Informed Consent Form for Parents/Guardians of Subjects

Do probiotics modulate the intestinal microbiome in extremely premature infants?

Principle Investigator: Dr. Harish Amin

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Parent/Legal Guardian – Informed Consent Form

Title of Research Project: **Do probiotics modulate the intestinal microbiome in extremely premature infants?**

Investigator(s):

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Co-Investigator	Dr. Belal Alshaikh
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This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your child's participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form

BACKGROUND

Bacteria in a baby's intestine have an important role in the baby's health. Very premature babies may have an imbalance of bacteria, which could contribute to conditions such as necrotizing enterocolitis (NEC), a serious ulcerative bowel condition that often develops in premature infants. Giving probiotics to babies might help get the bacteria in balance. We routinely give probiotics to babies born after 29 weeks' gestation, but we now want to try it with babies who were born even more premature.

NEC is one of the major illnesses affecting premature babies. It is associated with significant long-term consequences for babies, including long-term neurologic disability, and can also sometimes lead to death. Ways to predict and prevent NEC from happening have been difficult to determine. Feeding breast milk and colostrum (the yellow coloured first milk that is produced) are the main ways of preventing NEC that are currently known. This is likely through the effects on the bacteria in the gut as well the baby's gut itself. The bacteria in the gut play an essential role in nutrition, the baby's immunity, and maintaining the cells lining the baby's gut. Current evidence suggests that interactions between the altered bacteria and the cells lining the baby's gut have an important role in the development of NEC.

Probiotics are bacteria that have health benefits for humans. They are a potential solution to "faulty bacterial colonization" patterns in premature infants and could be a possible way to decrease NEC. This has shown positive results in some studies, but many questions remain.

Probiotics are proposed to normalize bacterial populations and decrease gut disease in premature infants. There is limited data linking clinical outcomes with the biology of probiotics.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to see if giving probiotics actually changes the bacterial balance in the baby's intestine, and if that improves their ability to feed and reduce the incidence of serious infection and necrotizing enterocolitis.

WHY HAS MY CHILD BEEN ASKED TO PARTICIPATE?

For this research study, we will study babies that are born prematurely. Your baby was born before 29 weeks of gestation, which is the group of infants we want to study.

DOES MY CHILD HAVE TO PARTICIPATE?

Your baby's participation in this research trial is completely voluntary. You can choose whether or not to participate. If you decide not to participate, there are no penalties, and your baby will not lose any benefits to which your baby would otherwise be entitled. If you decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form.

You are free to withdraw (stop your baby's participation) at any time, without giving a reason and without penalty or loss. Your decision to withdraw will not affect your baby's future medical care.
Should you choose to withdraw your baby from the study, the data already collected will only be kept with your permission.

WHAT WILL HAPPEN TO MY CHILD IF HE/SHE TAKES PART?

This is a randomized controlled study. Your baby will receive either probiotic or no.
Your baby will be fed like all premature babies and the only change will be that if your baby is randomized to get the probiotic he will receive it once daily. In contrast, if it happens that your baby is in the control group, he will get nothing. Stool (feces) will be examined four times to determine what bacteria are present in all babies in the study. Very small amounts of breast milk/colostrum (0.1ml to 0.2ml every 4 hours) are usually given to all premature babies within the first 48 hours of life. Actual feeds of breast and/or human milk (donor milk) are initiated from 72 hours onwards (starting at 10ml/kg/day and increasing slowly thereafter). The study probiotic containing live bacteria (at a dose of 0.5g per day) or placebo will be started at or after 72 hours of life. Intravenous fluids (fluids given through a vein) are also started after birth to provide your baby with additional nutrients (protein, fat, sugar, vitamins and minerals).
A research assistant and/or nurse will collect the stool (feces) samples at 4 time points: prior to, two weeks and four weeks after probiotic or placebo administration is commenced, and one week after it is stopped. Stool will be collected directly from your baby's diaper with a sterile spatula and will be examined for what bacteria are present. As soon as a sample is collected, the nurse will contact the investigators for sample processing.

If your baby is placed on "nothing by mouth" (NPO), the study drug will be stopped and then restarted with re-feeding. The study probiotic or placebo will be given until 34 weeks corrected gestational age.

WHAT ELSE DOES MY CHILD'S PARTICIPATION INVOLVE?

We will also be reviewing your baby's health record chart to gather information on the history of the pregnancy (including complications and medication used by the mother), the birth (including: gestational age, weight, need for resuscitation) and course in the neonatal intensive care units in Calgary (including: diagnoses during hospitalization, feeding and diet history, medications used, laboratory and diagnostic imaging results).

WHAT ARE THE ALTERNATIVES?

Your baby would receive the standard care provided to all babies in NICU with no probiotics or placebo.

WHAT ARE THE RISKS?

There is a very low risk of infection, although so far this has not happened in any of the several thousand

babies studied in clinical trials. Antibiotics will be given if your baby gets an infection.

ARE THERE ANY BENEFITS FOR MY CHILD?

If you agree for your baby to participate in this study there may or may not be a direct medical benefit to her/him. Your baby may benefit from participating in this study by not developing the illness of NEC. The indirect benefit of participating in our study is that the results will provide important information on how the intestinal microbiome (bacteria) is altered with use of probiotics.

WILL WE BE PAID FOR PARTICIPATING, OR DO WE HAVE TO PAY FOR ANYTHING?

There is no cost associated for participation in the study. You will receive no payments to have your baby participate in the study.

WILL MY CHILD'S RECORDS BE KEPT PRIVATE?

If you decide to have your baby participate in this research project, your baby's medical records will be reviewed by a research assistant or one of the primary investigators to collect information that will help understand the findings of the study. This information may also be looked at by representatives of the Health Authorities or the University of Calgary Conjoint Health Research Ethics Board, additionally to check that the research trial is being performed correctly. All will have a duty of confidentiality to your baby as a research participant, and a duty to observe any applicable data protection laws.
The information gathered on your baby will be kept confidential, with none of said information being released without your written consent. The results of our study will be reported as group data without any information that could identify the participants in the study. At the end of this research trial, the results may be published or used for teaching. Nothing that could reveal your baby's identity will be included.

A description of this clinical trial will be available on www.clinicaltrials.gov as required by the U.S law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

IF MY CHILD SUFFERS A RESEARCH-RELATED INJURY, WILL WE BE COMPENSATED?

In the event that you or your baby suffers injury as a result of participating in this research, no compensation will be provided to you by The University of Calgary, Alberta Health Services or the Researchers. Nothing said in this consent form alters your right to seek damages.

WHO HAS REVIEWED THE TRIAL?

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.

CONTACT DETAILS:

If you have further questions concerning matters related to this research, please contact:

Dr. Harish Amin (403) 955-7513 or
Dr. Belal Alshaikh (403) 955-2320 or
Dr. Amuchou Soraisham (403) 944-8101.

If you have any questions concerning your rights as a possible participant in this research, or if you have any complaints or concerns about the way the trial doctors have carried out the trial, you may contact the Chair, Conjoint Health Research Ethics Board, University of Calgary, at 403-220-7990.

SIGNATURES

Your signature on this form indicates that you have understood to your satisfaction the information regarding your baby's participation in the research project and agree to their participation as a subject. In no way does this waive your legal rights nor release the investigators, or involved institutions from their legal and professional responsibilities. You are free to withdraw your baby from the study at any time without jeopardizing their health care.

Parent/ Legal Guardian Informed Consent Form

Title of Research Project: Do probiotics modulate the intestinal microbiome in extremely premature infants?

- I have read and understood the above information and have been provided with a copy of this Subject or Parent/Legal Guardian Informed Consent form.
- I have had time to think about what is involved if I decide that my baby will participate in this research project.
- I can, at any time, if I want, stop my baby's participation without having to give any reason. I will inform the research team about my decision.
- For the purpose of this registry, I give my permission that members of the research team, and representatives of the health authorities and Ethics Committees may look at my baby's medical records, in respect of the current research trial. I agree to the collection and processing of some of my baby's personal medical data.
- By signing this form, I have not waived any legal rights I otherwise would have as a parent/legal guardian of a participant in a research trial.

If you have any unanswered questions or unsatisfactory answers to your questions, do not sign this form.

Name of subject:…….

Name of subject's parent or legal guardian:……

Relationship to subject: ……..

Signature: …… Date __ __ / __ __ __ / __ _____

(dd / mmm / yy)

Name of Investigator / delegate: …….

Signature Investigator / delegate: …….. Date __ __ / __ __ __ / __ _____

(dd / mmm / yy)

Name of witness (if applicable): ……

Signature of witness (if applicable): …… Date __ __ / __ __ __ / __ _____

(dd / mmm / yy)

A signed copy of this consent form has been given to you to keep for your records and reference.