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A multicentre study of the safety and efficacy of N-acetylcysteine in the treatment of acute liver failure in paediatric patients not caused by acetaminophen

Submission date
12/05/2010

Registration date
12/05/2010

Last Edited
14/07/2014

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Digestive System

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00248625

Secondary identifying numbers

6201

Study information

Scientific Title

Acronym
PALF

Study objectives
Acute liver failure (ALF) is a rare form of liver disease in children. The condition leads to failure of the function of the liver in a child with no previous history of liver disease. The causative agents include infections, drugs and sometimes metabolic defects that present for the first time as liver failure. However, the cause of the liver failure could only be identified in one-third of the patients.

There is no accepted specific treatment for ALF other than general supportive measures such as maintenance of blood sugar levels, prevention of superadded infections, administration of blood products, measures to reduce brain swelling and assisted breathing in the intensive care unit. In patients with severe disesase, liver transplantation is the only effective treatment.

The purpose of this study is to test whether a drug called N-acetylcysteine (NAC) improves outcome of patients with ALF. This drug is used as an antidote in patients with paracetamol overdose who usually develop liver failure. This drug has been very helpful in improving the survival of patients where overdose is likely to be fatal. N-acetylcysteine reduces cell injury induced by oxidative stress in liver failure not only in liver but other organs also. In a small number of adults in our hospital with liver failure not related to paracetamol overdose an improvement in various parameters of body function like blood pressure and oxygen utilisation was observed after administration of NAC. This drug has also been shown to improve cell function in situations of multi-organ failure not caused by liver failure. However a more recent study from Edinburgh failed to demonstrate these observations. This drug has been used without a definitive evidence of its efficacy in few centres (including ours) in the management of liver failure. This multinational randomised controlled trial will help to establish the safety and efficacy of this drug.

Ethics approval required
Old ethics approval format

Ethics approval(s)
MREC approved (ref: 02-186)

Study design
Multicentre randomised interventional treatment trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Topic: Medicines for Children Research Network; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
The study drug or placebo will be given as a 7-day continuous intravenous infusion to children with acute liver failure not due to acute acetaminophen toxicity.

Study drug: intravenous N-acetylcysteine
Total duration of therapy: 7 days. Duration may be less in the event of spontaneous recovery or liver transplantation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
N-acetylcysteine

Primary outcome measure
Comparison of survival without liver transplant

Secondary outcome measures
1. Length of intensive care unit and hospital stay
2. Number of organ systems failures

Overall study start date
01/01/2003

Completion date
01/12/2010

Eligibility

Key inclusion criteria
Enrolment in PALF registry:
1. Evidence of acute liver injury
2. International normalised ratio (INR) greater than or equal to 1.5 or prothrombin time (PT) greater than or equal to 15 with encephalopathy, or INR greater than or equal to 2.0 or PT

greater than or equal to 20 with or without encephalopathy
3. Aged less than 18 years, either sex
4. Informed consent, obtained from the patient or parent

Participant type(s)
Patient

Age group
Child

Upper age limit
18 Years

Sex
Not Specified

Target number of participants
Planned sample size: 184; UK sample size: 28

Key exclusion criteria
1. Acute paracetomol toxicity
2. Patient on N-acetylcysteine or received N-acetylcysteine during the course of this illness
3. Pregnancy
4. Known malignancy
5. Patient is on a liver support device
6. Sepsis
7. Signs of cerebral herniation
8. Intractable hypotension

Date of first enrolment
01/01/2003

Date of final enrolment
01/12/2010

Locations

Countries of recruitment
Canada

England

United Kingdom

United States of America

Study participating centre
Department of Liver Studies and Transplantation
London

United Kingdom
WC2R 2LS

Sponsor information

Organisation
King's College Hospital NHS Foundation Trust (UK)

Sponsor details
Denmark Hill
London
England
United Kingdom
SE5 9RS

Sponsor type
Hospital/treatment centre

Website
http://www.kch.nhs.uk/

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type
Government

Funder Name
National Institutes of Health (NIH) (USA)

Alternative Name(s)
Institutos Nacionales de la Salud, US National Institutes of Health, NIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/04/2013		Yes	No