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Investigating the impact of probiotic supplementation during pregnancy on maternal and infant health

Submission date
24/03/2020

Recruitment status
No longer recruiting

Registration date
30/03/2020

Overall study status
Completed

Last Edited
11/12/2023

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
During pregnancy, some molecules in the mother's blood can pass to the developing baby in the womb. This study is designed to investigate whether daily consumption of a probiotic in a food supplement form taken during pregnancy could change maternal inflammatory markers and affect the health and well-being of the mother. Inflammation is both a response of the immune system and a risk for certain diseases. Therefore, changes in inflammation of mothers may have the potential to improve health outcomes for mothers and their infants. This study will also investigate the effect probiotic supplementation may have on maternal well-being as measured using a number of validated questionnaires. This study will also look at whether taking this probiotic supplement will result in transfer of beneficial bacteria and probiotic strains from mum to baby. For this reason, supplementation with the probiotic will continue throughout pregnancy until 1 month after the baby is born.

Who can participate?
Healthy, pregnant women attending the study site for routine antenatal care, less than 18 weeks pregnant at the first visit, aged 18 to 45, BMI 18.5 to 35kg/m2, carrying a single pregnancy (not twins), have an understanding of the English language to fully understand study instructions and questionnaires, and are willing to take part and stop taking any probiotic products they currently consume. These products include supplemental and food sources of probiotics e.g. live yoghurts.

What does the study involve?
The study involves taking a capsule, either probiotic or placebo (dummy capsule), daily from between 14 and 20 weeks of pregnancy until delivery. Women will attend for the first study visit between 18 and 20 weeks, a second visit between 28 and 32 weeks, and a final visit between 1-4 weeks after birth with their infant. At each visit, while pregnant, women will be asked to provide a blood sample and answer some questionnaires on health and well-being. At the second visit, women will be asked to provide a stool sample as well. At the final postnatal visit, women will be asked to fill in the questionnaires once more, and provide a stool sample from both themselves and their infant.

What are the possible benefits and risks of participating?
There are no known risks to taking part in this study and no direct benefits either. Probiotic supplementation has been shown to be safe in pregnancy, for both mother and child. There may be some discomfort in providing stool samples. Women taking part in this study will have regular contact with both a midwife and nutritionist for the duration of the study. Women will also be providing invaluable information and contribution to the development of our knowledge of probiotics in pregnancy, which could improve pregnancy outcomes for mothers and infants in years to come.

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

When is the study starting and how long is it expected to run for?
November 2019 to June 2023

Who is funding the study?
1. Science Foundation Ireland
2. PrecisionBiotics will provide the capsules for this study

Who is the main contact?
Prof. Fionnuala McAuliffe
fionnuala.mcauliffe@ucd.ie

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
EC26.2019

Study information

Scientific Title
Investigation of the impact of Bifidobacterium supplementation in pregnancy on maternal immune markers

Acronym
MicrobeMom2

Study objectives
Targeted alteration of the maternal microbiota using a Bifidobacterium longum strain alters maternal inflammatory status during pregnancy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/12/2019, Research Ethics Committee at The National Maternity Hospital (Holles St, Dublin 2, Ireland; +353 (0)1 6373588; ethicsresearch@nmh.ie), ref: EC26.2019

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)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Pregnancy

Interventions

Eligible participants who provide written, informed consent and will be recruited into the study between 12- and 18-weeks' gestation. 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. These will then be put into an individual envelope for each participant and opened at the first study visit to reveal which group the participant is allocated. Study identifiers will be allocated to each participant sequential to randomisation. The group allocations will be communicated to the capsule manufacturers for labelling. Capsules will be prepacked in tubes labelled with the appropriate group allocation, 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.

Approximately 2 weeks post-recruitment, between 14-20 weeks' gestation, participants will be randomised to receive placebo or the intervention, a Bifidobacterium Longum strain probiotic. 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 109 colony forming units (CFU). Identical "Placebo" capsules will contain standard excipient only. They will be prepacked in tubes. Participants will be provided with up to a 3-month supply of capsules at this first visit and will be requested to bring the empty bottles to their next appointment. This will enable the researchers to monitor compliance with the intervention. Participants will be advised to take 1 capsule per day from randomisation until the final study visit between 1-4 weeks postpartum. The researchers have previously reported that this type of supplementation intervention is acceptable, and that compliance is high among pregnant women (Lindsay et al, 2014).

At recruitment, baseline details will be obtained to determine suitability to the study. At the randomisation visit between 14- and 20-weeks' gestation, baseline blood samples will be collected, as well as a lifestyle data questionnaire including physical activity, well-being and the use of supplements prior to enrolment in the study. The well-being section will include the World Health Organisation 5-Item well-being index, the Edinburgh Postnatal Depression Scale and the Perceived Stress Scale.

The second visit will take place between 28- and 32-weeks' gestation. Blood samples will be collected and also a stool sample, which will be used to determine gut microbiome. Dietary data will be collected using a food frequency questionnaire representing habitual dietary intakes of the previous 6 months. A lifestyle questionnaire will be collected using the same questions/tools as above and, in addition at this timepoint, data on sleep will be collected using the Pittsburgh Sleep Quality index Questionnaire and the Berlin Sleep Apnoea Questionnaire. A study feedback questionnaire will also be obtained at this point.

At delivery, cord blood samples where available and delivery information will be collected.

The final visit will take place between 1- and 4-weeks postpartum. Maternal and infant anthropometric measurements and stool samples will be collected. The lifestyle questionnaires will be repeated as per the first visit, with the addition of study feedback.

Intervention Type
Supplement

Primary outcome measure
Immune parameters (IL-10 after PBMC stimulation) measured using PBMC analysis at baseline and 28-32 weeks' gestation

Secondary outcome measures
1. Maternal inflammatory (TNF alpha and IL-6) and metabolic markers (HOMA, lipids) measured using venous blood samples at first visit (14-20 weeks) and second visit (28- 32 weeks gestation).
2. Stress/anxiety measured using Edinburgh Postnatal Depression Scale/Perceived Stress Scale /WHO well-being questionnaires at first visit (14-20 weeks), second visit (28- 32 weeks gestation) and postnatal visit (1-4 weeks postpartum)
3. Safety and tolerability of probiotic for the mother measured using questionnaires in late pregnancy and within 1 month postnatal
4. Pregnancy outcomes including gestational age, infant birthweight and infant length recorded from hospital records at birth
5. Transmission of probiotic from mother to baby stool measured using maternal and infant stool samples by strain-specific qPCR within 1 month postnatal

Overall study start date
01/11/2019

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Pregnant women less than 18 weeks' gestation
2. Aged over 18 years and younger than 45 years old
3. BMI of 18.5-35 kg/m2
4. Singleton pregnancy
5. Participants must also be willing to stop taking any other probiotic supplements or probiotic-containing foods where applicable
6. Women must have sufficient understanding of the English language

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants

Based on previous trials with the same probiotic strain in non-pregnant participants a sample size for 80% power analysis and an alpha significance of 0.05 is 68 (34 in each group) to allow differences to be detected in IL-10.

Total final enrolment
72

Key exclusion criteria
1. Multiple pregnancy or fetal anomaly
2. A poor standard of English

Date of first enrolment
01/05/2020

Date of final enrolment
01/01/2023

Locations

Countries of recruitment
Ireland

Study participating centre
National Maternity Hospital
Holles St
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Sponsor information

Organisation
University College Dublin

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Sponsor type
University/education

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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
PrecisionBioticsGroup

Results and Publications

Publication and dissemination plan
Additional documents can be made available upon reasonable request. Upon completion of data analysis and unblinding of the study, the researchers plan to publish their primary and secondary outcomes.

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Fionnuala McAuliffe (fionnuala.mcauliffe@ucd.ie).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		09/12/2023	11/12/2023	Yes	No