

# Scale-up Zinc Sulphate Use for Management of Childhood Diarrheal Diseases in Zambia Through Community Health Workers and Women's Support Groups

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#### Abstract

**Background:** In Zambia, diarrhea is one of the commonest diseases that affect under five children. It represents 12% of all causes of under-five mortality; and only 60% of children with diarrhea received oral rehydration treatment in 2012.

**Objective:** To assess if training of community health workers and establishment of women's support groups will enhance the use of zinc sulphate as adjuvant therapy for childhood diarrheal diseases and decrease child mortality in underserved areas. We therefore conducted a literature review of published clinical trials that were conducted in developing countries.

**Search methods:** We searched Medline through PubMed database and COCHRANE CRCT database. Our main focus was to identify literatures reporting on the effectiveness of oral zinc in reducing duration and severity of childhood diarrheal episodes; literatures published in developing countries, in English and French languages. We restricted our search to clinical trials. There was no time limit attached to our search.

Main results: After literature screening, 112 articles were excluded for not being clinical trials whilst 24 did not meet the main focus of our study. Only 28 articles were selected. Analysis reported a wide variety of diarrheal-related outcomes depending on number of considerations.

**conclusion:** Zinc supplementation in children reduces duration and/or severity of diarrheal episodes hence decreases child mortality.

Keywords: "diarrhea", "child", "zinc" and "therapeutic use".

## Introduction

Diarrhea, a condition characterized by frequent discharge of loose or watery stools for at least three times a day, is one of the major public health problems especially in children (1). According to World Health Organization (WHO) and the Centres for Disease Control and Prevention (CDC), diarrhea accounts for more than 760,000 of total child mortality every year and kills 2, 195 children every day, which is more than AIDS, malaria and measles combined (2, 3). In the majority of cases, this is preventable through exclusive breastfeeding, improved hygiene and sanitation and access to clean water, yet diarrhea is still one of the leading causes of death among children under five and it is the leading cause of malnutrition in the same age group (2). Causes of diarrhea are multiple (bacterial, parasitic, viral) but the contamination and spreading are mainly through unsafe food or water (1, 2). Diarrhea related deaths are more significant in low and middle income countries as access to safe water and good sanitation has remained poor in those countries (4).

Generally under-five children die from diarrheal diseases because of excessive loss of water and electrolytes that are associated with diarrheal diseases and; WHO and UNICEF recommend a diarrheal treatment package made of fluids replacement to prevent dehydration and zinc therapy (1). Zinc is known to be essential for the synthesis of proteins, cell growth and differentiation, immune function, and intestinal transport of water and electrolyte. For more than two decades, researchers have been assessing the benefit of zinc supplementation during diarrhea episodes. Studies have shown that zinc supplementation reduces diarrheal duration and treatment failure or death in persistent diarrhea. These studies also revealed that children receiving zinc experience a decrease in the severity of their diarrhea episodes. A ten days course as well as a five days course has proven to provide a prophylactic protection against future bouts of diarrhea for two to three months after the episode.(4).

ISSN: 2520-3134



## **Background and significance**

In Zambia, diarrhea is one of the commonest diseases that affect under five children (other diseases include malaria, respiratory infections, HIV/AIDS and neonatal causes with malnutrition underlying)(5). It represents 12% of all causes of under-five mortality; and only 60% of children with diarrhea received oral rehydration treatment in 2012 (6).

Poor access to safe water and adequate sanitation has continued to be one of the main drivers of diseases such as diarrhea in Zambia (7). According to Zambia Demographic and Health Survey 2013-14, 65% of households have access to improved sources of water and only 25.4% of households have improved and not shared sanitation facilities. This situation is more common in rural than in urban areas (e.g. 89.5% in urban vs 46.6% in rural for safe water and 35% in urban vs 18.5% in rural for having improved and not shared sanitation facilities) (8), and has significantly contributed in increasing the burden of diarrheal morbidity and associated mortality (7). Different strategies have been put in place by the government to help reduce the incidence of diarrheal diseases including diarrheal case fatality rate. Zinc supplementation is one of the strategies and has been implemented in the country since 2004. The implementation of these strategies in general and of zinc supplementation in particular has been challenged by a number of barriers. This is partially due to inadequate supply, geographical barriers, and constraints of time, distance and cost of transport and availability of qualified staff in rural areas. To prevent delays in accessing on time some vital health services, Zambia with the support of UNICEF and other partners, has introduced Integrated Community Case Management (ICCM) of pneumonia, malaria, diarrhea, and malnutrition in 23 selected districts out of 89 by 2010; this ICCM being run by Community Health Workers (CHW) Though, the health sector in Zambia is facing a major human resource crisis, with shortage of health workers at every service delivery level. Ministry of Health (MOH) has developed National Community Health Worker strategy aiming at repositioning and expanding the currently available CHW cadre. CHWs will deliver essential and priority health services, where there are gaps and reported deficiency through a taskshifting approach (from nurses to CHWs) (9). By the end of 2010, over 5,635 community health workers (CHWs) have been trained to support child health program in the country (10). CHWs undergo a year of formal training, and then return to their rural home communities to work. The majority of their work consists of household visits, but they also spend one day a week in the community health post and organize community health-education meetings. They are the first line of healthcare for Zambians living in the most remote areas of the country.

A recent review by the Child Health Epidemiology Reference Group (CHERG) estimated that community case management could result in reduction of childhood mortality. Oral rehydration salts (ORS) and zinc are effective against diarrhoea mortality in home and community settings, with ORS estimated to prevent 70 to 90 % of deaths due to acute watery diarrhea (11) and zinc estimated to decrease diarrhoea mortality by 11.5 % (12).

For these reasons, UNICEF, WHO and partners working in an increasing number of countries are supporting the ICCM strategy to train, supply and supervise front-line workers to treat children with diarrhoea, using ORS and zinc.

Despite this, the delivery of health services is often weakest where the needs are greatest, and low coverage of the most needed interventions results in a significant unmet need for treatment of diarrhea as one of the major child killers. E.g. in developing countries, current treatment levels are unacceptably low: only 39% of children receive correct diarrheal treatment (13).

Is this gap due to poor acceptability of ICCM services, lack or poor level of the community awareness, inadequate human resource? Increasing awareness in the context where this service is available and community health workers at community level, will they have a positive impact in accessing, utilizing zinc supplementation services and then reduce diarrheal related mortality in children aged under five?

We therefore intend to conduct a cluster randomized clinical trial that is going to assess the impact training of community health workers and establishment of women's support group on the use of zinc supplementation as adjuvant therapy in childhood diarrheal diseases at community level in rural areas of Western Province of Zambia where ICCM is being implemented as compared to where there is no implementation. The results from this study will provide evidence on how to scale up zinc

supplementation services in the ICCM implementing areas and later in the new districts. Knowing that, our messages to the community will be based on the efficacy of zinc supplementation in reducing the duration and severity of childhood diarrheal episodes.

We therefore conducted a literature review of published clinical trials that were conducted in low and middle income countries where Zambia belongs; methodology and results are presented below.

#### Literature review

## Formulation of an answerable question

PICO standardized format was used to formulate our research question as follow:

**Research question:** Can oral zinc supplementation be used to reduce duration and severity of childhood diarrheal episodes in children under five years old with acute or persistent diarrhea in rural areas of Zambia?

**Population:** Children under five years old with acute or persistent diarrhea in rural areas of Zambia **Intervention:** oral zinc supplementary therapy for diarrhea

**Comparison:** Children under five years old with acute or persistent diarrhea in rural areas of Zambia who did not receive oral zinc supplementary therapy

**Outcomes:** Reduction on the duration and the severity of childhood diarrheal episodes and its subsequent impact on child mortality in children under five years old in rural areas of Zambia.

#### **Methods**

#### Inclusion and exclusion criteria

We searched Medline through PubMed database on http://www.ncbi.nlm.nih.gov/pubmed/ and COCHRANE CRCT database. Our main focus was to identify literatures reporting on the effectiveness of oral zinc in reducing duration and severity of childhood diarrheal episodes; literatures published in developing countries, in English and French languages. We restricted our search to clinical trials. There was no time limit attached to our search. In PubMed, MeSh terms used were: diarrhea, zinc /therapeutic use and child. For COCHRANE CRCT, we used "diarrhea", "child", "zinc" and "therapeutic use" as keywords.

# **Search strategy**

#### PubMed search

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#1 search: "diarrhea" [MeSh terms]
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#2 search: "zinc/therapeutic use" [MeSh terms]

#3 search: ("child" [MeSh terms])

#4 search: (#1) AND #3

#5 search: (#4) AND #2

#6 search: (#4) AND #2 Filters: clinical trials

#### **COCHRANE CRCT search**

#1 search: "diarrhea" [keyword]

#2 search: #1 search AND "child" [keyword]

#3 search: #2 search AND "zinc" [keyword]

#4 search: #3 search AND "therapeutic use" [keyword]

### **Results**

After screening for clinical trials, focus to the topic under review; and duplication, 112 articles were excluded for not being clinical trials whilst 24 did not meet the main focus of our study either because they were not related to the effect of zinc supplementation in reducing duration and/or severity of diarrheal episodes or published in developed countries or in language other than English or French. Only 28 articles were selected (12 free full texts and 16 abstracts) by the end of the screening (Figure 1). Most studies were conducted in developing countries.

ISSN: 2520-3134

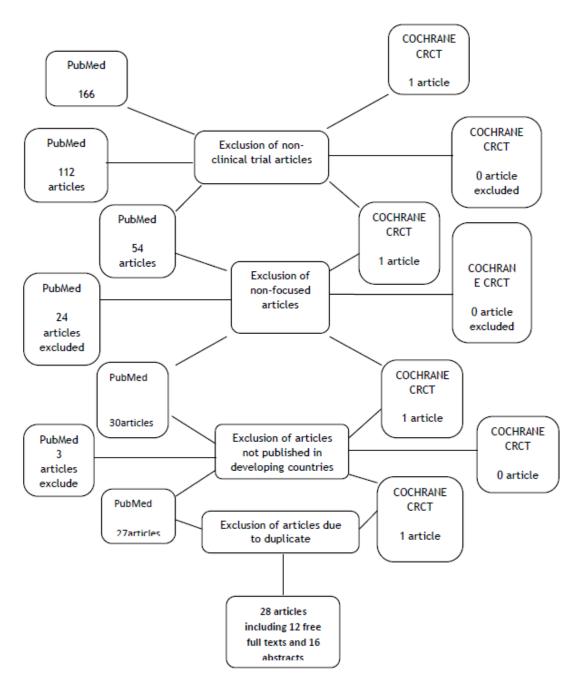


Figure 1. Literature research flow chart

Articles selected were organized in four sub topic groups according to their respective focus:

- 1. Impact of zinc supplementation in childhood diarrheal diseases
- 2. Impact of zinc and other micronutrients supplementation in childhood diarrheal diseases
- 3. Zinc and oral rehydration solution in acute diarrhea
- 4. Zinc in malnourished children with acute diarrhea

### Summary and synthesis of literature review

Randomized Controlled Trials (RCTs) assessing the therapeutic effects of zinc supplementation in childhood diarrheal diseases have reported a wide variety of diarrheal-related outcomes. Outcomes vary with different considerations:

### Impact of zinc supplementation in childhood diarrheal diseases

From the articles retrieved in our search, it shows that zinc supplementation, given alone, reduces drastically the duration and severity of acute or persistent diarrhea (16, 17, 22, 23, 24, 25). Associated with other additional information from other published randomized trials, these results indicate that zinc can have substantial clinical benefit and suggest that this supplementary therapy could reduce morbidity and mortality from diarrhea (16, 18, 19 and 23). Its effectiveness when given on daily or weekly schedule is still the same (16, 22 and 24). This applies also on the duration of adjuvant treatment; five days zinc treatment is as efficacious as ten days in preventing diarrhea in the subsequent three months (15).

Pooled analyses have a number of strengths. These include:

- 1. Evidence supported by statistical data (14)
- 2. Conclusions were made based on plasma zinc concentration and clinical findings (19)
- 3. Study conducted in areas of high prevalence of zinc deficiency (22)

Despite these strengths, analyses revealed also weaknesses such as:

- 1. The sample sizes in the stratified groups were insufficient to detect statistical significant differences in the 3-5-month and 6-11-month age-groups (16)
  - 2. No blinding was done; plasma levels do not always necessarily indicate zinc deficiency (20)
  - 3. Diarrheal episodes were detected by weekly surveillance during the supplementation period (23)

### Impact of zinc and other micronutrients in childhood diarrheal diseases

Articles reviewed revealed different outcomes depending on the micronutrients used in combination with zinc supplementation (27-33). Therapeutic Zinc or Zinc and Copper supplementation may not have a general beneficial impact on the duration of acute diarrhea in children (27); while Vitamin A and zinc supplementation was associated with distinct parasite-specific health outcomes (28). When compared with vitamin A alone, supplementation with zinc, or with zinc and multiple micronutrients, did not reduce diarrhea morbidity (29). Nevertheless, it was noted that zinc supplementation as adjunct therapy had a significant impact on the rate of prolonged diarrhea and some impact on duration and may be beneficial in children with diarrhea in developing countries (33).

Some of the strengths in our analyses are:

- 1. No difference noted in treatment adherence across the groups in the hospital stay or at home after discharge (27)
- 2. Treatment groups were similar at baseline with regard to the characteristics of the presenting episode, anthropometric data, and plasma zinc concentration (32)

Though weaknesses such as collection of only 1 stool per month for surveillance, was likely to miss enteric infections. There were no biochemical indicators of initial vitamin A and zinc status of children, no distinction between pathogenic and non-pathogenic E histolytica (28). Low dose of zinc as compared with other therapeutic studies as possible causes of the failure of a favourable response to treatment (27) was also noted.

# Zinc and oral rehydration solution (ORS) in acute diarrhea

An approach where caregivers are educated on the use of zinc supplementation in presence of easy access to oral rehydration salts appears more effective in diarrheal treatment (34). This approach does not adversely affect the use of oral rehydration salts; in fact, it greatly increases use of the same. Though, a controversial outcome from a study conducted in India (36) concluded that Zinc-ORS does not reduce the severity or duration of acute watery diarrhea in children who are brought to hospitals with diarrhea.

One of the strengths in our analyses was the engagement of private providers in the study which was an important factor in achieving high rates of intervention compliance (34). But the fact that zinc tablets were provided free of cost, possibility of a reporting bias in favor of the intervention groups for diarrhea prevalence could have been high (34).

ISSN: 2520-3134

#### Zinc in malnourished children with acute diarrhea

Literature reviewed showed that zinc supplementation in malnourished children with acute diarrhea may reduce the severity and duration of diarrhea, especially in children with low zinc levels (39). It reduces stool output, prevents weight loss and promotes earlier recovery (40).

Strengths related to studies include the fact that there was 24 hours observation and accurate weighing of stool output during the period of hospital management, while time to recovery was confirmed by direct observation (38). Intervention and control groups were comparable at admission in terms of severity and duration of diarrhea, as well as nutritional and anthropometric parameters (38). Despite these strengths, it was also noted that the control group in one of the studies did not received multivitamin syrup though it was appropriate for malnourished children (38) and the sample size in another study was insufficient to generalize findings (40).

## **Discussion**

From our literature review, we have noted that zinc supplementation is a new intervention for treating diarrheal episodes in children. It's an addition to the diarrhea treatment strategy. Findings of these trials, which were performed in several developing countries, indicate that therapeutic use of zinc is a diarrhea treatment strategy that promises to greatly improve diarrhea management and may have wide applicability. Though, they did not provide comparisons of zinc effects in different agegroups based on baseline investigations. Neither, interactions with other micronutrients nor its accessibility in the community were provided. In Zambia, despite World Health Organization (WHO) and UNICEF recommendation of use of zinc supplements in management of childhood diarrhea (42) and, the government policy of supportive community case management (CCM) and implementation for diarrhea, its use is not yet expanded countrywide (43).

At country level, few literatures have been published in line with the use of zinc in management of childhood diarrhea in the community. But results from other developing countries may be used to support the effectiveness of zinc supplementation in the treatment of diarrhea (14-41). Despite all, gaps still remain and they might be addressed by efficient implementation of training of CHW and establishment of women support groups. Gaps include issues of acceptability, community awareness, inadequate human resource hindering on access to ICCM services at community level.

#### Conclusion

Zinc supplementation reduces diarrheal duration and treatment failure or death in persistent diarrhea. It also decreases the severity of diarrhea episodes. A ten days course as well as a five days course has proven to provide a prophylactic protection against future episodes of diarrhea for two to three months after the initial episode.

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# Texila International Journal of Public Health Special Edition Apr 2019

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