ISRCTN76735966 https://doi.org/10.1186/ISRCTN76735966

Bowel surgery influences body's water, electrolyte and sugar control

Submission date
05/02/2013

Recruitment status
No longer recruiting

Registration date
21/03/2013

Overall study status
Completed

Last Edited
29/09/2021

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Familial adenomatous polyposis (FAP) is an inherited condition which mainly affects the large intestine (also known as the large bowel or colon and rectum). People with FAP develop many polyps (which are like small cherries on stalks) inside their large bowel. There are many different types of polyps but these particular polyps are called adenomas (the "adenomatous" in FAP). An adenoma can in time turn into a cancer which is why prophylactic surgery is offered. Patients with FAP undergo prophylactic removal of the colon usually in their late teens, to prevent the development of colorectal cancer. Until recently it was thought that the only effect of removing the colon (most of the large bowel) was loose faeces. There is now some evidence that this surgery has more profound effects, including alteration in the way the body handles water, electrolytes, glucose and fats. While preliminary animal work has been done, the metabolic disturbances caused by removal of colon have not yet been demonstrated in humans after ileo-rectal anastomosis (IRA - joining the last part of the small bowel to the last part of the large bowel) or restorative proctocolectomy (RPC - removal of whole of the large bowel and rectum and joining the last part of the small bowel to the last part of the gut), which are two most common forms of surgery involving removal of the colon in patients with FAP. This study aims to identify whether there is a disturbance of glucose, water and electrolyte metabolism in patients with no colon, and to see whether that can be easily corrected by taking a water and salt mixture (rehydration solution).

Who can participate?
Patients with FAP after colectomy (and those with intact colon for part 3 of the study).

What does the study involve?
The study is conducted in three stages at different time points.
Part 1 of the study aims to identify whether there is a disturbance of water, electrolyte and glucose metabolism in patients with no colon. The study involves no invasive investigations other than blood tests. Participant's blood samples are collected in the outpatient clinic after an overnight fast (12 hours of fasting). Participants are allowed to drink water, but are asked to avoid sugary drinks. The participant also provides a urine sample. The participant's blood pressure, body weight, height and test of muscle strength are recorded non-invasively. The participant is instructed to complete a 7-day food record for the assessment of both salt, energy

and nutrient intakes prior to attending the clinical investigation day. Quality of life or self-reported health status are also assessed using questionnaires.
Part 2 of the study aims to determine whether the disturbance in metabolism can be easily corrected by taking a rehydration solution. Participants are randomly allocated to one of two groups. One group receives a dummy (placebo) drink for 4 weeks, then after a 4-week break they are provided with the active rehydration drink to be consumed with meals every day for 4 weeks. The other group receive the active rehydration drink for 4 weeks, followed by a 4-week break, then they receive the placebo drink for 4 weeks.
Part 3 of the study aims to see whether taking the rehydration solution immediately after the removal of the colon can be used to prevent the problem altogether. Patients are randomly allocated to receive either the placebo drink or the active rehydration drink immediately after the removal of the colon.
Following discharge from the study, patients have a consultation and are given individual dietary advice based on their dietary record. They are also advised to continue with the rehydration solution.

What are the possible benefits and risks of participating?
If resection of the colon leads to disturbances in the water, electrolyte balance, sugar and fat metabolism, irrespective of underlying disease state, then rehydration therapy to restore sodium and fluid balance to normal control levels could form a simple, effective and cost-effective strategy to correct these disturbances. Participants receive the routine post-operative follow-up as an out-patient. In addition to the routine follow-up tests, the only burden to the participant is the time spent being told about the research project and thinking about whether they wish to participate. Upon obtaining consent, the other burden is the time spent to complete the quality of life questionnaire, the time spent in giving information about their dietary habits, and providing additional blood and urine samples for analyses. By taking part in this study there are no risks of physical injury or harm. All the necessary information is given and the blood tests are performed where possible at an existing out-patient appointment to reduce the burden and to avoid unnecessary inconvenience to the participant.

Where is the study run from?
St Mark's Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2011 to December 2014

Who is funding the study?
1. Royal College of Surgeons/Norman Williams IA Research Fellowship (UK)
2. St Mark's Hospital Foundation Seedcorn Fund (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Metabolic consequences following colectomy

Study objectives
Colon (large bowel) is an active metabolic organ, removal of which leads to adaptation of other tissues in the body. Until recently it was thought that the only effect of removing the colon (most of large bowel) was loose faeces. There is now some preliminary evidence that this surgery has more profound effects, including alteration in the way the body handles water, electrolytes, glucose and fats. Disturbance of this control by the body can lead to serious metabolic disturbances and poor quality of life.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London-Stanmore, 16/08/2011, ref: 11/LO/1014

Study design
Part 1 - Prospective observational study
Parts 2 and 3 - Prospective randomised controlled trials

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

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

Health condition(s) or problem(s) studied
Metabolic disturbances following colectomy

Interventions
Part 1 (Observational study)
Experimental design: To measure indices of sodium intake (diet diary), sodium loss (urine Na+, K+, plasma aldosterone) and insulin resistance (insulin, glucose, adiponectin, fasting lipids and blood pressure) in a large cohort of patients.
Methods: 50 IRA, 25 RPC and 25 colectomy with ileostomy patients will be recruited. Patients will attend one clinical investigation day. As part of the clinical investigation day, participant's blood samples will be collected in the outpatient clinic after an overnight fast (12 hours of fasting). Participant will be allowed to drink water, but will be asked to avoid sugary drinks. The participant will also provide a urine sample to be tested. The participant's blood pressure, body weight, height and test of muscle strength will be recorded non-invasively. The participant will be instructed to complete a 7 day food record for the assessment of both salt, energy and nutrient intakes prior to attending the clinical investigation day. Quality of life, or self-reported health status will also be assessed using the SF-36 and FACIT (F)version-4 questionnaires and compared to reference values from the general population.

Part 2
Experimental design: To perform a single-blind, placebo-controlled randomised cross-over trial of the effects of rehydration on the hyperaldosteronism and abnormal glucose tolerance in patients after IRA or RPC or colectomy with ileostomy.
Methods: 30 patients with demonstrated hyperaldosteronism from part 1 will be recruited.
Arm A: 15 patients will receive the 'placebo' drink for 4 weeks. Patients will then attend a clinical investigation day as for part 1 of the study. Patients will then have a 4-week washout period following which they will attend St Mark's Hospital for their second clinical investigation day. Patients will be provided with the active rehydration drink sachets (1 sachet in 1 litre of water to be consumed 1 tumbler with meals everyday). Patients will be advised to consume the active rehydration drink for 4 weeks following which they will attend St Mark's Hospital for their third clinical investigation day.
Arm B : As above, but 15 patients will receive the active rehydration drink for 4 weeks, followed by a 4 week washout period and will then receive the 'placebo' drink for 4 weeks. Patients will attend St Mark's Hospital for clinical investigation days as above.

Part 3
Experimental design: To perform a single-blind, placebo-controlled randomised trial of the effects of rehydration on the hyperaldosteronism and abnormal glucose tolerance in patients

after IRA.
Methods: 20 patients scheduled for IRA will be recruited.
Following recruitment, patients will attend St Mark's Hospital for a pre-operative clinical investigation day as described in part 1 and 2 of the study. Patients will be randomised to receive either the 'placebo' drink (as in part 2) or the active rehydration drink (as in part 2) starting from the immediate post-operative period.
Arm A: 10 patients will receive 'placebo' drink. Arm B: 10 patients will receive active rehydration drink.
Patients will attend St Mark's Hospital for clinical investigative day at 3, 6 and 12 months post surgery.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
To determine how prevalent sodium depletion and hyperaldosteronism are in well adapted patients following ileorectal anastomosis (IRA) or restorative proctocolectomy (RPC) or colectomy with ileostomy.

Secondary outcome measures
1. To determine if sodium depletion in well adapted patients following IRA or RPC or colectomy with ileostomy is associated with and causative of abnormal glucose tolerance.
2. To ascertain if these metabolic changes can be reversed with a simple rehydration therapy which could be easily incorporated into patient aftercare.
3. To ascertain if these metabolic changes can be prevented from developing post-operatively with a simple rehydration therapy which could be easily incorporated
4. Differences in health-related quality of life scores as assessed using SF-36 and FACIT- F questionnaires

Overall study start date
05/12/2011

Completion date
31/12/2014

Eligibility

Key inclusion criteria
1. Participants who have undergone IRA or RPC or colectomy with ileostomy
2. Surgery >1 year previously, or preoperative patients (part 3)
3. Absence of small bowel disease, Crohn's, Coeliac disease etc
4. No recent use of steroid medication (< 1 year)
5. 18 < BMI < 30 kg/m2
6. Minimal small bowel resection (<10 cm)
7. Aged 14-70 years

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
150

Key exclusion criteria
1. Patients with diabetes
2. Patients who are unwilling to consent
3. Patients who are regularly taking the electrolyte mix
4. Patients with any known adrenal gland disorder

Date of first enrolment
05/12/2011

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Mark's Hospital
Harrow
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Sponsor information

Organisation
North West London Hospitals NHS Trust (UK)

Sponsor details

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04cntmc13

Funder(s)

Funder type
Research organisation

Funder Name
Royal College of Surgeons/Norman Williams IA Research Fellowship granted in July 2012. The applicants (Miss S Mallappa) clinical salary is covered by the Fellowship for one year in the first instance.

Funder Name
St Marks Hospital Foundation Seedcorn Fund: £18k + £10k granted in October 2011 and May 2012 respectively.

Results and Publications

Publication and dissemination plan
The results are in the write-up phase, with the aim of submitting to peer-reviewed journal by the end of 2017. The results have already been presented at a number of international meetings.

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		22/06/2015	29/09/2021	No	No
Thesis results		01/11/2016	29/09/2021	No	No