course of acute dengue infections in Vietnamese subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Pending from the Oxford Tropical Medicine Research Ethics Committee (OXTREC) (UK) as of 25 /07/2008.

Primary study design
Interventional

Study design
Randomised placebo-controlled partially blinded (drug versus placebo) trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Dengue fever

Interventions
Suitable patients admitted to hospital within the first 3 days of fever will be randomised to receive:
1. Low dose oral prednisolone daily for 3 days (see below for details of dosage)
2. High dose oral prednisolone daily for 3 days (see below for details of dosage)
3. Identical placebo

Dosage:
1. Body weight = 20 - 29 kg:
1.1. Low dose = 10 mg in 0.5 mg/kg increments
1.2. High dose = 40 mg in 2 mg/kg increments
2. Body weight = 30 - 39 kg:
2.1. Low dose = 15 mg in 0.5 mg/kg increments
2.2. High dose = 60 mg in 2 mg/kg increments
3. Body weight = 40 - 49 kg:
3.1. Low dose = 20 mg in 0.5 mg/kg increments
3.2. High dose = 60 mg in 2 mg/kg increments
4. Body weight = 50 - 59 kg:
4.1. Low dose = 25 mg in 0.5 mg/kg increments
4.2. High dose = 60 mg in 2 mg/kg increments
5. Body weight = greater than 60 kg:
5.1. Low dose = 30 mg in 0.5 mg/kg increments
5.2. High dose = 60 mg in 2 mg/kg increments

Blood tests:
1. Haematocrit and platelet measurements will be carried daily or more frequently if clinically indicated
2. Renal and liver function tests, electrolytes and blood glucose measurements, and coagulation profiles, will be carried out at enrolment, day 5 - 6 of illness and at the follow up visit

3. Conventional serological and virological tests will be carried out to confirm dengue infection and indentify the infecting serotype. The daily plasma samples will be assessed for viral shedding and NS1 production. Three samples (study enrolment, 48 hours later, follow-up visit) will be obtained to look at the effect of steroid use on immune function/cytokine regulation.

Summary statistics will be used to describe the baseline characteristics of the three groups. Standard statistical methodology will be used to compare the proportion of adverse events such as mucosal bleeding, shock, vomiting etc., and of laboratory safety data including haematological (platelets, coagulation screening tests) and biochemical (liver function tests, blood glucose, electrolytes) parameters. All serious adverse events will be reported promptly to the DSMB. The dynamics of viral shedding and NS1 profiles will be assessed using techniques such as AUC, Kaplan Meier, etc.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
Safety (clinical parameters): comparison of incidence of shock, mucosal bleeding, jaundice, haematological and biochemical abnormalities in the steroid and placebo groups

Key secondary outcome(s)
1. Safety (virological parameters): comparison of viral shedding in terms of viral load and NS1 clearance between the groups
2. Evaluation of the immune response to infection (cytokine profiles, microarrays) between the groups

Completion date
31/10/2010

Eligibility

Key inclusion criteria
1. Aged between 6 and 20 years, either sex
2. Weight at least 20 kg
3. Clinical suspicion of dengue, with a positive rapid test for dengue non-structural protein 1
4. Fever for less than or equal to 72 hours
5. Informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Other

Sex
All

Key exclusion criteria
1. Signs or symptoms suggestive of any other acute infectious disease
2. Any evidence of significant complications of dengue, e.g., mucosal bleeding, jaundice, neurological compromise, shock, inability to tolerate oral medication
3. Any prior history of serious physical illness, or any chronic condition requiring regular follow up
4. Any history of psychiatric disorder or behaviour disturbance
5. Current or recent (within 3 months) use of any medication other than drugs for symptomatic relief (analgesics, decongestants, etc.)
6. Any history of an adverse drug reaction to any medication
7. Pregnancy (enrolment within one month of last menstrual period [LMP] in post-pubertal females)

Date of first enrolment
20/10/2008

Date of final enrolment
31/10/2010

Locations

Countries of recruitment
Viet Nam

Study participating centre
The Oxford University Clinical Research Unit (OUCRU)
Ho Chi Minh City
Viet Nam
Q5

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
The Wellcome Trust (UK) (grant ref: 077078)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2012		Yes	No