

Probiotic treatment for acute watery diarrhoea in Vietnamese children

Submission date 25/04/2012	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 14/06/2012	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/10/2020	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

If your child has three or more loose watery stools without solid pieces per day, for less than 14 days, it is called acute watery diarrhoea. Diarrhoea is a very common disease in young children all over the world including Vietnam. Diarrhoea can be caused by bacteria, viruses and parasites, but in developing countries, rotavirus is the most common cause. This is also the case in Vietnam. The standard treatment for diarrhoea is an oral rehydration solution (ORS), which is a solution containing salts and sugars. When there is slime (mucous) and/or blood in the diarrhoea, and when it is caused by bacteria, doctors may also give antibiotics to some children. Some doctors recommend probiotics to help the intestines clear the infection. Probiotics are live bacteria which, when you drink enough of it, are said to be good for your intestines. They may help the good bacteria that normally live in your intestine to fight the bad bacteria or viruses that make you sick. Many scientists have looked at whether probiotics work for diarrhoea and overall, these studies suggest that they are good for the intestines. However, overall the quality of these studies is not high. The studies had many differences in the groups of patients that were studied, the way the studies were done, and which, how much and for how long the probiotics were taken. Not all studies had control groups that were given a placebo (dummy) treatment, which is essential for a reliable result. It is difficult to use all the different results to make one treatment guideline for treating children with acute watery diarrhoea. In conclusion, we are not sure if probiotics really work and how much to give. In Vietnam, probiotics are regularly prescribed by doctors treating children who have been admitted to the hospital for acute watery diarrhoea. Many people buy probiotics themselves because probiotics are thought to work and can be bought over the counter at pharmacies. One type of bacteria that are probiotics are *Lactobacillus acidophilus*. There are only a few studies looking at how *L. acidophilus* helps to reduce acute watery diarrhoea in children, but many probiotic brands in Vietnam contain them. Based on earlier studies, we think that therapy with *L. acidophilus* will reduce diarrhoea. Our main study question is to see if *L. acidophilus* therapy reduces diarrhoea by measuring the time from when your child takes his/her first dose of study medication to the first 24-hour period he/she no longer has diarrhoea. Other study questions are:

1. How much shorter the diarrhoea lasts. Parents/guardians will be provided with the diarrhoeal assessment and study drug administration chart card, where they will mark X when the child passes stool, and we will look at the time from when your child has taken his/her first dose of study medication to the first 24-hour period he/she has not had diarrhoea.

2. How long the diarrhoea lasted in your child, including the time before your child was admitted.
3. How many times your child has diarrhoea during the first three days of therapy.
4. In how many children the treatment does not work.
5. The amount of rotavirus, norovirus and L. acidophilus in your child's stool (faeces) by doing faecal tests at certain points in time.
6. The time your child has to stay in the hospital.
7. By how much diarrhoea is reduced in children who are treated with L. acidophilus, who get antibiotics and those that do not, during hospitalisation.

Who can participate?

Vietnamese boys and girls can enter this study if they are admitted to the hospital in Ho Chi Minh City for acute watery diarrhoea. Your child has to be between the ages of 9 months and 5 years, has to have diarrhoea for less than 3 days, and must have written permission from you (parents/guardians) for taking part in the study. Your child cannot take part if he/she has slimy (mucoid) or bloody diarrhoea, or has had diarrhoea in the month before he/she is admitted, or has a disease of the intestines that will not go away and will probably last for the rest of his/her life (chronic), or has a disease where the immune system does not work properly, or if your child takes medicine to suppress the immune system, or has lost so much fluid from his/her body that she is very ill. We would like 300 children to take part in the study.

What does the study involve?

Participating children will be randomly allocated into one of two groups: one group will receive L. acidophilus and the other group will receive a placebo. Your child will receive two sachets, twice a day, which is twice the regular dose. The total duration of the therapy will be 5 days.

What are the possible benefits and risks of participating?

There may be a bruise from taking a blood sample or the place where the blood sample has been taken may get infected. In Vietnam, probiotics are given regularly as treatment for children with watery diarrhoea. In earlier, published studies, scientists used a higher amount of probiotics than we will use, and no side effects were seen. So, we do not expect to see side effects from taking the study medication.

Where is the study run from?

Children's Hospital 2 in Ho Chi Minh City, Vietnam.

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

The study started in September 2014 and recruitment is expected to finish in September 2015.

Who is funding the study?

The Li Ka Shing Foundation (Hong Kong/Canada) and the Wellcome Trust (UK)

Who is the main contact?

Dr Stephen Baker
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Contact information

Type(s)

Scientific

Contact name

Dr Stephen Baker

Contact details

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

04EN

Study information

Scientific Title

A randomised placebo-controlled trial for the treatment of non-complicated acute watery diarrhoea using oral probiotics in children attending Childrens Hospital 2 in Ho Chi Minh City, Vietnam

Study objectives

This trial is designed to study the effect of a readily available and commonly used brand of probiotics (in Vietnam) containing *Lactobacillus acidophilus*. The study hypothesis is that probiotics are superior to placebo in the treatment of acute watery diarrhoea in children.

On 18/09/2014 the following changes were made to the trial record:

1. The scientific title was changed from 'A multi-centre randomised placebo-controlled trial for the treatment of non-complicated acute watery diarrhoea using oral probiotics in Vietnamese children' to 'A randomised placebo-controlled trial for the treatment of non-complicated acute watery diarrhoea using oral probiotics in children attending Childrens Hospital 2 in Ho Chi Minh City, Vietnam'
2. The anticipated start date was changed from 01/09/2012 to 26/09/2014
3. The anticipated end date was changed from 31/08/2013 to 26/09/2015
4. The study design was changed from 'Multi-centre randomised double-blinded placebo-controlled interventional trial' to 'Randomised double-blinded placebo-controlled interventional trial'

Ethics approval required

Old ethics approval format

Ethics approval(s)

Study design

Randomised double-blinded placebo-controlled interventional trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Prevention

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

Acute diarrhoea

Interventions

Current interventions as of 22/09/2014:

Lactobacillus acidophilus 2×10^8 (CFU) twice per day for the duration of 5 days versus placebo, twice daily for the duration of 5 days; both to be dissolved in water and ingested orally.

Previous interventions:

Lactobacillus acidophilus 2×10^9 (CFU) twice per day for the duration of 5 days versus placebo, twice daily for the duration of 5 days; both to be dissolved in water and ingested orally.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

The time from the first dose of study medication to the start of the first 24 hour diarrhoea free-period as assessed by the parents/guardians

Secondary outcome measures

Current secondary outcome measures as of 18/09/2014:

1. The total duration of acute watery diarrhoea (including the pre-enrolment duration), from admission to the start of the first 24-hour diarrhoea-free period, as assessed by the participant's parent/guardian
2. Treatment failure:
 - 2.1. No resolution of diarrhoea after 5 days of treatment course
 - 2.2. Severe symptoms for which treatment is stopped, such as the development of severe

dehydration, renal failure, (septic) shock, respiratory distress, or other syndromes associated with diarrhoeal disease (e.g. pneumonia)

2.3. Required additional anti-diarrhoeal treatment

3. The stool frequency in the first three days after the first dose of study medication as assessed by the nurse

4. The daily norovirus and rotavirus load in copies per millilitre of viral transport medium, by PCR on faecal swabs from admission until discharge, and at follow-up

5. The duration of hospitalisation defined as the number of days from hospital admission until discharge

6. The extent of intestinal *L. acidophilus* colonisation of faecal samples collected on admission, on discharge, and at outpatient follow-up

Secondary outcome measures from 11/07/2012 to 18/09/2014:

1. The time from the first dose of study medication to the start of the first 24-hour diarrhoea-free period, as assessed by the nurse on duty

2. The total duration of acute watery diarrhoea (including the pre-enrolment duration), from admission to the start of the first 24 hour diarrhoea free-period, as assessed by the participant's parent/guardian

3. Treatment failure:

3.1. No resolution of diarrhoea after 5 days of treatment course

3.2. Severe symptoms for which treatment is stopped, such as the development of severe dehydration, renal failure, (septic) shock, respiratory distress, or other syndromes associated with diarrhoeal disease (e.g. pneumonia)

3.3. Required additional anti-emetic or anti-diarrhoeal treatment

4. The stool frequency in the first three days after the first dose of study medication as assessed by the nurse

5. The daily norovirus and rotavirus load in copies per millilitre of viral transport medium, by PCR on faecal swabs from admission until discharge, and at follow-up

6. The duration of hospitalisation defined as the number of days from hospital admission until discharge

7. The extent of intestinal *L. acidophilus* colonisation of faecal samples collected on admission, on discharge, and at outpatient follow-up

8. The number and severity of adverse events.

Original secondary outcome measures until 11/07/2012:

1. The time from the first dose of study medication to the start of the first 24 hour diarrhoea free-period, as assessed by the nurse on duty

2. The total duration of acute watery diarrhoea (including the pre-enrolment duration), from admission to the start of the first 24 hour diarrhoea free-period, as assessed by the participant's parent/guardian

3. Treatment failure:

3.1. No resolution of diarrhoea after 5 days of treatment course

3.2. Severe symptoms for which treatment is stopped, such as the development of severe dehydration, renal failure, (septic) shock, respiratory distress, or other syndromes associated with diarrhoeal disease (e.g. pneumonia)

3.3. Required additional anti-emetic or anti-diarrhoeal treatment

4. The stool frequency in the first three days after the first dose of study medication as assessed by the nurse

5. The daily norovirus and rotavirus load in copies per millilitre of viral transport medium, by PCR on faecal swabs from admission until discharge, and at follow-up

6. The duration of hospitalisation defined as the number of days from hospital admission until discharge

7. The extent of intestinal *L. acidophilus* colonisation of faecal samples collected on admission, on discharge, and at outpatient follow-up
8. The time from the first dose of study medication to the start of the first 24 hour diarrhoea free-period, as assessed by the parents/guardians, between those participants who received antimicrobial therapy during hospitalisation and those that did not

Overall study start date

26/09/2014

Completion date

26/09/2015

Eligibility

Key inclusion criteria

1. Between 9 to 60 months of age with acute, non-bloody, non-mucoid, watery diarrhoea presenting at a study site with symptoms of less than 3 days duration, and
2. Written informed consent from a parent or guardian

We used the definition of diarrhoea as defined by the WHO diarrhoea treatment guidelines: the passage of unusually loose or watery stools, usually at least three times in a 24 hour period ± 4 .

Participant type(s)

Patient

Age group

Child

Lower age limit

9 Months

Upper age limit

60 Months

Sex

Both

Target number of participants

300

Key exclusion criteria

1. Patients with bloody or mucoid diarrhoea
2. Those who had ≥ 1 episode of diarrhoeal disease in the month prior to admission
3. Those who are known to have short bowel syndrome
4. Another underlying chronic (inflammatory) gastrointestinal disease
5. Systemic illnesses rendering the patient immunocompromised
6. Those on chronic steroid therapy
7. Those on immunosuppressive therapy, or
8. Those diagnosed as severely dehydrated, according to the definitions of the WHO guidelines for the treatment of diarrhoea, a manual for physicians and other senior health workers

Date of first enrolment

26/09/2014

Date of final enrolment

26/09/2015

Locations

Countries of recruitment

Viet Nam

Study participating centre**Head of Enteric Infections**

Ho Chi Minh City

Viet Nam

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Sponsor information

Organisation

University of Oxford (UK)

Sponsor details

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Sponsor type

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Funder(s)

Funder type

Charity

Funder Name

The Li Ka Shing Foundation (Vietnam)

Funder Name

Wellcome Trust (UK), grant ref: 089276/Z/09/Z

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?
Protocol article	protocol	28/01/2013		Yes	No
Results article	results	24/04/2017	15/10/2020	Yes	No