Short-Course Prophylactic Zinc Supplementation for Diarrhea Morbidity in Infants of 6 to 11 Months

WHAT’S KNOWN ON THIS SUBJECT: Randomized controlled trials have shown that zinc supplementation during diarrhea substantially reduces the incidence and severity. However, the effect of short-course prophylactic zinc supplementation has been observed only in children >12 months of age.

WHAT THIS STUDY ADDS: The current study was able to show that short-course prophylactic zinc supplementation significantly reduced diarrhea morbidity in apparently healthy infants of 6 to 11 months even after 5 months of follow-up.

abstract

BACKGROUND: Zinc supplementation during diarrhea substantially reduces the incidence and severity of diarrhea. However, the effect of short-course zinc prophylaxis has been observed only in children >12 months of age. Because the incidence of diarrhea is comparatively high in children aged 6 to 11 months, we assessed the prophylactic effect of zinc on incidence and duration of diarrhea in this age group.

METHODS: In this randomized, double-blind, placebo-controlled trial, we enrolled infants aged 6 to 11 months from an urban resettlement colony in Delhi, India, between January 1, 2011, and January 15, 2012. We randomly assigned 272 infants to receive either 20 mg of zinc or a placebo suspension orally every day for 2 weeks. The primary outcome was the incidence of diarrhea per child-year. All analyses were done by intention-to-treat.

RESULTS: A total of 134 infants in the zinc and 124 in the placebo groups were assessed for the incidence of diarrhea. There was a 39% reduction (crude incident rate ratio [IRR] 0.61, 95% confidence interval [CI] 0.53–0.71) in episodes of diarrhea, 39% (adjusted IRR 0.61, 95% CI 0.54–0.69) in the total number of days that a child suffered from diarrhea, and reduction of 36% in duration per episode of diarrhea (IRR 0.64, 95% CI 0.56–0.74) during the 5 months of follow-up.

CONCLUSIONS: Short-course prophylactic zinc supplementation for 2 weeks may reduce diarrhea morbidity in infants of 6 to 11 months for up to 5 months, in populations with high prevalence of wasting and stunting. Pediatrics 2013;132:e46–e52

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KEY WORDS zinc, diarrhea, infants, randomized control trial

ABBREVIATIONS CI—confidence interval
IRR—incident rate ratio
RR—rate ratio

Dr Malik formulated the research question and contributed to designing the study, wrote the research grants, carried out the field investigations, carried out the initial data analyses, and drafted the initial manuscript; Dr Taneja contributed to designing the study, contributed to developing the standard operating procedures, implemented randomization and blinding, and reviewed and revised the manuscript; Dr Devasenapathy supervised the data collection and managed the data, analyzed the data, and interpreted the findings; Dr Rajeshwari supervised the clinical data collection and management, and contributed to developing the standard operating procedures; and all authors approved the final manuscript as submitted.

This trial was registered with the Clinical Trial Registry-India, No. CTRI/2010/091/00147.

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Zinc is required for multiple cellular tasks and the immune system depends on the sufficient availability of this essential trace element. Zinc deficiency is common in several developing countries, including India. This is because the commonly consumed staple foods have low zinc contents and are rich in phytates, which inhibit the absorption and utilization of zinc. Randomized controlled trials have shown that zinc supplementation during acute diarrhea reduces the duration and severity, as well as the incidence of subsequent diarrheal episodes. However, recently published meta-analyses conclude that prophylactic zinc supplementation significantly reduces the incidence of diarrhea only in children >12 months of age. Because the incidence of diarrhea is comparatively high in children 6 to 12 months of age (4.8 episode per year), coinciding with the starting of complementary feeding, the current study aimed to evaluate whether zinc prophylaxis for a short duration has any role in reducing the morbidity due to diarrhea in this age group. Although the original trial included additional outcomes, such as acute respiratory tract infections and growth, the results of these will be reported separately.

METHODS

Study Setting and Participants

This is a community-based, randomized, double-blind, parallel-arm placebo-controlled trial, conducted from January 1, 2011, to January 15, 2012. We included all children 6 to 11 months of age residing in Gokulpuri, an urban resettlement colony in the northeast district of Delhi, India, who were likely to stay until the completion of the study. Gokulpuri has ~2500 houses divided into 4 blocks, A, B, C, and D, with a predominantly migrant population of ~23,000. Most of the population belongs to the middle and lower socioeconomic strata. To achieve the final sample size, additional children were recruited from the similar adjacent area of Gangavihar. The study was approved by the Institutional Ethical Committee of Maulana Azad Medical College, New Delhi, and Associated Lok Nayak Hospitals. The trial is registered with the Clinical Trial Registry-India, number CTRI/2010/091/001417.

We hypothesized that zinc prophylaxis for 2 weeks would reduce the incidence of diarrhea in subsequent months. Thus, we excluded any child receiving zinc supplement at the time of study or who had received it in the preceding 3 months, those who were severely malnourished, immune-deficient, currently on steroid therapy, severely ill requiring hospitalization, or of families likely to migrate from the study area. A house-to-house survey was done at the beginning of the study to identify and recruit the eligible infants. The study purpose was explained to the family and an informed consent was obtained from parents of all infants before they were included in the trial. The recruitment was done during the first 2 weeks of January and July, followed by subsequent 5 months of follow-up, respectively. This ensured the assessment of outcomes for a complete year from January 2011 to January 2012, to minimize the effect of seasonality.

Randomization and Blinding

Random sequence was generated by simple randomization method using computer-generated random numbers (Excel 2010). The bottles were labeled with serial numbers in the Department of Community Medicine, Maulana Azad Medical College, by DKT, without the knowledge of the field investigator (AM). The field investigator and parents were blinded to the treatment allocation and unblinding was done at the end of the follow-up period for all 272 infants.

Intervention

The zinc and placebo syrups were prepared by Abyss Pharma (Delhi, India). Each 5 mL of the preparation containing placebo (syrup base) or zinc (20 mg elemental zinc as zinc sulfate) was packed in similar-looking bottles. The syrups were of similar color, taste, and consistency. During the survey, after ascertaining the eligibility and obtaining informed consent, the infants were enrolled sequentially. The mother received the bottles with prelabeled serial numbers. The field investigator administered the first dose of the intervention at the time of enrollment and advised the mother to give 5 mL of syrup (using a standard 5-mL plastic spoon) daily to the infant for the remaining 13 days. Subsequently, visits were made on the 7th and the 14th days to ensure compliance. If the syrup had not been given regularly, a maximum of 1 week was given to complete the dosages. We collected data for any possible side effects as reported by the caregivers during these visits. To ensure that the child did not receive additional doses of zinc, we provided mothers with identity cards indicating the study title and that the infants had received zinc syrup. These cards were to be produced whenever the child was taken to any medical practitioner.

Outcomes and Follow-up

The primary outcome was the incidence of diarrhea per child-year. Diarrhea was defined as 3 or more loose, liquid, or watery stools or any change in consistency or frequency of stools or at least 1 loose stool containing blood in a 24-hour period. Secondary outcomes included incidence density of acute diarrhea, dysentery, and persistent diarrhea; duration of diarrhea; and side effects. Acute diarrhea was defined as an episode of diarrhea lasting up to 14 days. If an episode lasted for >14 days, it was defined as persistent diarrhea. The episode was classified as dysentery if the stool contained blood. Duration was assessed as the number of days with diarrhea.
and as mean number of days a diarrheal episode lasted. A baseline assessment (Table 1) was done at the time of recruitment, which included weight and length measurements using a Salter weighing scale (up to 100 g [Model no. AM 1744; ATICO Medical Pvt Ltd, Haryana, India]) and an Infantometer (up to 1 mm [model no: AM 235 6M; Salter India Ltd, Daryaganj, New Delhi, India]) and an Infanometer (up to 1 mm [model no: AM 235 6M; Salter India Ltd, Daryaganj, New Delhi, India]) respectively. All the outcomes were assessed by a trained field investigator.

Follow-up for diarrhea began on the 15th day after intervention. Each child was followed-up fortnightly ±3 days and the follow-up continued for 5 months after the completion of zinc/placebo supplementation. At each follow-up, the mother/caregiver was asked about the occurrence of diarrheal disease during the previous 15 days. Recovery from a diarrheal episode was considered when the last day of diarrheal disease was followed by a 72-hour diarrheal-free period.6 Subsequent episodes were considered to be new diarrheal episodes.

Sample Size
The sample size was calculated taking into account 4 primary outcomes: decrease in incidence of diarrhea, acute respiratory tract infections, and increase in length and weight. For diarrhea, previous studies in similar populations estimated an incidence of 9.1 episodes (SD = 4.5) per child-year.7,9 Thus, for a 20% reduction in the incidence of diarrhea (α = 0.05 and power 80%), we required 90 infants in each group. However, the largest sample size required (for acute respiratory tract infection) was 258; thus, we recruited the entire population of 216 infants from Gokulpuri and an additional 56 infants from Gangavihar (total = 272). The outcomes for diarrheal disease were assessed for all recruited infants.

Statistical Analysis
The data were collected and checked for accuracy on a daily basis and entered into SPSS version 16 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The data were collected and checked for accuracy on a daily basis and entered into SPSS version 16 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). We included all children who had taken at least 2 doses of the intervention for the analyses. The follow-up visits for which the infant outcomes were not available were imputed using the worst-case (2 episodes of diarrhea) and best-case scenarios (no episodes). However, this did not change the study results; thus, we present in this article results from complete data set analysis. We decided to compare the monthwise mean episodes of diarrhea in the 2 groups. We also decided to compare the monthwise mean episodes of diarrhea in the 2 groups.

Socioeconomic status was assessed by using the Modified Kuppuswamy Scale (based on education and occupation of family head and total family income) modified for Consumer Price Index for industrial workers of India for 2011.13 The z-scores for length and weight were calculated by using World Health Organization reference tables for length and weight.14,15

Observation and Results
From a total of 3155 households identified during the house to house survey, we assessed 272 infants for eligibility (Fig 1). As there were no exclusions and refusals, all the infants were recruited. A total of 141 infants received zinc and 131 received placebo. Both groups shared similar baseline characteristics

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**TABLE 1** Baseline Characteristics of the Study Subjects at the Time of Recruitment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Zinc (n = 141)</th>
<th>Placebo (n = 131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>67 (47.5)</td>
<td>68 (51.9)</td>
</tr>
<tr>
<td>Female</td>
<td>74 (52.5)</td>
<td>63 (48.1)</td>
</tr>
<tr>
<td>Age, mo, mean ± SD</td>
<td>8.77 ± 1.73</td>
<td>8.76 ± 1.86</td>
</tr>
<tr>
<td>Socioeconomic status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>4 (2.8)</td>
<td>4 (3.1)</td>
</tr>
<tr>
<td>Upper Middle</td>
<td>39 (27.7)</td>
<td>30 (22.9)</td>
</tr>
<tr>
<td>Lower Middle</td>
<td>65 (46.1)</td>
<td>58 (44.3)</td>
</tr>
<tr>
<td>Lower</td>
<td>33 (23.4)</td>
<td>39 (29.8)</td>
</tr>
<tr>
<td>Average floor space per person, square meters ± SD</td>
<td>7.75 ± 4.13</td>
<td>8.26 ± 5.21</td>
</tr>
<tr>
<td>Household water purification device, n (%)</td>
<td>31 (22.0)</td>
<td>23 (17.6)</td>
</tr>
<tr>
<td>Feeding type, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>13 (9.2)</td>
<td>16 (12.2)</td>
</tr>
<tr>
<td>Complementary feeding</td>
<td>12 (8.5)</td>
<td>11 (8.4)</td>
</tr>
<tr>
<td>Both</td>
<td>116 (82.5)</td>
<td>104 (79.4)</td>
</tr>
<tr>
<td>Length, cm, mean ± SD</td>
<td>67.4 ± 3.86</td>
<td>67.5 ± 3.82</td>
</tr>
<tr>
<td>Mean Z score</td>
<td>−1.76 ± 1.46</td>
<td>−1.69 ± 1.48</td>
</tr>
<tr>
<td>Stunted (&lt;22 WHID), n (%)</td>
<td>51 (36.0)</td>
<td>54 (41.0)</td>
</tr>
<tr>
<td>Weight, kg, mean ± SD</td>
<td>7.26 ± 1.1</td>
<td>7.21 ± 1.2</td>
</tr>
<tr>
<td>Mean Z score</td>
<td>−1.50 ± 1.15</td>
<td>−1.58 ± 1.21</td>
</tr>
<tr>
<td>Wasted (&lt;−2Z WHID), n (%)</td>
<td>44 (31.2)</td>
<td>53 (41.0)</td>
</tr>
</tbody>
</table>

WHID, World Health Organization.
Seven families ($n = 4$ in the zinc group and $n = 3$ in the placebo group, respectively) migrated during the study period. The mean number of follow-ups was 10 in each group (zinc: $10.0 \pm 0.75$, placebo: $10.0 \pm 0.76$, $P = .721$). The final analyses included 134 infants in the zinc group and 124 in the placebo group, who had completed the study. A total of 19 infants (13.5%) in the zinc group and 26 infants (20%) in the placebo group were given an additional 1 week to complete the intervention, as they were found to be initially noncompliant.

### Effect on Diarrhea

Zinc supplementation for 14 days caused a significant reduction in the number of episodes of diarrhea. Of the total 829 episodes observed, 329 episodes occurred in the zinc group and 500 in the placebo group, accounting for an incidence of 6.07 and 9.90 per child year respectively, at the end of 5 months (Table 2). Generalized estimating equation regression model showed that there was a reduction of 39% (adjusted IRR 0.61, 95% CI 0.53–0.71) in episodes of diarrhea in the zinc group as compared with the placebo group after the model was adjusted for wasting.

When types of diarrhea were analyzed separately (Table 2), we found a significant decrease of 31% in the episodes of acute diarrhea (adjusted IRR 0.69, 95% CI 0.59–0.81), 70% in the episodes of persistent diarrhea (adjusted IRR 0.30, 95% CI 0.17–0.51), and more than 95% in the episodes of dysentery (adjusted IRR 0.03, 95% CI 0.01–0.24) in the zinc group.

Zinc supplementation led to a significant reduction of 39% (adjusted rate ratio [RR] 0.61, 95% CI 0.54–0.69) in overall days with diarrhea. The results of these will be reported separately.

Zinc significantly reduced the mean episodes of diarrhea for each of the 5 months (Table 4). However, the level of significance decreased after the third month.

### Side Effects

Reported side effects were diarrhea, vomiting, and constipation. The percentage of children reporting these were 9.0%, 10.4%, and 1.5%, respectively, in the zinc group and 7.3%, 4.8%, and 0%, respectively, in the placebo group, and the difference was nonsignificant in the 2 groups.

One death due to diarrhea was reported in the zinc group 3 months after recruitment. Verbal autopsy revealed severe dehydration due to nonadministration of oral rehydration solution or the available home fluids were the cause of death. The fact that the death took place 3 months after intervention, and the incorrect management revealed in the verbal autopsy, rules out any possible role of zinc.

### DISCUSSION

In the current trial, we report that prophylactic zinc supplementation for 2 weeks significantly reduced the incidence and duration of diarrhea during follow-up of 5 months. Although we studied additional outcomes (ie, acute respiratory tract infections and growth), the results of these will be reported separately.

Zinc depletion leads to upregulation of neuropeptides, such as cyclic guanosine monophosphate, and acute-phase reactants, such as interleukin 1, which creates secretory conditions in the intestine leading to diarrheal episodes. Thus, zinc prophylaxis in zinc-deficient populations reduces diarrheal morbidity.

The major limitation of this study is that serum zinc levels were not done to assess the deficiency and the subsequent effect on serum zinc levels. Nevertheless, previous studies in similar populations...
of Delhi have shown high prevalence of zinc deficiency (normal: 11.5–22.2 μM) to the extent of 73.3% for values <10.4 μM and 33.8% for values <9.0 μM. Moreover, in our study, the proportion of stunted infants was >20%, which suggests an elevated risk of zinc deficiency, because stunting is a proxy indicator of zinc deficiency in population studies. Also, baseline data on incidence density of diarrhea in this age group were not available.

Among the studies in which short-course zinc prophylaxis of 2 weeks was used, only 1 study had shown significant reduction in the incidence of diarrhea in a 12- to 35-month age group. Previous studies, which were carried out in infants of 6 to 11 months, have shown similar results to the current trial but after continuous zinc supplementation. One of these trials was carried out in a cohort of low birth weight infants. Trials have also shown the effectiveness of continuous zinc prophylaxis among wider age groups (6–41 months and 6–35 months, respectively), but subgroup analysis for children <12 months of age was not done. In a large study done in a similar population of Delhi as the current trial, zinc prophylaxis of 4 months was found to be effective only in children >12 months of age. Thus, unlike the previous studies, the current trial showed that short-course zinc prophylaxis significantly reduced diarrheal incidence in an age group of 6 to 11 months.

Zinc prophylaxis was shown to reduce the incidence of diarrhea in both continuous as well as short-course supplementation trials, in 2 meta-analyses. However, the beneficial effect was limited to children >12 months of age.

In the current trial, a significant reduction of days with diarrhea per child and duration per episode of diarrhea was observed. In contrast, results of 2 previous trials have shown no effect of continuous zinc prophylaxis on the duration of diarrhea. Of these, 1 study was done in the age group of 6 to 9 months and another in the age group of 18 to 36 months. Of the 2 meta-analyses, 1 with continuous zinc supplementation trials showed fewer total days with diarrhea, whereas the other, which included studies with continuous and short-course zinc supplementation, showed no effect on duration of diarrhea.

A significant reduction in incidence was seen when diarrhea was further classified into acute diarrhea, persistent diarrhea, and dysentery in the current trial. In the past, only 1 study concluded that the incidence of acute diarrhea was reduced significantly by zinc supplementation, but in a wider age group (6–35 months). Three studies, which had a similar age group or analyzed results for children <12 months of age, showed no significant decrease in persistent diarrhea in the zinc group. Although both the meta-analyses show that risk of persistent diarrhea did decrease with zinc supplementation, subgroup analysis for the 6 to 11 months age group is not available. Also one of these meta-analyses included studies with continuous zinc supplementation only. Regarding dysentery, only 1 study showed significant reduction in incidence of dysentery following zinc supplementation, that too in a wide age group of 6 to 35 months with continuous supplementation.

### TABLE 2: Effect of Zinc Supplementation on Incidence of Diarrhea on the Study Subjects

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Child Years Observed</th>
<th>Incidence (Episodes Child⁻¹year⁻¹)</th>
<th>Crude IRR (95% CI)</th>
<th>Adjusted IRR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>54.08</td>
<td>6.07</td>
<td>0.61 (0.56–0.74)</td>
<td>0.61 (0.53–0.71)</td>
</tr>
<tr>
<td>Placebo</td>
<td>50.25</td>
<td>9.90</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Acute diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>54.08</td>
<td>5.77</td>
<td>0.68 (0.57–0.83)</td>
<td>0.69 (0.59–0.81)</td>
</tr>
<tr>
<td>Placebo</td>
<td>50.25</td>
<td>8.33</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Persistent diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>54.08</td>
<td>0.28</td>
<td>0.29 (0.17–0.51)</td>
<td>0.30 (0.18–0.53)</td>
</tr>
<tr>
<td>Placebo</td>
<td>50.25</td>
<td>1.01</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Dysentery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>54.08</td>
<td>0.02</td>
<td>0.032 (0.004–0.24)</td>
<td>0.030 (0.01–0.24)</td>
</tr>
<tr>
<td>Placebo</td>
<td>50.25</td>
<td>0.58</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Adjusted for wasting.

### TABLE 3: Effect of Zinc Supplementation on Days with Diarrhea and Duration per Episode of Diarrhea

<table>
<thead>
<tr>
<th>Duration</th>
<th>Intervention</th>
<th>P Value*</th>
<th>Crude RR (95% CI)</th>
<th>Adjusted RR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD days of diarrhea</td>
<td>Zinc (n = 118)*</td>
<td>Placebo (n = 118)*</td>
<td>&lt;.001</td>
<td>0.60 (0.53–0.76)</td>
</tr>
<tr>
<td>Mean ± SD days per episode</td>
<td>3.60 ± 2.23</td>
<td>5.34 ± 2.16</td>
<td>&lt;.001</td>
<td>0.63 (0.55–0.77)</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test, P < .05 considered significant.

### TABLE 4: Monthwise Episodes of Diarrhea in the 2 Study Groups

<table>
<thead>
<tr>
<th>Month</th>
<th>Zinc</th>
<th>Placebo</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>First</td>
<td>0.44 (0.60)</td>
<td>0.85 (0.84)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Second</td>
<td>0.40 (0.56)</td>
<td>0.83 (0.87)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Third</td>
<td>0.49 (0.65)</td>
<td>0.88 (0.77)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Fourth</td>
<td>0.58 (0.65)</td>
<td>0.82 (0.78)</td>
<td>0.14</td>
</tr>
<tr>
<td>Fifth</td>
<td>0.61 (0.80)</td>
<td>0.77 (0.73)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test, P < .05 considered significant.
A study with short-course zinc supplementation showed a nonsignificant reduction in incidence of dysentery in the age group of 12 to 35 months. Of the 2 meta-analyses, 1 is in agreement with the current trial, although the age group is wide in this meta-analysis and studies with only continuous zinc supplementation have been included.

Among the previous studies in similar populations, we found that 1 study may have insufficient power to detect a significant decrease in diarrhea morbidity in infants 6 to 11 months of age. In other studies, zinc prophylaxis was given to a subset of the population that had already received therapeutic zinc for acute diarrhea, which might have led to reduced effectiveness of the subsequent zinc prophylaxis. However, the current study was done in a population that had not received zinc supplementation for the preceding 3 months, was apparently healthy, and had a high proportion of wasted and stunted infants. This, coupled with the fact that the maximum burden of diarrhea is seen in the age group of 6 to 11 months, may have been responsible for such significant results in the current study.

CONCLUSIONS

Previous trials and meta-analyses have shown the beneficial effect of zinc prophylaxis on diarrhea either by continuous supplementation for a long duration, ranging from 3 months to 1 year, or in age groups of >12 months. The current study was able to show significant reduction in diarrhea morbidity in infants of 6 to 11 months, even 5 months after short-course zinc prophylaxis.

The advantage of zinc given as a community-based prophylactic intervention is that all children in the target population will be covered. This in turn will reduce the overall incidence of diarrhea in the community compared with administration of zinc only to children who seek treatment for diarrhea. This is because many children suffering from diarrhea may not come to a health facility, as is common in the slum populations, and thus keep suffering from repeated episodes of diarrhea. The difficulty of having to give zinc to apparently healthy children is that the delivery strategy has to be community based, thus requiring additional time and work on the part of the health workers/community volunteers.

The results of this study have important cost and operational implications, as short-course prophylaxis of zinc in an adequate dose might be more feasible than continuous therapies.

The results of this study may be extrapolated to similar zinc-deficient populations only. Future trials on the effect of zinc prophylaxis on diarrhea should concentrate on zinc-deficient pockets in both developed and developing countries. It is desirable that such trials follow a standardized procedure regarding the duration and dose of zinc prophylaxis. This would ensure that policy makers have reliable and valid evidence to implement zinc prophylaxis programs for those child populations that will benefit the most from them.

REFERENCES


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