ISRCTN21069375 https://doi.org/10.1186/ISRCTN21069375

Investigation of dermal metabolism in burned and unburned human skin using the microdialysis method to quantify peripheral resuscitation following burn injury

Submission date
29/09/2006

Recruitment status
No longer recruiting

Registration date
29/09/2006

Overall study status
Completed

Last Edited
24/08/2015

Condition category
Injury, Occupational Diseases, Poisoning

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Mr NSM Moiemen

Contact details
Burns & Plastics
Selly Oak Hospital
Birmingham
United Kingdom
B29 6JD

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N0265174144

Study information

Scientific Title
Investigation of dermal metabolism in burned and unburned human skin using the microdialysis method to quantify peripheral resuscitation following burn injury: a randomised controlled trial

Study objectives
Purpose:
1. To validate the microdialysis technique for use as a bedside monitoring device to measure changes in the biochemistry of the skin, allowing greater accuracy of fluid management in burns patients.
2. To quantify the biochemical changes in the skin as a result of burn injury.

Design:
Prospective, controlled study
To fulfill our primary objective of assessing biochemical changes in the burn wound, we must first establish normal levels of these substances in healthy skin in similar circumstances. Burns patients are treated in a warmed room, as their injury prevents them from controlling their own body heat. Injured patients have a raised metabolic rate. It is therefore important to establish values within normal skin at rest, in a warm environment, and during exercise (to raise metabolic rate). This gives us appropriate control values for the conditions in which a burns patient is tested.

The few published studies on microdialysis sampling of normal skin have assessed lactate, pyruvate and glucose levels at rest and during a glucose tolerance test, but have not assessed changes in relation to temperature.

The one study which looked at the effect caused by exercise measured lactate alone. To fully assess adequacy of oxygenation, the lactate and pyruvate must both be measured, and quoted as a ratio. Lactate levels alone are not adequate for our study. It is therefore necessary to perform a study on a group of healthy volunteers to establish a normal range.

Secondly, there are significant differences in the body's response to small and large burns. In small burns (<15% total body surface area), the responses are limited to the area of the wound, with no major changes affecting the rest of the body. By contrast, extensive burns (>30% total body surface area) have an exaggerated response to injury involving not only the burn wounds, but the entire body, including unburned skin. These patients require intensive monitoring and treatment if they are to survive. Since these two groups of patients have different responses and receive different treatments, it is necessary to treat them separately for this study. Patients with small burns will have less confounding factors, and will be most useful to obtain a clear picture of the different biochemistry between the zones of burn. Their unburned skin is expected to act as a normal control. Patients with extensive burns are likely to show a very different picture. Their wound environment is likely to change with the fluid treatment they are given. Their unburned skin is unlikely to show levels resembling normal.

Thirdly, in order to fully assess the adequacy of resuscitation required to validate the microdialysis method, it is important to include the most accurate current indicators of fluid status for patients in Study 3. These methods have been validated in a recent clinical trial on our unit. Gastric Tonometery is a sensitive measure of the blood flow in the stomach which alters if there is insufficient fluid in the body. Changes in gastric Tonometery occur before changes in the more traditional measure of urine volume. Microalbuminuria is a measure of the protein leak

from the kidneys as analysed in the urine. It parallels the leakage of fluid from blood vessels and will be invaluable when interpreting microdialysis results.

Hypothesis:
1. Is biochemical assessment of tissue fluid (particularly lactate, pyruvate, glucose and glycerol) within the burn wound an accurate measure of the adequacy of fluid management in burns patients?
2.1 What is the normal biochemistry of tissue fluid from healthy skin?
2.2 Does the biochemistry of tissue fluid from healthy skin change with room temperature or with exercise?
2.3 How is the biochemistry of tissue fluid different in burned skin?
2.4 Is there a characteristic difference in the biochemistry of tissue fluid in each of three defined zones of injury surrounding a burn?
2.5 Is there a difference in tissue fluid between patients with small, uncomplicated burns and patients with extensive burns?
2.6 How does the tissue fluid change in response to resuscitation in the major burns patient?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

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
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Burn injury

Interventions
Three studies are proposed:

Study 1: Normal Volunteers -
12 healthy volunteers will be recruited. Each volunteer will be asked to attend the Burns Unit for a 4-hour period at their convenience. Once informed consent is obtained, a topical anaesthetic

cream will be applied to a site on the forearm. This will be left in place for 30 minutes until anaesthesia has been achieved. The skin will be cleaned, and a microdialysis probe inserted into the skin using a needle (1.4 mm diameter). The needle is the same size as a standard intravenous cannula. The needle and the probe are sterile. The needle will be removed and the flexible probe left in the skin. This will be secured in place with tape. The probe is connected to a small pump, the size of a mobile phone. This pumps sterile, neutral fluid at a very low rate through the probe (less than 1ml per hour), and a sample is collected from the other end of the probe into a small plastic vial which will be changed every 10 minutes. After placement, the volunteer will be asked to rest for 90 minutes in a room at 20 degrees Celsius. The temperature will then be raised to 30 degrees Celsius for 30 minutes. Following this the room will be cooled to 17 degrees Celsius for 30 minutes. The volunteer will then be asked to exercise on an exercise bicycle for 20 - 30 minutes. The volunteer will then be allowed to rest for 30 minutes. At the end of this period, the probe will be removed, and a small dressing placed over the site. The volunteer will be allowed to leave, and will not be required for further input.

Study 2: Small burns -
Twelve patients will be recruited. Any patient admitted to the Burns Unit at Selly Oak Hospital with total burn less than 15% body surface area, and including arm or leg in the burn distribution will be considered for inclusion. Once initial assessment has been completed and therapy commenced, the study will be started. Details of the distribution and depth of the burns will be recorded for correlation with the results. Zone of stasis will be determined by application of a blood pressure cuff on the limb above the burned area. The cuff will be inflated for a maximum of 3 minutes until the zone of stasis is defined. The zone of stasis will be marked with a skin marking pen, then the cuff will be released. A local anaesthetic injection will be given at two of the three areas to be studied: the zone of stasis (as defined above) and the normal area of unburned skin. The zone of coagulation (centre of burn) has no feeling, so anaesthesia is unnecessary. Once anaesthesia is attained (approximately 5 minutes), a microdialysis probe will be placed in the skin at each of these sites. The probe will be perfused with solution via the pump. Dressings will be standardised: Jelonet, gauze and crepe. This is currently the standard dressing for the first 48 hours. Microdialysis samples will be taken every 30 minutes throughout the first 36 hours following injury. Patient activity, medical intervention and events will be noted throughout the study period. Medical notes will also be reviewed subsequent to patient discharge, and events in relation to surgical procedures, skin grafting and wound healing will be noted.

Study 3: Large Burns -
Twelve patients will be recruited. Any patient admitted to the Burns Unit or Intensive Care Unit at Selly Oak Hospital with total burn greater than 30% body surface area, will be considered for inclusion. Once initial assessment has been completed and therapy commenced, the study will be started. Details of the distribution and depth of the burns will be recorded for correlation with the results. Zone of stasis will be determined using the cuff method as above. Three microdialysis probes will be inserted under local anaesthesia as above. Samples will be collected every 30 minutes. A gastric probe will be inserted through the nostril to the stomach. This probe is equivalent to the standard nasal feeding tube routinely inserted to feed patients with extensive burn wounds. Measurements are recorded via a bedside machine. Urine samples will be collected every 30 minutes from a standard urinary catheter for measurement of microalbumin. Details of fluid therapy, urine output, gastric tonometry and urine microalbuminuria will be collected and noted. Medical notes will be reviewed subsequent to discharge and surgical procedures, skin grafting, wound healing and patient outcome will be noted. At the end of the 36 hour period, the probes will be removed and the study will be concluded. Patients will receive treatment as per standard protocol in the burns unit. Treatment will not be altered as a result of measurements taken during the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Lactate/pyruvate ratio for each group.

Secondary outcome measures
1. Wound healing
2. Graft take
3. Infection rate
4. Mortality rate
5. Length of hospital stay

Overall study start date
02/02/2006

Completion date
02/02/2008

Eligibility

Key inclusion criteria
Study 1:
1.1. Potential healthy volunteers will be sought amongst colleagues and contacts locally. The reasons for the study and the procedure will be explained, but only those who show an interest and are keen to be involved will be recruited. No pressure will be put on anyone to volunteer. Appropriate volunteers will be given an information pack, and if they agree to go ahead, will be asked to sign a consent form. Should there be a large response, volunteers will be drawn at random after being grouped by age and sex.
1.2. Aged between 18 - 80 years (the burn population at Selly Oak does not include children. Persons over the age of 80 years are likely to have substantial co-morbidity, and have an extremely poor survival rate in large burns)

Study 2:
2.1. Once the study is commenced, consecutive patients who are to be admitted to Selly Oak Hospital Burns Unit with small burns and fitting the inclusion criteria will be invited to join the study. Clinical staff will be made aware of the study, and will alert the investigator when a suitable patient is admitted. The investigator will approach the patient to explain the study. An information leaflet will be given to the patient. Should they agree to involvement they will be asked to sign consent.
2.2. Aged between 18 - 80 years
2.3. Admission to Selly Oak Hospital (Selly Oak Hospital is the regional Burns Unit, so all burns in the region will come through this hospital)
2.4. Burns < 15% (these patients do not require formal resuscitation and will be unlikely to have a systemic inflammatory response associated with their injury)

Study 3:
3.1. All patients admitted to Selly Oak Hospital Burns Unit or Critical Care Unit with major burns will be highlighted to the investigator by clinical staff. Patients will be approached as soon as possible after admission and invited to join the study. The information leaflet will be explained to the patient and they will be invited to sign the consent form.
3.2. Aged between 18 - 80 years
3.3. Admission to Selly Oak Hospital
3.4. Burns greater than 30% (These patients will all be formally resuscitated. They will also have a systemic inflammatory response.)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
36

Key exclusion criteria
Study 1:
1.1. Pre-existing skin or other medical conditions (these may interfere with the assessment of normal values)
1.2. Alcohol intake in past 6 hours (alcohol may affect metabolism)

Study 2:
2.1. Pre-existing skin or other medical conditions
2.2. Coexisting trauma (trauma can exacerbate the inflammatory response leading to a false reading)
2.3. Alcohol intake in past 6 hours

Study 3:
3.1. Pre-existing skin or other medical conditions
3.2. Coexisting trauma
3.3. Alcohol intake in past 6 hours

Date of first enrolment
02/02/2006

Date of final enrolment
02/02/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Selly Oak Hospital
Birmingham
United Kingdom
B29 6JD

Sponsor information

Organisation
Record Provided by the NHSTCT Register - 2006 Update - Department of Health

Sponsor details
The Department of Health
Richmond House
79 Whitehall
London
United Kingdom
SW1A 2NL
+44 (0)20 7307 2622
dhmail@doh.gsi.org.uk

Sponsor type
Government

Website
http://www.dh.gov.uk/Home/fs/en

Funder(s)

Funder type
Government

Funder Name
University Hospital Birmingham NHS Trust (UK) - NHS R&D Support Funding

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