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Investigating whether the magnitude of postoperative inflammatory and insulin resistant responses is related to body composition and physiological function of skeletal muscle and adipose tissue

Submission date
25/11/2011

Recruitment status
No longer recruiting

Registration date
25/11/2011

Overall study status
Completed

Last Edited
25/05/2018

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
Up to 3 million surgical procedures are performed annually in Britain. Although patients may undergo the same operation, some patients go on to develop greater degrees of inflammatory stress than others. This results in certain patients developing marked inflammation and insulin resistance. Insulin resistance means the body does not respond appropriately to important hormones. The degree of insulin resistance the body develops determines whether patients develop serious complications and how rapidly they recover after surgery. We do not know why these stress responses after major surgery differ so greatly between patients, but think this occurs due to the make-up and function of the body's muscle and fatty tissues. By studying and understanding these mechanisms we will be able to identify patients at risk of developing marked stress responses and improve their preparation before surgery, thereby possibly improving the outcomes of thousands of patients undergoing major surgery. Our study will investigate the roles that different types of muscle and fat in the body play in the development of inflammatory stress and insulin resistance. This is of importance as in the UK patients undergoing surgery are becoming more obese. We will also identify better ways of predicting the development of inflammatory stress and insulin resistance in surgical patients. This would allow us to select those patients whom we know will develop marked inflammatory stress and insulin resistance, and optimise their preparation before surgery.

Who can participate?
Patients aged 18-75 due to have a major abdominal operation.

What does the study involve?
Participants are asked to attend the hospital in the week before surgery. We perform some tests to look at the way that the body reacts to insulin (a hormone that allows the body to use energy from food). This involves blood tests, a small muscle biopsy (sample) and a low-dose X-ray.

Before surgery, participants are randomly allocated to drink either a carbohydrate (sugary) drink or a placebo (dummy) drink. It is possible that drinking this carbohydrate drink may improve how participants recover following surgery and this is one of the things we want to test in this study. Many studies have demonstrated that drinking these specially designed carbohydrate drinks before surgery is safe. During the operation under general anaesthetic, the surgeon takes a few samples of muscle and fat from your body and a small amount (30ml, three tablespoons) of blood. On the day after the operation, we perform a few more blood tests, take another small muscle biopsy and repeat the test to see how the body responds to insulin after major surgery.

What are the possible benefits and risks of participating?
Although the study (carbohydrate) drink has been previously shown to make patients feel better before/after surgery (less thirst/nausea/vomiting and quicker recovery after surgery) there is no guarantee that participants will experience these benefits. We cannot promise the study will help participants but the information we get will help improve the treatment of future patients who undergo surgery. There is a small risk of bleeding (much less than a 1 in a 100 chance) when we take the muscle/fat biopsies. If this occurs the person performing the biopsy will apply pressure or use a special instrument to stop the bleeding. The muscle or fat biopsies may be uncomfortable but we will inject plenty of local anaesthetic beforehand to numb the area. There is a very small chance of developing side effects when we perform the special tests to see how participants react to insulin. Participants will be monitored with a heart monitor and blood pressure measurement and a study doctor will always be present during the insulin infusion.

Where is the study run from?
The study is taking place at Queens Medical Centre, Nottingham and the University of Nottingham Medical School (which is on the Queens Medical Centre site).

When is the study starting and how long is it expected to run for?
September 2011 to September 2013

Who is funding the study?
The study is being funded by CORE charity, The European Society for Clinical Nutrition and Metabolism (ESPEN), Nottingham Digestive Diseases Centre NIHR Biomedical Research Unit, the Division of Gastrointestinal Surgery and the School of Biomedical Sciences (University of Nottingham).

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11276

Study information

Scientific Title
Investigating whether the magnitude of postoperative inflammatory and insulin resistant responses is related to body composition and physiological function of skeletal muscle and adipose tissue: a randomised controlled trial

Study objectives
Preoperative fasting and surgery induce stress, inflammation and insulin resistance (IR). The development of IR is clinically significant as it increases length of hospital stay, surgical morbidity and mortality. A recent study demonstrated that for every 1mg/kg/min decrease in intraoperative insulin sensitivity (i.e. IR), the development of major postoperative complications is increased (OR 2.23, P=0.004). Measures to attenuate IR may, therefore, be of clinical benefit. Such measures include administering carbohydrate-based drinks preoperatively. Surgical patients undergoing the same operative procedure develop differing magnitudes of IR postoperatively, however, the reasons underlying this remains unknown. To date, few studies have examined whether differences in body composition and physiology contribute to the development of postoperative inflammation and IR. We, therefore, plan to undertake this proof of concept study to investigate:
1. The cellular pathways leading to postoperative inflammation/IR
2. Correlation between the magnitude of postoperative IR and body composition. These mechanisms are of importance given the increasing prevalence among surgical patients of sarcopenia (reduction in muscle mass) and obesity, and the associations between sarcopenia, obesity, inflammation and IR.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service (NRES) Committee East Midlands Northampton First MREC approval date 15/08/2011, ref: 11/EM/0232

Study design
Randomised; Interventional; Design type: Process of Care

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

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
Topic: Generic Health Relevance and Cross Cutting Themes; Subtopic: Generic Health Relevance (all Subtopics); Disease: Surgery

Interventions
Preoperative carbohydrate load, Single intervention: Preoperative carbohydrate loading using a commercially available preparation given to patients undergoing abdominal surgery. Participants will receive 2 servings of the drink on the evening before surgery and one serving on the morning of surgery. The drink will be compared to a placebo drink that will be administered in the same quantities and at the same times.

Study Entry : Registration and One or More Randomisations

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Within subject differences in perioperative insulin sensitivity amongst obese, non-obese, carbohydrate loaded and non carbohydrate-loaded patients. Timepoint(s): End of study

Secondary outcome measures
1. The correlation between body composition and changes in perioperative insulin sensitivity
2. Differences in cytokine gene expression
3. Differences in muscle and fat genes and protein expression
4. The incidence of post-operative infectious and non-infectious complications
5. Differences between the groups in length of hospital stay

Overall study start date
28/09/2011

Completion date

28/09/2013

Eligibility

Key inclusion criteria
1. Age 18-75 years
2. Correct body mass index (BMI) and waist circumference criteria (Obese group BMI >=30 or waist circumference > 94 cm in men and > 80 cm in women. Non obese group BMI 18.5-25) or
3. Waist circumference (<=94cm in men and <=80 cm in women)
4. Due to undergo elective major abdominal surgery
5. American Society of Anaesthesiologists physical status (ASA IIII)
6. Caucasian patients
7. Able to give informed consent and comply with study protocol
Target Gender: Male & Female; Upper Age Limit 75 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
Planned Sample Size: 32; UK Sample Size: 32

Key exclusion criteria
1. History of significant preoperative weight loss (>10% over preceding 3 months)
2. Clinical history of pulmonary aspiration
3. Known gastrooesophageal reflux disease (GORD) or hiatus hernia
4. History of difficult intubation or conditions leading to the latter such as: previous neck radiotherapy/rheumatoid arthritis/presence of thyroid goitre
5. Metabolic disorders (e.g. diabetes mellitus, thyroid disease, Cushings Syndrome)
6. Simultaneous participation in another clinical study or involvement in a clinical study within the preceding 3 months
6. Patients with suspicion of alcohol/drug abuse
7. Pregnancy

Date of first enrolment
28/09/2011

Date of final enrolment
28/09/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen's Medical Centre
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
University of Nottingham (UK)

Sponsor details
Department of GI Surgery - E floor
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Sponsor type
University/education

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Charity

Funder Name
Core - The Digestive Disorders Foundation (UK)

Funder Name
European Society of Clinical Nutrition and Metabolism (ESPEN)

Funder Name
National Institute for Health Research (NIHR) (UK) - Biomedical Research Unit

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?
Results article	results	01/02/2019		Yes	No