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Study of zinc and copper supplementation in treatment of children suffering from diarrhoea

Submission date 31/08/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 24/09/2007	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/05/2013	**Condition category** Digestive System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diarrhoea causes an estimated 2.5 million child deaths in developing countries each year, 35% of which are due to acute diarrhoea. Zinc and copper stores in the body are known to be depleted during acute diarrhoea. Our objectives were to evaluate the efficacy of zinc and copper supplementation when given with standard treatment to children with acute watery or bloody diarrhoea.

Who can participate?
Inclusion Criteria
1. Children with Six to 60 months of age, either sex
2. Presence of diarrhoea
3. Duration of diarrhoea ≤ 72 hours prior to admission
4. Ability to take oral feeds or breast feeds
5. Caretaker willing to sign informed consent
Exclusion criteria
1. Serious complicating illness/disease
2. Clinically apparent kwashiorkor (malnutrition)
3. Residence more than 30 km from Nagpur
4. Previously enrolled in this trial

What does the study involve?
The treatment groups were:
1. Zinc alone
2. Zinc and copper
3. Placebo with each of these treatment groups divided in two sub-groups based on frequency of dose
Each treatment was administered either once a day or 6 hourly during hospitalisation and the allocation ratio across all the six groups was uniform. After discharge, the supplements were only administered as a single daily dose to all children. These doses of supplements were administered for a total duration of two weeks from enrolment in the trial including after discharge from hospital.

What are the possible benefits and risks of participating?
There are no known side effects from taking zinc and copper supplements in the amounts that will be given to your child during this study. It is possible that these supplements will hasten your childs recovery from diarrhoea and prevent further illnesses following discharge from hospital. Two additional blood collections will be required and these may cause some pain and distress to your child. To minimize this discomfort we will use a cream on the skin to reduce any pain.

Where is the study run from?
Indira Gandhi Government Medical College, Nagpur, India

When is the study starting and how long is it expected to run for?
The study started in September 2003 and ended in October 2006.

Who is funding the study?
The Welcome Trust (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
GR068664AIA

Study information

Scientific Title
Zinc and copper supplementation in treatment of acute diarrhoea in children: a randomised controlled clinical trial

Acronym
CDP

Study objectives
In a randomised controlled trial of supplementation for 2 weeks of 2 mg/kg/day of zinc or 2 mg /kg/day of zinc and 0.2 mg/kg/day of copper together with standard treatment, given to children hospitalised for acute diarrhoea, the children supplemented with zinc alone in comparison to the placebo group, or the children supplemented with zinc and copper in comparison to placebo group will at least experience the following.

Primary hypotheses:
1. 15% reduction in the mean duration of diarrhoea following admission to hospital
2. 50% reduction in the proportion of children with acute diarrhoea lasting more than seven days from onset
3. 25% reduction in the total stool output weight

Secondary hypotheses:
4. 30% increase in the proportion of children who are successfully rehydrated with oral rehydration solution
5. Increasing the frequency of dosage will increase the beneficial impact of zinc and copper supplementation on the clinical outcomes of acute diarrhoeal disease
6. 20% reduction in predicted mean total cost of treating patients with acute diarrhoea in the zinc and copper supplemented study groups as compared to the placebo group from the patient and providers perspective

Tertiary hypotheses:
7. 50% reduction in the proportion of children with acute diarrhoea who experience any the following complications:
7.1. Haemolytic uraemia syndrome
7.2. Septicaemia
7.3. Death
8. The effect of zinc and copper supplementation on each specific clinical indicator is different depending on the initial zinc status, initial anthropometric status, age and breastfeeding status

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from:
1. Indira Gandhi Government Medical College (IGGMC) on the 18th January 2003 (ref: 19/8/10/02)
2. University of Newcastle Ethics Committee (ref: H-500-0203)

Study design
Randomised, double blind, placebo controlled clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Acute diarrhoea

Interventions
The treatment groups were:
1. Zinc alone
2. Zinc and copper
3. Placebo with each of these treatment groups divided in two sub-groups based on frequency of dose

Each treatment was administered either once a day or 6 hourly during hospitalisation and the allocation ratio across all the six groups was uniform. After discharge, the supplements were only administered as a single daily dose to all children. The dose of zinc was 2 mg/kg body weight /day and that of copper was 0.2 mg/kg body weight/day. These doses of supplements were administered for a total duration of two weeks from enrolment in the trial including after discharge from hospital.

Intervention Type
Supplement

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Zinc supplementation, copper supplementation

Primary outcome measure
In-hospital:
1. Mean duration of diarrhoea of 3.9 days, measured every day for two weeks
2. Duration of diarrhoea (mean duration greater than 7 days from onset of episode), measured every day for two weeks
3. Time/rate of rehydration, measured every day for two weeks
4. Total stool output (weight), measured every day for two weeks
5. Amount of Oral Rehydration Solution (ORS) used, measured every day for two weeks
6. Amount of Intravenous (IV) fluids used, measured every day for two weeks
7. Weight change: on admission, after 4 hours and then every 24 hours

Secondary outcome measures
In-hospital:
1. Cost of supplements versus standard treatment
2. Rates of complications (measured every day for two weeks):
2.1. Electrolyte imbalance
2.2. Haemolytic uraemic syndrome
2.3. Septicemia
2.4. Death
3. Differential effects depending on clinical indicators:
3.1. Initial zinc status, measured once at baseline and on 14th day
3.2. Age, measured every fortnight over a 3 month period following discharge
3.3. Breastfeeding status, measured every fortnight over a 3 month period following discharge
3.4. Anthropometric indicators, measured every fortnight over a 3 month period following discharge

Overall study start date
01/09/2003

Completion date
30/10/2006

Eligibility

Key inclusion criteria
1. Six to 60 months of age, either sex
2. Presence of diarrhoea
3. Duration of diarrhoea less then or equal to 72 hours prior to admission
4. Ability to take oral feeds or breast feeds
5. Caretaker willing to sign informed consent

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
60 Months

Sex
Both

Target number of participants
808

Key exclusion criteria

1. Serious complicating illness/disease
2. Clinically apparent kwashiorkor
3. Residence more than 30 km from Nagpur
4. Previously enrolled in this trial

Date of first enrolment
01/09/2003

Date of final enrolment
30/10/2006

Locations

Countries of recruitment
India

Study participating centre
125, Katol Road
Nagpur
India
440013

Sponsor information

Organisation
University of Newcastle (Australia)

Sponsor details
c/o Dr Michael J. Dibley
Senior Lecturer in Epidemiology
Centre for Clinical Epidemiology & Biostatistics
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Sponsor type
University/education

Website
http://www.newcastle.edu.au/

ROR
https://ror.org/00eae9z71

Funder(s)

Funder type
Charity

Funder Name
The Wellcome Trust (UK) (grant ref: 068664)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2013		Yes	No