Buckinghamshire Healthcare NHS
NHS Trust
The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS
NHS Foundation Trust

Department of Nutrition & Dietetics
Direct Line: 01296 315775
Our Ref:

INFORMATION SHEET FOR PATIENTS

Study title:
Effect of *Lactobacillus casei* Shirota in preventing antibiotic associated diarrhoea including *Clostridium difficile* associated diarrhoea in patients with spinal cord injuries: a multicentre, randomised, double-blind, placebo-controlled trial

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

This information sheet consists of two parts:

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1
What is the research about?
We would like to invite you to take part in this project.
The aims of this study are to investigate if a probiotic preparation – Lactobacillus casei Shirota (Yakult) can prevent the development of antibiotic associated diarrhoea (AAD) and clostridium difficile associated diarrhoea (CDAD).
In addition, we would like to see if the change in gut flora (bacteria), nutritional status and the use of the so-called “proton pump inhibitors” such as lansoprazole, omeprazole, pantoprazole and esomeprazole are risk factors for AAD and CDAD.
We hope to include approximately 360 individuals in the study.

Why have I been invited?
We hope to know if the use of probiotic yoghurt drinks can prevent antibiotic or clostridium difficile associated diarrhoea. This study will provide important information to help us develop the standards of care for patients with spinal cord injuries.
If you are being prescribed antibiotics, we would like to invite you to participate in this study.

Do I have to take part?
Your participation is entirely voluntary. You have the right to refuse. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You have the right to withdraw from the study at any time, for any reason, without explanation and without detriment to your future health care.

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Patients aged above 18 years, with spinal cord injuries who have commenced antibiotic therapy, whilst on an acute spinal ward, are welcome to join this study.

What will happen to me if I take part?
If you agree to take part:

1. We may offer you a probiotic drink (Yakult, containing 6.5 x 10^9 *Lactobacillus casei* Shirota) once daily. This will continue through your course of antibiotics, and then for an extra 7 days after you finish the course of antibiotic treatment. To compare, we will have an equal number of patients in a second group who will take the placebo (an identical looking yoghurt drink without *Lactobacillus casei* Shirota). Whether you are in the group to receive additional probiotics or take placebo will be decided by chance.
2. We will collect a stool specimen to test the presence of gut flora. This will be taken approximately 15 minutes of your time (at baseline, 7 days and 30 days after you finish the antibiotic course). The following test will be carried out.
    a. Clostridium difficile toxin test will be carried out in the Trust's microbiology laboratory under supervision of Consultant Microbiologist.
    b. Anonymised Stool specimen will be stored in a dedicated fridge for delivery to our collaborator's laboratory for TaqMan PCR test, a more specialised test which can detect particles of the bacteria.
3. We will assess your nutritional status. This will take approximately 10 minutes and will take place on the ward. The following measurements will be carried out.
    a. Height (measured or estimated).
    b. Weight (measured or estimated).
    c. We will also ask a few simple questions about your recent health (e.g. any recent changes in weight and / or appetite).
4. We will record if you are on proton pump inhibitors (from your medication chart).
5. We will monitor your bowel record chart and record your clinical state - such as your level of spinal cord injury, and routine blood biochemistry results will be collected if available.
6. No additional blood samples will be collected in this study.
7. The above will be reassessed at 7 days and 30 days after you finish your antibiotics.

What are the alternatives?
If you so choose, you can stop taking the drink at any time. This will not affect your treatment in hospital or afterwards. If you do not take part in the study you will not receive the probiotic or the additional monitoring described above, but your care will otherwise be the same

Buckinghamshire Healthcare NHS
NHS Trust
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NHS Foundation Trust

What are the possible disadvantages and risks of taking part?
We do not expect any risks from being involved in this study.

What will happen to any samples I give?
Stool samples will be analysed by our Microbiology Laboratory and disposed of in the usual way within the Trust. Anonymised stool specimens will be sent to our collaborator's laboratory for TaqMan PCR test, a more specialised test which can detect particles of the bacteria. After the test, the samples will be destroyed.

What are the side-effects of any treatment received while taking part?
We do not expect any side effects from the treatment we give in this study.

Are there any possible benefits?
This study is designed to promote medical knowledge of whether probiotics can prevent the development of AAD and CDAD. It may be of no benefit to you personally but we hope that it will help to inform us and allow us to give better advice on the treatment of hospital patients in the future.

What happens when the research study stops?
When the study stops, we will offer you a further 2 weeks supply of Yakult Light for you to continue if you wish.

What if there is a problem?
If at anytime you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through NHS complaints procedure. Details can be obtained from the hospital in this instance. Please find relevant details in part 2 of this letter.

Will my taking part in the study be kept confidential?
Yes. We will follow standard ethical and legal practice. All information about you will be handled in confidence. The details are included in Part 2.

Will my GP know that I am involved in this study?
Your GP will not be informed that you have participated in this study. However you may discuss your participation with any health and social care professional as well as with any other person.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

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PART 2

What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your research doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your research doctor will ensure that your care continues as normal. If you decide to continue in the study we may ask you to sign an updated consent form. If this happens, your research doctor might consider you should withdraw from the study. He/she will explain the reasons and arrange for your care to continue. If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time. This will not affect the care you receive. Information collected may still be used. Any stored samples that can still be identified as yours will be destroyed if you wish. Please ask to speak to the researchers who will do their best to assist you.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (contact number supplied). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

If you are seeking advice and support on all aspects of healthcare, you can contact our patient advice and liaison service (PALS), our "one-stop-shop" for patients, carers and relatives. You can contact PALS on: Stoke Mandeville Hospital: 01296 316042; Email: pals@buckshealthcare.nhs.uk; The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust: 01691 404606; Email: pals.officer@rjah.nhs.uk

Will my taking part in the study be kept confidential?

All information collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the hospital will have your name, address and any other personal information removed so that you cannot be recognised.

What will happen to any samples I give?

If you develop diarrhoea, samples of your diarrhoea will be analysed by the microbiology laboratory and disposed of in the usual way. No other samples will be taken because of the study.

What will happen to the results of the research study?

The findings of this study will be published in suitable professional scientific journals and presented at an appropriate scientific conference.

Those who participated in the study will not be identified in any publication or presentation of the study results.

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Who is organising and funding the research?
This study has been organised by staff of the National Spinal Injuries Centre at the Stoke Mandeville Hospital (www.buckinghamshirehospitals.nhs.uk/spinal , the Midland Centre for Spinal Cord Injury (http://www.rjah.nhs.uk/Our-Services/Spinal-Injuries-Unit.aspx), Centre for Health Service Research at City University London (http://www.city.ac.uk/health/research/centre-for-health-services-research), Centre for Gastroenterology and Clinical Nutrition at University College London (www.ucl.ac.uk/medicine/gastroenterology-and-nutrition) and Norwich Medical School (http://www.uea.ac.uk/medicine) . Funding comes from the Industry Yakult Honsha Co. Ltd. (www.yakult.co.uk).

Who has reviewed the study?
This study has been given approval for conduct in the NHS by the National Research Ethics Service at South-Central Oxford C Research Ethics Committee.

What do I do now?
Details of the procedure and instructions will be given to you again before the measurements take place.
The person named below will be very happy to answer any additional questions you may have about this project. The ward staff will be able to contact them for you.

Contact person: Edmund Chiu Phone / bleep: Ext. 5836

Thank you for your time in considering this study. Please discuss this information with your hospital consultants, family, friends or GP if you wish.

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