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To study the transit of beneficial bacteria from mother to infant

Submission date
16/08/2016

Recruitment status
No longer recruiting

Registration date
18/08/2016

Overall study status
Completed

Last Edited
18/09/2023

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The healthy development and maturation of a newborn baby depends not only on the genetic information inherited from both parents, but also on the bacteria which come to live in their gut. These bacteria are collectively known as the microbiota and are passed mainly from mother to baby at the time of birth, and some additional bacteria come from the environment. This study will focus on a specific group of bacteria called bifidobacteria as these are the dominant bacteria in healthy infants' guts and are associated with positive health outcomes. This study investigates whether a daily bifidobacterial probiotic capsule taken during pregnancy and breastfeeding results in transfer of these beneficial bacteria from mother to baby. This study also explores whether the probiotichas a beneficial effect on the mother's blood sugars and lipid levels.

Who can participate?
Pregnant women with a body mass index (BMI) of ≥20kg/m2 and ≤35kg/m2, who are otherwise healthy

What does the study involve?
Participants are asked to avoid food and yoghurts that contain probiotics for the duration of the study. When they are 16 weeks pregnant they are asked to provide a stool sample, complete a 3-day food diary, provide blood samples, and have a skin swab, mouth swab/rinse and a vaginal swab. Participants are also offered a fetal ultrasound at this visit. They are then randomly allocated to receive either probiotic or placebo (dummy) capsules, which they take daily from 16 weeks of pregnancy until the baby is 3 months old. The research doctor/midwife meets them at regular antenatal appointments to ensure they have enough capsules and that they are having no difficulties. When they are 34 weeks pregnant participants are again asked to provide a stool sample, complete a 3-day food diary, provide blood samples, and have a skin swab, mouth swab /rinse and a vaginal swab. At this time participants have an additional growth scan of their baby. At the time the baby is born, a sample of blood is taken from the umbilical cord and a sample of the placenta and membranes (afterbirth) is taken if they deliver by elective caesarean section. Participants are also asked to take a sample of their baby's first bowel movement, and to provide a small sample of breast milk and a swab from the skin of the breast. When the baby is 1

month old participants are asked to complete a 3-day food diary, provide stool samples (both mother and baby), and provide a sample of breast milk. This is repeated when the baby is 3 months old.

What are the possible benefits and risks of participating?
There are no health benefits from participating in the study but the knowledge gained may influence future medical care. There are no known risks associated with this study. Probiotics have been shown to be safe to take during pregnancy, with no risks for mother or baby. Participants may experience some discomfort in providing the requested samples but this will be brief and minimised as much as possible. Remembering to take the probiotic or placebo capsules each day may also be a minor inconvenience for participants.

Where is the study run from?
The National Maternity Hospital (Ireland)

When is the study starting and how long is it expected to run for?
December 2015 to December 2018

Who is funding the study?
National Maternity Hospital Ireland Medical Fund

Who is the main contact?
Prof. Fionnuala McAuliffe

Contact information

Type(s)
Public

Contact name
Prof Fionnuala McAuliffe

ORCID ID
http://orcid.org/0000-0002-3477-6494

Contact details
UCD Department of Obstetrics & Gynaecology,
65-66 Lower Mount Street,
Dublin 2
Dublin
Ireland
None

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EC 35.2015

Study information

Scientific Title
To study the transit of bifidobacteria from mother to infant: a randomised controlled trial

Study objectives
Maternal dietary supplementation with a specific bifidobacterial strain during pregnancy and lactation will result in colonization of the neonatal gut with that specific strain.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Research Ethics Committee at The National Maternity Hospital, Holles St, Dublin 2, 15/02 /2016, ref: EC 35.2015

Study design
Single-centre double-blind interventional randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Probiotics, pregnancy, Bifidobacteria, microbiome

Interventions
Eligible participants will be recruited from the outpatients' department of the hospital at approx. 12 weeks' gestation. Once a patient has given written informed consent to participate in the trial, she will be randomised to receive one of the following: daily Bifidobacteria probiotic capsule or daily placebo capsule. The study statistician, who will not be involved in data collection, will produce computer-generated sets of random allocations before the study starts. This will be done by block randomisation with randomly permuted block sizes, with the group allocation linked to a unique study identifier for each participant, the allocation and identifier will be communicated to the capsule manufacturer.

All study products will be manufactured under Good Manufacturing Practice conditions. The trial products, both probiotic and placebo will be provided as identical white, size #1 hydroxypropylmethylcellulose capsules. The probiotic capsules will contain approx. 10 mg of probiotic as freeze-dried powder blended with standard excipients at a dose of approx. 1 x 10 to the power of 9 colony forming units (CFU). Identical placebo capsules will contain standard excipient only. They will be prepacked in tubes and consecutively numbered for each woman according to the randomisation schedule, thereby concealing allocation from the trial staff and the participants. The consecutively numbered tubes will be allocated in sequence to each woman on recruitment. Treatment allocation will be concealed from the investigators until the data analysis is complete.

Participants will be provided with a 1-month supply of capsules at 16 weeks' gestation and will be requested to bring the empty bottles to their next appointment. This will enable us to monitor compliance with the intervention. Presence of the specific bacterial strain in faecal samples of the expecting mother will also serve to demonstrate compliance. Participants will advised to take 1 capsule per day from 16 weeks' gestation until 3 months postpartum. We have previously reported that this type of supplementation intervention is acceptable and that compliance is high among pregnant women (Lindsay et al, 2014).

Baseline blood samples, an oral rinse, a high vaginal swab, a stool sample and a nutritional assessment (3-day food diary) will be collected at 16 weeks' gestation (pre-supplementation) and again at 34 weeks' gestation. At delivery cord blood will be collected. At one point on days 2-5 postpartum, a small sample (< 5 ml) of breast milk and a sample of baby's stool will be collected.

At 1 month and 3 months postpartum a maternal 3-day food diary, a sample of breast milk, mother's stool and baby's stool will be collected.

Intervention Type
Supplement

Primary outcome measure
Presence of the supplemented bifidobacterial strain in the infant's stool in the 1st week postpartum, at 1 month postpartum and at 3 months postpartum. To measure this the infant stool will be analysed for the presence of the supplemented bifidobacterial strain.

Secondary outcome measures
Differences in the following between the probiotic and placebo groups:
1. Maternal lipids
2. Maternal insulin resistance as measured by fasting glucose and HOMA-IR
3. Maternal C Reactive Peptide
Maternal bloods will be taken in early (approx. 16 weeks gestation) and late (approx. 34 weeks gestation) pregnancy and will be analysed for these metabolic parameters.

Overall study start date
01/12/2015

Completion date
31/12/2019

Eligibility

Key inclusion criteria
Participant inclusion criteria as of 14/11/2018:
1. Pregnant women over the age of 18, capable of giving informed consent
2. With adequate understanding of the English language and an understanding of the study to enable them to give informed consent to participate
3. With a Body Mass Index of ≥18.5kg/m2 and ≤35kg/m2

Previous participant inclusion criteria:
1. Pregnant women over the age of 18, capable of giving informed consent
2. With adequate understanding of the English language and an understanding of the study to enable them to give informed consent to participate
3. With a Body Mass Index of ≥20kg/m2 and ≤35kg/m2

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Our sample size was estimated based on colonization of the neonatal gut at any time point. A target power of 80% will be used, at a type I error rate of 0.05. The default (placebo) colonization rate will be 0% as the strain we are using is not present in the maternal diet. In the intervention group, a minimal clinically relevant difference was not possible to obtain from the literature, thus, we took 15% as a target. The sample size required to show at least this difference between arms (0% versus 15%) is 60 per group. We will therefore need 120 participants to complete the study.

Total final enrolment
160

Key exclusion criteria
1. A history of gestational diabetes in a previous pregnancy
2. Pre-gestational diabetes e.g. Type 1 or Type 2 diabetes
3. A multiple pregnancy or fetal anomaly
5. A poor standard of English
6. A previous perinatal death

Date of first enrolment
29/08/2016

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
Ireland

Study participating centre
The National Maternity Hospital
Holles Street
Dublin
Ireland
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Sponsor information

Organisation
University College Dublin

Sponsor details
Belfield Downs
Dublin
Ireland
D14 YH57

Sponsor type
University/education

ROR
https://ror.org/05m7pjf47

Funder(s)

Funder type
Government

Funder Name
Science Foundation Ireland

Alternative Name(s)
SFI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

Funder Name
Alimentary Health

Alternative Name(s)
Alimentary Health Ltd., AH

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Ireland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		16/08/2016	15/09/2016	No	Yes
Preprint results		29/03/2023	31/03/2023	No	No
Other publications	Secondary analysis	31/08/2023	18/09/2023	Yes	No