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Probiotic treatment for acute watery diarrhoea in Vietnamese children

Submission date	Recruitment status	[X] Prospectively registered
25/04/2012	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/06/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
15/10/2020	Infections and Infestations	

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 childs 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?
Childrens 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

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Additional identifiers

Protocol serial number
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)
Oxford Tropical Research Ethical Committee, 18/04/2012, ref. 14-12

Study design
Randomised double-blinded placebo-controlled interventional trial

Primary study design

Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Acute diarrhoea

Interventions
Current interventions as of 22/09/2014:
Lactobacillus acidophilus 2 x 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 x 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(s)
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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Child

Lower age limit
9 months

Upper age limit
60 months

Sex
All

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)

ROR
https://ror.org/052gg0110

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

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	24/04/2017	15/10/2020	Yes	No
Protocol article	protocol	28/01/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes