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Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients

Submission date 19/09/2002	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/09/2002	**Overall study status** Completed	
Last Edited 08/11/2022	**Condition category** Signs and Symptoms	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Robyn Norton

Contact details
The George Institute for International Health
Level 24, Maritime Trade Towers
207 Kent Street
Sydney
Australia
NSW 2021
+ 61 2 9657 0381
rnorton@george.org.au

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
153711

Study information

Scientific Title
Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients

Acronym
SAFE Study (Saline versus Albumin Fluid Evaluation)

Study objectives
When 4% albumin is compared to 0.9% sodium chloride (normal saline) for intravascular fluid resuscitation in patients in the Intensive Care Unit (ICU) there is no difference in 28-day all-cause mortality.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval at Royal North Shore Hospital (affiliated with the University of Sydney and the Institute for International Health) was issued on 27 November 2000 (protocol ref: 0010-173M). Each participating institution also received ethics approval.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Critically ill patients requiring intravenous fluid resuscitation

Interventions

The study treatment will be randomly allocated with stratification within the ICU and across the study population for patients admitted for trauma causes or non-trauma causes. Administration of the study treatments will be double blinded. Each eligible participant will be randomised to receive either 4% human albumin or 0.9% sodium chloride.

Co-sponsor for this trial:
Australian and New Zealand Intensive Care Society Clinical Trials Group
Level 3, 10 Ievers Terrace
Carlton, Melbourne 3053
Australia
Phone: +61 3 9340 3400
Fax: +61 3 9340 3499
Contact person: Professor Simon Finfer (sfinfer@george.org.au)

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Human albumin solution or normal saline

Primary outcome measure
Death from all causes at 28 days after randomisation

Secondary outcome measures
1. Survival time during the first 28 days
2. The proportion of patients with one, two, three, four and five new organ failures (defined as documented change in cardiovascular, respiratory, renal, haematologic or hepatic component of the Sepsis-related Organ Failure [SOFA] score from zero, one or two at base-line to three or four during ICU stay)
3. Duration of mechanical ventilation
4. Duration of renal replacement therapy
5. Duration of ICU and hospital stay

Overall study start date
01/01/2003

Completion date
31/12/2004

Eligibility

Key inclusion criteria
Patients are eligible for inclusion in the study if ALL the following requirements are met:
1. Fluid resuscitation is required for intravascular fluid depletion that is in addition to intravenous fluid that is required for nutrition or to replace ongoing insensible losses, urinary losses, ongoing losses from other sites (e.g., fistula losses from the gastrointestinal tract, urinary losses from diabetes insipidus, cerebral salt wasting syndrome or the polyuric phase of acute

renal failure) or to restore normonatraemia
2. The ICU clinician considers that both 4% human albumin solution and 0.9% sodium chloride are equally appropriate for the patient and that no specific indication or contraindication for either exists
3. The requirement for fluid resuscitation must be supported by AT LEAST ONE of the following clinical signs:
a. Heart rate greater than 90 beats/min
b. Systolic Blood Pressure (SBP) less than 100 mmHg or Mean Arterial Pressure (MAP) less than 75 mmHg or a 40 mmHg decrease in SBP or MAP from the baseline recording
c. Central venous pressure less than 10 mmHg
d. Pulmonary artery wedge pressure less than 12 mmHg
e. Respiratory variation in systolic or mean arterial blood pressure of greater than 5 mmHg
f. Capillary refill time greater than one second
g. Urine output less than 0.5 ml/kg for one hour

Participant type(s)
Patient

Age group
Adult

Sex
Not Specified

Target number of participants
7000

Key exclusion criteria
Patients are excluded from the study if one or more of the following are present:
1. A known previous adverse reaction to human albumin solution
2. Any known religious objection to the administration of human blood products (for example if patient is a Jehovahs Witness)
3. A requirement for the patient to receive plasmapheresis during this ICU admission
4. An admission to the ICU following cardiac surgery
5. An admission to the ICU for the treatment of body burn
6. An admission to the ICU following liver transplantation surgery
7. Age less than 18 years
8. Brain death or brain death that is likely to be diagnosed within in the next 24 hours of fluid resuscitation being required
9. If the patient is moribund and expected to die within the next 24 hours - defined as having a treatment limitation order in place that exceeds a not for resuscitation order and that indicates the treating clinicians are not committed to full supportive care
10. If the patient has previously been enrolled and has completed follow up in the SAFE study
11. If the patient has previously received fluid resuscitation that was prescribed within the study ICU and during this current ICU admission
12. If the patient has been transferred to the study ICU from a non-study ICU and received a fluid bolus or fluid resuscitation for the treatment of volume depletion in that non-study ICU

Date of first enrolment
01/01/2003

Date of final enrolment
31/12/2004

Locations

Countries of recruitment
Australia

New Zealand

Study participating centre
The George Institute for International Health
Sydney
Australia
NSW 2021

Sponsor information

Organisation
The George Institute for International Health (Australia)

Sponsor details
c/o Professor Simon Finfer
The George Institute for International Health
Level 24, Maritime Trade Towers
207 Kent Street
Sydney
Australia
NSW 2021

Sponsor type
Research organisation

Website
http://www.thegeorgeinstitute.org

ROR
https://ror.org/023331s46

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Funding has been from several organisations (listed in alphabetical order):

Funder Name
Auckland Hospital (New Zealand)

Funder Name
Commonwealth Department of Health and Aged Care (Australia)

Funder Name
CSL Limited, Melbourne (Australia)

Funder Name
Middlemore Hospital, Auckland (New Zealand)

Funder Name
National Health and Medical Research Council (Australia) - three year project grant (ref: 153711)

Funder Name
National Health Research Council (New Zealand) (ref: 01/386)

Funder Name
New South Wales Health Department

Funder Name
Northern Territory Health Services (Australia) - grant from the Australian Health Care Agreement 1998 - 2003 Quality Improvement and Enhancement Funds

Funder Name
Queensland Health Services Department (Australia)

Funder Name
Royal Hobart Hospital, Tasmania (Australia)

Funder Name
South Australia Department of Human Services (Australia)

Funder Name
Victoria Department of Human Services (Australia)

Funder Name
Western Australia Health Department (Australia)

Funder Name
The SAFE study was initiated and designed by the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Australian and Red Cross Blood Service. The study design, protocol and procedures have been finalised in collaboration with the Institute for International Health, independently of the aforementioned funding bodies. The data will be collected, analysed and published independent of the funding bodies and a copy of the final report will be distributed to them on completion of the study.

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

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		18/11/2006		Yes	No
Results article		30/08/2007		Yes	No