ISRCTN16554977 https://doi.org/10.1186/ISRCTN16554977

Can supplementation with a probiotic reduce the crying time and modify the gut microbiome in a group of infants with colic?

Submission date
14/05/2020

Recruitment status
No longer recruiting

Registration date
16/05/2020

Overall study status
Completed

Last Edited
02/12/2020

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
Colic is when a baby cries a lot and is difficult to console, without an obvious cause. This is a common problem that should get better on its own, but can be distressing and exhausting for parents. The exact causes of infantile colic are not fully understood. Likely causes could be problems with gut motility and food intolerance. Growing evidence suggests that the gut microbiota (the microorganisms that live in the gut) could be also involved in colic.

Certain compositions of the gut microbiota, where a type of bacteria called Coliforms are in high concentrations and a type of bacteria called Lactobacilli are in a low concentration, have been found to be more common in infants with colic than in infants without colic.

Probiotic supplementation with Lactobacilli has been shown to be effective in treating this condition in some clinical trials of breastfed infants. However, changing the composition of the gut bacteria during the early stages of gut development can induce lasting shifts in immunity as a result of inflammation of the gut.

A specific bacterial species called Lactobacillus rhamnosus may have anti-inflammatory properties. Supplementation with a probiotic of this bacteria may improve colic and reduce inflammation. The aim of this study was to investigate how effective a Lactobacillus rhamnosus probiotic was in treating infantile colic, in addition to maternal diet avoidance of cow’s milk.

Who can participate?
Newborns with colic aged between 2 and 10 weeks who are breastfed.

What does the study involve?
Participants are randomly allocated to one of two groups. Infants will either have normal care and breastfeeding or they will take 5 drops of the probiotic each day for 28 days and their mother will avoid consuming cow's milk over this period. Fecal samples will be collected from nappies before the trial starts and after 28 days. Their mother will also report how often the infant is crying at the start and end of the study.

What are the possible benefits and risks of participating?
This probiotic is well know and safe. There could be a reduction in colic symptoms of crying and fussing of the baby and parental discomfort.

Where is the study run from?
University Hospital City of Health and Science of Turin (Italy)

When is the study starting and how long is it expected to run for?
April 2017 to October 2019

Who is funding the study?
Office of the Governer (USA)

Who is the main contact?
Dr Francesco Savino
francesco.savino@unito.it

Study website
https://www.cittadellasalute.to.it/

Contact information

Type(s)
Scientific

Contact name
Dr Francesco Savino

ORCID ID
https://orcid.org/0000-0001-9163-1016

Contact details
Department of Pediatrics
Ospedale Infantile Regina Margherita
Azienda Ospedaliera Citta' Della Salute E Della Scienza Di Torino
Piazza Polonia, 94
Italy
Italy
10126
+39 (0)113135618
francesco.savino@unito.it

Additional identifiers

EudraCT/CTIS number
2020-002496-35

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Supplementation with the probiotic L rhamnosus GG to reduce the crying time and modify gut microbiota, or fecal calprotectin values in a group of infants with colic (Lactobacillus GG): a randomized controlled pilot study

Acronym
Lactobacillus GG

Study objectives
The aim of this study is to investigate whether supplementation with the probiotic Lactobacillus rhamnosus ATCC 53103 and maternal dietary elimination of cow's milk is effective in treating infantile colic of breastfed infants and reducing gut inflammation by measuring fecal calprotectin levels and composition of gut microbiota compared to placebo control.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/04/ 2017, Ethics Committee of the University Hospital City of Health and Science of Turin (Ospedale Mauriziano di Torino , Corso Spezia 60, Torino 10126 Italy; +39 (0)113134079), ref: 7/2017

Study design
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 file in Italian ISRCTN16554977_PIS_Italian (added 08/06/2020)

Health condition(s) or problem(s) studied
Infantile colic

Interventions
At enrollment, each infant underwent a medical examination by a pediatrician, and parents completed a questionnaire to obtain data concerning type of delivery, birth weight, and gestational age. The pediatrician asked the parents to report full-force crying by means of a well-validated three-day diary before the faecal sample collection at baseline and again after the 28 day intervention. The mean daily minutes of crying were calculated as a sum of crying, fussing, and unsuitable crying using a parental diary.

Eligible participants will be randomized to either receive the intervention or placebo control:
1. The intervention arm received Lactobacillus rhamnosus GG (5 x10^9 colony units per day). The probiotic study product consisted of a suspension of freeze-dried L rhamnosus ATCC53103 in a mixture of mais oil and mono and diglyceride oil supplied in a 5 mL dark bottle fitted with a dropper cap.
2. The control arm received a placebo. The placebo was a mixture of mais oil and mono and diglyceride oil supplied in a 5 mL dark bottle fitted with a dropper cap, without probiotic.

Both arms were instructed to take 5 drops of either the probiotic or placebo in the morning 30 minutes before feeding each day for 28 days. For both arms, maternal avoidance of cow's milk was requested for the 28 days study period.

Randomization was performed by the random-digit method, on the basis of a computer-generated numbers. A two treatments randomization scheme with random block of varying size was used (Stata Statistical Software: Release 9. StataCorp LP, College Station, TX. Ralloc Procedure).

Intervention Type
Supplement

Primary outcome measure
Colic measured by changes in the parent-reported crying time per day of infants at baseline and 28 days

Secondary outcome measures
Gut inflammation assessed using real-time PCR analysis of gut microbiota from fecal samples, and fecal calprotectin levels measured via a quantitative assay at baseline and 28 days

Overall study start date
05/04/2017

Completion date
30/11/2019

Eligibility

Key inclusion criteria
1. Aged between 2 and 10 weeks
2. Gestational age between 37 and 40 weeks
3. Birth weight between 2700 g and 4200 g,
4. Exclusively breastfed
5. Colic, as diagnosed according to the Wessel definition modified by Roma IV criteria (infants have at least three episodes of unexplained full-force crying lasting more than three hours per

day on at least three days a week for at least one week)
6. Maternal willingness and ability to avoid dietary cow’s milk

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
20

Total final enrolment
57

Key exclusion criteria
1. Clinical evidence of chronic illness or gastrointestinal disorders
2. Antibiotic or probiotic treatment in the week preceding recruitment

Date of first enrolment
01/03/2018

Date of final enrolment
31/10/2019

Locations

Countries of recruitment
Italy

Study participating centre
Ospedale Infantile Regina Margherita (ORIM)
Children's Hospital Regina Margherita
University Hospital City of Health and Science of Turin
Piazza Polonia, 94
Torino
Italy
10126

Sponsor information

Organisation

Azienda Ospedaliera Citta' Della Salute E Della Scienza Di Torino

Sponsor details
Piazza Polonia, 94
Torino
Italy
10126
+39 (0)113135059
fsavino@cittadellasalute.to.it

Sponsor type
Hospital/treatment centre

Website
https://www.cittadellasalute.to.it/

ROR
https://ror.org/001f7a930

Funder(s)

Funder type
Government

Funder Name
Office of the Governer

Alternative Name(s)

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United States of America

Results and Publications

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

Intention to publish date
01/06/2020

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Dr Francesco Savino, francesco.savino@unito.it.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			08/06/2020	No	Yes
Results article	results	05/06/2020	02/12/2020	Yes	No