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Inflammatory response in major injury and recovery - erythropoietin

Submission date	Recruitment status	[X] Prospectively registered
17/09/2015	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/03/2016	Stopped	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
07/01/2019	Injury, Occupational Diseases, Poisoning	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Blunt trauma, also known as blunt force trauma, is a severe physical injury caused by impact of the head or body with a blunt object or surface. One of the most common injuries associated with blunt trauma is damage to the kidneys. The kidneys play a vital role in the body, producing a number of different hormones. One of these hormones, erythropoietin (EPO) stimulates the bone marrow to produce more red blood cells. Previous studies have shown that giving patients a manufactured version of this hormone, known as recombinant human erythropoietin (rhEPO) can help to protect patients with severe injuries from death. The reason why this happens is not known, however further studies have suggested that rhEPO may actually influence the immune system, reducing the risk of infection. The aim of this study is to find out whether treatment with rhEPO can help reduce organ failure rates and improve recovery in adults admitted to intensive care with injuries caused by blunt trauma.

Who can participate?
Adults admitted to intensive care unit (ITU) with blunt trauma with an injury severity score of at least 16.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first groups are given an injection under the skin (subcutaneous injection) of rhEPO 1, 8 and 15 days after they are admitted to the ITU. Participants in the second group are given a subcutaneous injection of a dummy (placebo) 1, 8 and 15 days after they are admitted to the ITU. Participants in both groups are monitored for 30 days after they are discharged from ITU in order to establish how many have multiple organ failure, how many survive and the time spent on the ITU ward.

What are the possible benefits and risks of participating?
Participants who receive rhEPO may benefit from a faster recovery as a result of the treatment. Risks of taking part are small however some patients may experience side-effects of rhEPO such as high blood pressure.

Where is the study run from?
Morriston Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2015 to December 2017

Who is funding the study?
Abertawe Bro Morgannwg University Health Board (UK)

Who is the main contact?
Professor Ian Pallister

Contact information

Type(s)
Scientific

Contact name
Prof Ian Pallister

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Additional identifiers

Protocol serial number
4

Study information

Scientific Title
Inflammatory response in major injury and recombinant human erythropoietin

Acronym
IRMINE

Study objectives
The use of recombinant human erythropoietin (rhEPO) reduces organ failure after severe trauma in adults, by effects on the clinical, cellular & biomolecular manifestations of the systemic inflammatory response to injury and the haemopoeitic bone marrow.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC 3, 26/01/2016, ref: 15/WA/0361

Study design

Multi-centre single-blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Major Trauma (Injury Severity Score 16+)

Interventions
Participants are randomly allocated to one of two groups.

Intervention group: Participants receive rhEPO (40,000 units) via subcutaneous injection on day 1, 8 and 15 post admission, while the patient remains in ITU.
Control group: Participants receive a subcutaneous injection of a placebo on day 1, 8 and 15 post admission, while the patient remains in ITU.

Participants are followed up for 30 days after discharge from ITU to calculate mortality rates at 30 days.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
Multiple organ failaure is monitored using the Denver multiple organ failure score at baseline, day 3 and then daily until discharge from ITU, mortality or 30 days.

Key secondary outcome(s))
1. Treatment plan (surgery and/or interventional radiology) is recorded at baseline
2. Length of ITU stay is determined at 30 days, time of discharge from ITU or death
3. Critical care support required is measured by mode and duration of mechanical ventilation and inotrope infusion daily throughout ITU stay
4. Length of hospital stay is determined from patient notes at 30 days, discharge or death
5. Thromboembolic vascular events (TVE) rate is determined from reviewing patient notes at 30 days, discharge or death
6. The inflammatory response to injury is measured using the Systemic Inflammatory Response clinical score (SIRS) calculated daily and using cytokine and cellular protein assays at on blood samples taken daily, while on ITU
7. Presence of Persistent Inflammation/Catabolism syndrome (PICS) is calculated from clinical observations and protein assays from day 10, only in those remaining on ITU at that point
8. Leukocyte progenitor proliferation/differentiation in bone marrow aspirates is assessed using flow cytometry and colony forming unit assays obtained on day 2 while on ITU, and subsequently in those requiring pelvic fracture surgery

9. Mitochondrial respiratory function is measured using bioenergetic profile assays on blood obtained daily until while on ITU

Completion date
30/12/2017

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

Eligibility

Key inclusion criteria
1. Aged between 18-60 years
2. Blunt trauma patients admitted to ITU
3. Injury severity score (ISS) at least 16
4. ITU stay expected to last at least 3 days

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
1. Pregnancy (an admission pregnancy test is routine in all female trauma patients who are of child-bearing age)
2. Presence of a severe isolated traumatic brain injury
3. Presence of any blood-borne infections e.g. HIV, hepatitis B or C.
4. Presence of any known malignancies
5. Presence of not been consented by a personal legal representative or a professional legal representative if the former is not available
6. Are already participating in another clinical trial
7. Presence of a contra-indication to thromboprophylaxis
8. Presence of contra-indications for rhEPO:
8.1. Uncontrolled hypertension
8.2. Known sensitivity to mammalian cell derived products
8.3. Hypersensitivity to the active substance or to any of the excipients
8.4. Severe coronary, peripheral arterial, carotid or cerebral vascular disease, including patients

with recent myocardial infarction or cerebral vascular accident
8.5. Patients who have developed Pure Red Cell Aplasia (PRCA) following treatment with any erythropoietin
8.6. A history of thrombo-embolic vascular (TVE) events

Date of first enrolment
04/10/2016

Date of final enrolment
04/01/2017

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Morriston
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SA6 6NL

Sponsor information

Organisation
Abertawe Bro Morgannwg University Health Board

ROR
https://ror.org/04zet5t12

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Abertawe Bro Morgannwg University Health Board

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes