

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	Recruitment status No longer recruiting	☐ Prospectively registered
		☐ Protocol
Registration date 12/05/2010	Overall study status Completed	☐ Statistical analysis plan
		☒ Results
Last Edited 14/07/2014	Condition category Digestive System	☐ 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

ClinicalTrials.gov (NCT)

NCT00248625

Protocol serial number

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 disease, 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)

Primary study design

Interventional

Study design

Multicentre randomised interventional treatment trial

Study type(s)

Treatment

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(s)

Comparison of survival without liver transplant

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Child

Upper age limit

18 Years

Sex

Key exclusion criteria

1. Acute paracetamol 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**

United Kingdom

England

Canada

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)

ROR

<https://ror.org/01n0k5m85>

Funder(s)

Funder type

Government

Funder Name

National Institutes of Health (NIH) (USA)

Alternative Name(s)

US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United States of America

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary****Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2013		Yes	No