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CRASH2 Trial, a large randomised placebo-controlled trial among trauma patients with significant haemorrhage of the effects of an antifibrinolytic treatment on death and transfusion requirement

Submission date
13/07/2004

Recruitment status
No longer recruiting

Registration date
10/09/2004

Overall study status
Completed

Last Edited
09/07/2014

Condition category
Signs and Symptoms

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

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.crash2.lshtm.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00375258

Secondary identifying numbers
HTA 06/303/20; HTA 09/102/01; SLCTR/2007/008

Study information

Scientific Title

Acronym
CRASH2

Study objectives
Because the coagulation abnormalities that occur after injury are similar to those after surgery, it is possible that antifibrinolytic agents might also reduce blood loss, the need for transfusion and mortality following trauma. However, to date there has been only one small randomised controlled trial (70 randomised patients, drug versus placebo: 0 versus 3 deaths) of the effect of antifibrinolytic agents in major trauma. As a result, there is insufficient evidence to either support or refute a clinically important treatment effect. Systemic antifibrinolytic agents have been used in the management of eye injuries where there is some evidence that they reduce the rate of secondary haemorrhage.

CRASH2 aims to determine the effect of the early administration of the antifibrinolytic agent tranexamic acid (TXA) on death and transfusion requirement in adult trauma patients with ongoing significant haemorrhage, or who are considered to be at risk of significant haemorrhage. In addition, the effect on the risk of non-fatal vascular events (either haemorrhagic or occlusive) will be assessed.

The initial stages of the trial was funded by the London School of Hygiene, the Bupa Foundation and the Moulton Charitable Trust. In 2007, this trial obtained main funding from the NIHR Health Technology Assessment Programme, which will fund this trial from April 2007 to September 2010.

More information on the CRASH2 trial can be found at: http://www.nets.nihr.ac.uk/projects/hta/0630320

As of 16/06/2008, the CRASH2 trial will conduct sub-group analyses "CRASH-2 Intracranial Bleeding Study (IBS)" (start date: October 2009) to study the effect of TXA in participants who also have traumatic brain injury (TBI). About 40% of participants out of 9,000 enrolled so far have TBI. Details of this sub-study can be found at: http://www.nets.nihr.ac.uk/projects/hta/0910201

Hypothesis: Early administration of TXA can prevent the occurrence or increase of intracranial bleeding in patients with TBI and significant bleeding.

On 21/08/2009 the anticipated start and end dates of this trial were changed from 01/05/2005 and 30/04/2010 to 01/04/2007 and 30/09/2010, respectively.

This trial completed follow-up on the 02/03/2010, and the record was updated to reflect this on 09/07/2010.

Ethics approval required
Old ethics approval format

Ethics approval(s)
All trial centres will seek ethics approval before recruiting participants. As of 10/06/2008, over 275 approvals have been received.

Study design
Randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information can be found at: http://www.crash2.lshtm.ac.uk/prot_EngPIS.htm

Health condition(s) or problem(s) studied
Trauma

Interventions
Tranexamic acid 2 g intravenously over 8 hours versus placebo.

Please note that as of 24/03/10 this trial has completed recruitment, analysis is ongoing.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Tranexamic acid

Primary outcome measure

The primary outcome measure is death in hospital within 4 weeks of injury (causes of death will be classified).

An additional outcome measure for the sub-group analyses (added as of 18/06/2008):
1. Increase in volume of intracranial bleeding. A repeat CT scan will be carried out 24-48 hours after injury and compared to a clinical baseline CT scan.

Secondary outcome measures
Secondary outcome measures will be receipt of a blood transfusion, volume of blood transfused, surgical intervention and the occurrence of vascular events (haemorrhagic stroke, occlusive stroke, myocardial infarction, pulmonary embolism, clinically diagnosed deep vein thrombosis). Data will be recorded on a single sided outcome form which can be completed entirely from the hospital notes. There will be no additional tests.

Additional outcome measures for the sub-group analyses (added as of 18/06/2008):
A repeat CT scan will be carried out 24 - 48 hours after injury and compared to a clinical baseline CT scan to assess the following:
1. Frequency of progressive haematomas
2. Frequency of delayed haematomas
3. New focal ischaemic lesions

Overall study start date
01/04/2007

Completion date
02/03/2010

Eligibility

Key inclusion criteria
All adult trauma patients who are considered to be at risk of significant haemorrhage and are within 8 hours of the injury, are eligible for trial entry if they appear to be at least 16 years old. There are no other pre-specified exclusion criteria, as the fundamental eligibility criterion is the responsible doctor's 'uncertainty' whether or not to use tranexamic acid (TXA) in a particular adult with traumatic haemorrhage. Patients for whom there is considered by the responsible doctor to be a clear indication for TXA should not be randomised. Likewise, any for whom there is considered to be a clear contraindication to TXA (such as, perhaps, those who have clinical evidence of a thrombotic disseminated intravascular coagulation) should not be randomised. All those for whom the responsible doctor is substantially uncertain as to whether or not to use an anti-fibrinolytic agent are eligible for randomisation, and as many such patients as possible should be considered for the trial.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
20,000 (Target number of participants for the sub-group analyses: up to 1,000)

Key exclusion criteria
The fundamental eligibility criterion is the responsible doctor's 'uncertainty' as to whether or not to use an antifibrinolytic agent in a particular adult with traumatic haemorrhage. Patients for whom the responsible doctor considers there is a clear indication for antifibrinolytic therapy should not be randomised. Likewise, patients for whom there is considered to be a clear contraindication to antifibrinolytic therapy (such as, perhaps, those who have clinical evidence of a thrombotic disseminated intravascular coagulation) should not be randomised. Where the responsible doctor is substantially uncertain as to whether or not to use an antifibrinolytic, all these patients are eligible for randomisation and should be considered for the trial. There are no other pre-specified exclusion criteria.

Date of first enrolment
01/04/2007

Date of final enrolment
02/03/2010

Locations

Countries of recruitment
Albania

Argentina

Australia

Austria

Bangladesh

Belgium

Cameroon

Canada

China

Colombia

Cuba

Czech Republic

Ecuador

Egypt

El Salvador

England

Georgia

Ghana

India

Indonesia

Iran

Iraq

Italy

Jamaica

Japan

Kenya

Malaysia

Mexico

Montenegro

Nigeria

Peru

Poland

Saudi Arabia

Serbia

Singapore

Slovakia

South Africa

Spain

Sri Lanka

Tanzania

Thailand

Tunisia

United Kingdom

Zambia

Study participating centre
London School of Hygiene and Tropical Medicine
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Sponsor information

Organisation
London School of Hygiene and Tropical Medicine (UK)

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Sponsor type
University/education

Website
http://www.lshtm.ac.uk/

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research organisation

Funder Name

NIHR Health Technology Assessment Programme - HTA (UK)

Funder Name
Bupa Foundation (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Moulton Charitable trust (UK)

Funder Name
London School of Hygiene and Tropical Medicine (UK)

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?
Other publications	Letter to the Editor	21/06/2006		Yes	No
Results article	initial progress results	27/10/2006		Yes	No
Results article	effects of tranexamic acid results	03/07/2010		Yes	No

Results article	tranexamic acid results	01/12/2010	Yes	No
Other publications	reduced environmental impact of trials	03/02/2011	Yes	No
Results article	early treatment results	26/03/2011	Yes	No
Results article	cost-effectiveness analysis results	03/05/2011	Yes	No
Results article	tranexamic acid results	01/07/2011	Yes	No
Results article	tranexamic acid results	01/07/2012	Yes	No
Results article	tranexamic acid mortality results	11/09/2012	Yes	No
Results article	results	01/03/2013	Yes	No
Results article	results	01/06/2014	Yes	No