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Effects of fermented milk on prevention of antibiotic-associated diarrhoea and Clostridium difficile infection in patients undergoing planned bone surgery

Submission date
26/12/2014

Recruitment status
No longer recruiting

Registration date
18/01/2015

Overall study status
Completed

Last Edited
19/02/2020

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Antibiotics are used in many conditions and are often given to patients to protect them against infection at the time of surgery. Diarrhoea can occur after the use of antibiotics and is a common problem that is difficult to avoid. It can delay recovery from surgery and in the worst cases can be a serious problem for the patient's health. Evidence is emerging that probiotics, 'friendly' bacteria usually in special drinks or yoghurts, might reduce this risk. The aim of this study is to investigate whether a daily bottle of Yakult, compared with placebo, can reduce the rate of antibiotic-associated diarrhoea in patients having planned orthopaedic surgery at the Elective Orthopaedic Centre (UK).

Who can participate?
Patients who have been referred for an elective orthopaedic operation at the Elective Orthopaedic Centre (UK)

What does the study involve?
Participants are randomly allocated to one of two groups: Yakult or placebo. They need to refrain from consuming any probiotics in the 8 weeks before their surgery. They might be telephoned around 3 weeks before the operation as a reminder, and to check that nothing has changed and that they meet the criteria for entry into the study. Patients are then provided with a supply of Yakult or placebo and should start drinking one bottle per day for 2 weeks before the surgery and for a further 2 weeks after the surgery, recording this information on the sheets provided. The operation and treatments proceed as normal and patients' care is as standard. After the operation, and for the next 4 weeks, patients need to record their stool appearance using a chart that they are provided with. If they have diarrhoea in the 4 weeks following the operation, as defined by three or more watery stools on two or more consecutive days, they need to inform us by telephone or email and send a stool sample for testing. This testing is part of the patients' clinical care because diarrhoea can be serious in some cases and can be treated if the stool sample shows the cause. Patients also need to complete a questionnaire about

gastrointestinal symptoms, which is short and simple, at the time of providing consent, in the hospital 2 weeks and and 4 weeks after surgery.

What are the possible benefits and risks of participating?
The main possible benefit would be a reduced risk of antibiotic-associated diarrhoea, which could otherwise prolong recovery from surgery and could be detrimental to health. There are no known safety issues surrounding this study.

Where is the study run from?
Epsom General Hospital, Elective Orthopaedic Centre (UK)

When is the study starting and how long is it expected to run for?
April 2010 to August 2014

Who is funding the study?
1. Yakult Ltd (UK)
2. Elective Orthopaedic Centre (UK)
3. St George's Charitable Trust (UK)

Who is the main contact?
Dr Carl Moran

Contact information

Type(s)
Scientific

Contact name
Dr Carl Moran

Contact details
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Additional identifiers

Protocol serial number
v9

Study information

Scientific Title
Effects of Yakult (Lactobacillus casei Shirota) on prevention of antibiotic-associated diarrhoea and Clostridium difficile infection in patients undergoing elective orthopaedic surgery

Study objectives

Maintenance of a healthy commensal microbiota and the gut's colonisation resistance by the administration of once daily probiotic Lactobacillus casei Shirota in the form of fermented milk (Yakult), before and after elective orthopaedic surgery, can help reduce the risk of diarrhoea associated with antibiotics and Clostridium difficile.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service, North London REC 3, 27/09/2010, ref: 10/H0709/52

Study design
Single-centre double-blind randomised placebo-controlled study

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Infections

Interventions
Patients will be randomly allocated to one of two groups. One group will receive a daily Yakult drink for 2 weeks before and 2 weeks after the elective operation. The other group will receive a placebo version of the drink for the same period. The placebo drink will not have the active ingredient of Yakult, but will look and taste identical and will be packaged in the same way. The placebo drink will also be manufactured by Yakult.

Intervention Type
Supplement

Primary outcome(s)
Incidence of antibiotic-associated diarrhoea during 4 weeks after surgery. This will be assessed in a hospital and then reported by participants following discharge through direct contact with us or records of their bowel habits over the 4 weeks following the operation. The stool chart will then be sent back to us in a pre-paid envelope.

Key secondary outcome(s))
1. Duration of antibiotic-associated diarrhoea: this will either be recorded directly if the diarrhoea occurs while the patient is still in hospital or by the participant on a stool chart that covers the 4 weeks after the operation. The recorded information is then sent back by the participant in a pre-paid envelope.
2. The incidence of Clostridium difficile diarrhoea, as diagnosed with a positive Clostridium difficile toxin test and stool culture to exclude other enteric pathogens in all patients with undiagnosed diarrhoea. Any inpatients with diarrhoea will have a stool sample sent for analysis, as per standard hospital care. Participants are asked to inform the trialists of the diarrhoea if it occurs in the 4 weeks after surgery, but following discharge from hospital, so that they can have a stool sample taken (as part of standard care).

3. Gastrointestinal symptoms recorded with the Gastrointestinal Symptom Rating Scale before and after surgery. They are recorded face-to-face at the time of consent and at the time of the operation. Participants record the symptoms themselves at 2 weeks and 4 weeks after the surgery and send the results in pre-paid envelopes.

Completion date
01/08/2014

Eligibility

Key inclusion criteria
1. Undergoing elective joint replacement surgery at the Elective Orthopaedic Centre (UK)
2. Must be able to adhere to the protocol requirements
3. Must be capable of giving informed consent
4. At least 18 years old

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Diarrhoea on pre-admission or within the preceding week
2. Lactose intolerance or intolerance to dairy products
3. Regular probiotic consumption in the previous 8 weeks
4. Antibiotic use in the previous 4 weeks
5. Patients unable to give written informed consent
6. Immunosuppression
7. Active inflammatory bowel disease or bowel surgery less than 6 months ago, cancer, leukaemia or pancreatitis

Date of first enrolment
21/07/2011

Date of final enrolment
15/08/2012

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
Epsom General Hospital
Elective Orthopaedic Centre
Denbies Wing
Surrey
United Kingdom
KT18 7EG

Sponsor information

Organisation
St George's University of London

ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Industry

Funder Name
Yakult UK Ltd (UK)

Funder Name
Elective Orthopaedic Centre (UK)

Funder Name
St George's Charitable Trust (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes