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Is a vitamin and mineral supplement containing a small amount of iron as useful as one with a higher amount of iron in supporting the health of Bangladeshi children living in areas with a high level of iron in drinking water sources?

Submission date 24/06/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/07/2019	**Overall study status** Completed	
Last Edited 02/09/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Iron deficiency anemia occurs when your body doesn't have enough iron to produce hemoglobin. Hemoglobin is the part of red blood cells that gives blood its red color and enables the red blood cells to carry oxygenated blood throughout your body. Anemia is a global public health problem and Bangladesh is no exception. However, unlike the widely held assumptions, iron deficiency is not the principal reason for anemia in the Bangladeshi population. Iron status in population is good and iron present in drinking water (i.e. groundwater) is attributed for that. The country has a policy of MNP programming for control of anemia in young children. However, the program suffers from poor coverage, and side effects of MNP e.g. diarrhea, vomiting, nausea are identified as one of the limiting factors. We think iron from MNP and groundwater is causing the excess load of iron in the intestines and thereby causing the side effects. Hence we hypothesize that an MNP with a low dose of iron might be effective and result in fewer side effects.

Micronutrient Powder (MNP) is a mixture of the key nutrients which helps prevent anemia and promote health. MNP is an established intervention to control anemia in children in the low and mid-income countries. Despite its proven usefulness, studies have shown that MNP intake has been associated with side effects in children, such as diarrhea, vomiting, abdominal discomfort, etc. Recent studies in Africa have shown that MNP or iron supplementation have resulted in the adverse changes in the composition of gut microbiota (bacteria living in human intestines), with the growth of disease-causing (pathogenic) bacteria and suppression of the health promoting good bacteria. Iron, which is a key element of MNPs/supplements is implicated for the adversaries.

Bangladeshi people are exposed to a high level of iron from groundwater on which 97% of the rural population depends for potable supplies. Studies have shown that a high level of iron from groundwater leads to good iron status, and resulted in a low iron deficiency in Bangladeshi

children. Iron from groundwater alongside the iron from MNP may build up an excess of iron leading to the adverse effects. The burden of diarrhea has been observed to be higher in the MNP program areas of Bangladesh than the national prevalence estimate of the condition. The program evaluations have shown that the effective coverage of the program has been low, largely attributed to the side-effects.

Who can participate?
Children aged 24-53 months

What does the study involve?
Children will take one sachet of MNP every day for 2 months.

What are the possible benefits and risks of participating?
Participants received the MNPs - a nutritious food supplement - for 2 months, free of charge. Their health was assessed every week and if they were ill, treatment was provided free of charge. There was a risk of pain during the taking of blood; however, the blood was taken by experienced specialists in blood-taking who aimed to reduce stress for the children as much as possible. Some children might also experience loose stools or feeling sick as a result of taking the supplement, but this effect was expected to reduce with time. The children were monitored closely and treated for any health problems.

Where is the study run from?
1. Griffith University, Gold Coast, Australia
2. Institute of Nutrition and Food Science, University of Dhaka, Bangladesh

When is the study starting and how long is it expected to run for?
October 2018 to November 2018

Who is funding the study?
Nestlé Foundation.

Who is the main contact?
Sabuktagin Rahman,
sabuktagin.rahman@griffithuni.edu.au

Contact information

Type(s)
Scientific

Contact name
Mr Sabuktagin Rahman

Contact details
Public Health, School of Medicine
Building GO1
Room 3.30
Gold Coast Campus
Griffith University
Gold Coast
Australia

4222
+61475074577
sabuktagin.rahman@griffithuni.edu.au

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Ref # 46 /Biol. Scs. /2017-2018

Study information

Scientific Title
Efficacy of Micronutrient Powder (MNP) with low-dose of iron in Bangladeshi children living in areas with a high level of iron in groundwater

Acronym
MNP-low-Fe

Study objectives
Micronutrient powder (MNP) with a low dose of iron is not inferior to the standard MNP in terms of haemoglobin outcome.
MNP with a low-dose of iron would have less number of adverse events than that of the standard MNP

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 16/07/2017, Research Ethical Committee of Faculty of Biological Science, Dhaka University (University of Dhaka, Dhaka-1000, Bangladesh; +88 02 58613243, +88 02 9673387; deanbio@du.ac.bd), ref: 46 /Biol. Scs. /2017-2018
2. Approved DATE, Griffith University Human Research Ethics Committee, Australia.

Study design
Interventional randomised controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Iron deficiency anaemia

Interventions

The study is a randomized controlled trial in a community setting in rural Bangladesh. At the screening, the children aged 22-54 months were selected if the concentration of iron of the water of the tube-wells (i.e. groundwater) they drink from were >= 2 mg/L, and the guardians of the children were willing to participate in the trial.

Selection for blood and stool parameters:
Roughly over two-third of the enrolled children as per the required sample size was randomly selected for blood sample collection. A total of 327 children were enrolled who were roughly sex-matched. Each day on average 13 screened children were considered for the baseline data collection. Of the 13, nine children were selected by simple random sampling for blood parameters, e.g. hemoglobin, serum ferritin, sTfR, CRP, AGP and the presence of any congenital hemoglobin disorders (e.g. thalassemia). For selection of stool sample, we applied a stratified random sampling to select 4 children everyday considering the children selected for blood parameters and their peers non-selected for blood parameters at a ratio of 3 to 1. In this way, three children were randomly selected from the nine selected for blood sample collection and 1 child was randomly picked from the 4 children not selected for blood sample collection. This distribution worked towards a balance for stool sample selection across all study children, thus minimizing bias.

Randomization to treatment group:
The enrolled children (n=327) were randomly allocated to either the MNP (n=164) and the low-iron MNP (n=163) groups. Simple randomization was done using an online randomization software (www.startrek.com).

Children will be randomized to receive the micronutrient powder with a low dose of iron (referred to as MNP-low-Fe containing 5 mg of iron) and the standard MNP (containing 12.5 mg of iron). The children will feed 60 sachets of their allocated MNP at a dose of 1 sachet per day. The composition of the MNPs include five nutrients- iron, zinc, vitamin A, vitamin C and foiic acid in similar concentrations except for the dose of iron which is 12.5 mg and 5 mg respectively in the standard MNP and MNP-low-Fe. The sachets will be packed in identical looking foils with a code imprinted to indicate the different MNPs. Both researchers and the study participants are unaware of which group code belongs to which MNP.

Low iron MNP contains MNP with 5 components- Iron (5 mg elemental Fe), zinc, vitamin A, vitamin C, and Folic acid. Standard MNP contains - Iron (12.5 mg elemental Fe), zinc, vitamin A, vitamin C, and Folic acid. The dose of the other nutrients is the same between the two groups except for iron (5 mg vs. 12.5 mg). Enrolled children will be given at 1 sachet (1 g MNP powder) every day for 2 months.

After taking the written informed consent the mother of the enrolled child will be requested to provide information on household information, e.g. occupation of the head of the household, mother's education level, living conditions e.g. type of household, type of toilet used, household food insecurity, household possession of assets, spend on food items etc. Information will be gathered on the child's age, gender, sufferings of sickness over the past 2 weeks, e.g. loose stool, diarrhea, nausea, vomiting, fever, cold etc. Blood sample will be collected from the children after proper aseptic precaution for the parameters, e.g. hemoglobin ferritin, STFR. Stool parameters will be collected on a sub sample of children for the assay of gut microbiota. Their participation in the study is voluntary and they have the rights to withdraw from the study at any time point. Confidentiality of the data will be maintained strictly. Their identity will be coded and that the results will reveal only the aggregated data and not their identity.

Intervention Type

Supplement

Primary outcome(s)
1. Haemoglobin level in blood at baseline and endline (2 months after the start of treatment)
2. Serum ferritin level at baseline and endline (2 months after the start of treatment)
3. Soluble transferrin receptor (sTfR) level in blood at baseline and endline (2 months after the start of treatment)
4. Composition of gut microbiota from analysis of stool sample at baseline and endline (2 months after the start of treatment)
5. Incidences of morbidity, e.g. diarrhea, vomiting, respiratory infections, etc monitored weekly throughout the intervention until endline (2 months after the start of treatment)

Key secondary outcome(s))
1. Nutritional status assessed by measuring the weight and height of the children at baseline and endline (2 months after the start of treatment)

Completion date
31/01/2019

Eligibility

Key inclusion criteria
1. Children aged 24-53 months
2. Children drinking from groundwater with a high level of iron (>=2 mg/L)
3. Guardians willing for children to participate

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Child

Lower age limit
24 months

Upper age limit
53 months

Sex
All

Total final enrolment
327

Key exclusion criteria
1. Children receiving antibiotic in the preceding 2 months of the enrollment.
2. Children receiving MNP or other iron supplements in the preceding 2 months of the

enrollment.
3. Children with any congenital or chronic debilitating ailment.
4. Mother and the head of the household not willing to allow their child to participate in the trial.

Date of first enrolment
18/10/2018

Date of final enrolment
20/11/2018

Locations

Countries of recruitment
Australia

Bangladesh

Study participating centre
Griffith University
Public Health, School of Medicine
Gold Coast Campus
Parklands Dr.
Southport
Gold Coast
Australia
4215

Study participating centre
Institute of Nutrition and Food Science, University of Dhaka
Suhrawardi Udyan Rd
Dhaka
Bangladesh
1000

Sponsor information

Organisation
Griffith University

ROR
https://ror.org/02sc3r913

Funder(s)

Funder type
Charity

Funder Name
Fondation Nestlé

Alternative Name(s)
Nestlé Foundation, Fundación Nestlé

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

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?
Results article	results	13/11/2019	27/11/2019	Yes	No
Results article	results	01/02/2021	01/03/2021	Yes	No
Results article	Thalassemia carrier status and groundwater iron	18/08/2023	02/09/2024	Yes	No