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Impact of zinc supplementation on diarrhoeal morbidity in rural children of West Bengal, India

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Aim: To determine the role of zinc supplementation in reducing diarrhoeal morbidity in children. *Methods:* A randomized, double-blind, community-based intervention study was conducted in 280 rural children aged between 6 and 41 mo. Children were randomly allocated into three groups. One group received a daily dose of 10 mg zinc for 5 d wk^{-1}, another group received 50 mg zinc once weekly and the remaining group received placebo. Zinc was supplemented for 16 wk from November 1999. Diarrhoeal episodes were detected by weekly surveillance during the supplementation period. *Results:* Eighty diarrhoeal episodes were detected among 59 children in all 3 groups. The groups were compared with each other at baseline and as regard to the outcome variable (incidence of diarrhoea). The proportion of children suffering from diarrhoea during the period was significantly lower in the zinc-supplemented groups (15.8% in daily and 16.5% in weekly group) than in the placebo group (30.8%). The incidence of diarrhoea in the daily and weekly zinc-supplemented groups was 0.68 and 0.69 episodes $child^{-1}$ y^{-1}, and that in the placebo group was 1.67 episodes $child^{-1}$ y^{-1} (relative risk 0.41, 95% confidence interval 0.24–0.71). Diarrhoeal incidence of <4 d duration was found to occur significantly less often in the supplemented groups. There was no difference in diarrhoeal incidence between the daily and weekly zinc-supplemented children. There were no detected adverse reactions in any of the supplemented groups.

Conclusion: The study indicates that zinc supplementation is effective in reducing diarrhoeal morbidity when administered either daily or in a weekly schedule.

Key words: *Children, diarrhoea, double blind, zinc*

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Malnutrition and diarrhoeal disease remain major public health problems, particularly in developing countries (1–5). Repeated attacks of diarrhoea are commonly associated with malnutrition, leading to further malnutrition, and resulting in a vicious cycle (6–7). Macronutrient deficiency is the main cause of malnutrition, but almost all malnourished children also suffer from micronutrient deficiency (8). Zinc is one of the most important micronutrients, deficiency of which leads to reduce immune function and increased morbidity from infectious diseases, including diarrhoea (9–10). A correlation between zinc deficiency and causation of diarrhoea has recently been documented in human subjects (11–14). Several community-based studies of zinc supplementation in children have also documented a substantial reduction in diarrhoeal incidence (15–17). In those studies zinc was supplemented daily, but daily supplementation may not be feasible. Weekly supplementation of zinc may have operational advantages over daily supplementation for mass distribution in future programmes. Therefore, a double-blind, placebo-controlled study was carried with two dosing schedules, daily and weekly dose, of zinc supplementation to determine the efficacy in reducing diarrhoeal morbidity among children below 4 y of age in the rural community in West Bengal, India.

Patients and methods

Study design

A community-based, placebo-controlled, double-blind, randomized intervention study was undertaken to assess the impact of daily versus weekly supplementation of zinc on diarrhoeal morbidity. The project proposal was reviewed and approved by the institutional ethics committee.

Study area and population

The study was conducted in three adjoining villages

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about 10 km away from Kolkata, West Bengal, India. Children aged between 6 and 41 mo, who were residing permanently in these villages with their parents, were included in the study. Selection of children of this age group was based on the earlier observation of a high incidence of diarrhoea in this group (18). Children below 6 mo of age were excluded, as breastfeeding may have a protective impact on the incidence of diarrhoea (19). Informed consent was obtained from the parents of the children before inclusion in the study. Before starting supplementation, relevant demographic and epidemiological information on the study families was collected through a baseline survey and recorded on the predesigned and pretested proforma.

Sample size and enrolment of study children

With the expectation of a 30% reduction in the prevalence of diarrhoea in both zinc-supplemented groups compared with the placebo, the calculated sample size was 85 children in each group, using the formula for comparison of two proportions (20).

Zinc supplementation

Randomization. Study children were randomized into 3 groups to receive either 10 mg elemental zinc (zinc sulfate in 5 ml syrup base) for the first 5 consecutive days in a week, or only placebo as 5 ml syrup for the same 5 d a week, or 50 mg elemental zinc (in 5 ml syrup) on the first day of the week followed by placebo syrup for the next 4 d. The randomization was done by a statistician using random number tables.

Blinding. For blinding, two bottles with the same serial number were supplied to the parents of each child. One small bottle of 30 ml syrup contained either 10 mg zinc 5 ml^{-1}, 50 mg zinc 5 ml^{-1} or placebo, and one bottle contained 120 ml syrup of either 10 mg zinc 5 ml^{-1} or placebo. The 30 ml bottle was fixed to one specific day (first day of the week) and the 120 ml bottle to the other 4 d of the week. After the first round of supplementation, bottles were replaced to continue the supplementation up to 16 wk. The two zinc syrups and placebo were similar in colour and taste and were prepared in identical bottles. Both 30 and 120 ml bottles were numbered according to the random number by the pharmaceutical company, which kept the code number to maintain confidentiality. Zinc supplementation was started from November 1999 and carried out for 16 wk.

Surveillance and data collection

Eight female locally resident surveillance workers, with an educational level up to 10th grade, were engaged for the surveillance of diarrhoea. They were properly trained for active surveillance to detect diarrhoeal episode(s) by visiting the study children once a week and to record the information only on the predesigned proforma. They were also trained to manage diarrhoea cases at a community level. They supervised the administration of supplemented syrup and observed any adverse effects following supplementation, e.g. vomiting. The diarrhoea cases detected by surveillance workers were further followed up for the nature of stool, presence of blood, mucus and duration of each episode by the field team of the institute, using a standard pretested proforma. A physician from the Epidemiology Division carried out overall supervision of the project work.

Data entry and analysis

Data were scrutinized for consistency and accuracy before being entered into a personal computer using a database software package, dBase IV, and converted into Epiinfo version 6.0 for matching consistency and validity. The validated data were randomly checked. The 3 groups were identified and relative risks (RR) with 95% confidence intervals (95% CI) were obtained using Epiinfo version 6.0.

The χ^2-test with Yates' continuity correction was used to compare the incidence of diarrhoea between groups. Fisher's Exact test was used when the expected cell frequency was less. After analysis of the data, decoding was done to identify the supplemented groups.

Definitions

- Diarrhoea: three or more loose or watery or mucoid stool (presence of only mucus in stools) in 24 h. The presence of visible blood in loose stool, even on a single occasion during the episodes, was considered as bloody diarrhoea.
- Incidence: the number of new episode of diarrhoea within the stipulated time-frame. The denominator was number of child-weeks of observation in the stipulated time, which was converted to child-years.
- New diarrhoeal episode: when there were at least 2 diarrhoea-free days between the episodes.

Results

In total, 290 children aged 6–41 mo were included in the study during the baseline survey. However, 10 children were excluded as they reached the age of 41 mo at the time of supplementation. Therefore, 280 children were included in the study. Baseline information of the study families in three groups was comparable (Table 1). Parameters of baseline information such as average number of family members (4.12–4.33), mud-structure housing (50%) and monthly income within Rs 2000 (US $45) in 80.0% of the families, and other parameters such as sanitary latrine, occupation of the head of the family and literacy of the parents did not differ significantly.

Fifty-nine children developed 80 episodes of diarrhoea during the study period, of which 18 episodes

Table 1. Comparability of study and control families in the three groups of children (6–41 mo).

Information	Daily 10 mg	Weekly 50 mg	Placebo
No. of children	95	91	94
No. of families	92	88	87
Total population	399	363	373
Average people family^{-1}	4.33	4.12	4.28
Gender			
Male	45.26%	42.86%	50.00%
Female	54.74%	57.14%	50.00%
Housing condition			
Kuccha	47.8%	48.9%	52.9%
Other (mixed)	52.1%	51.1%	47.1%
Latrine (sanitary)	91.3%	85.2%	83.9%
Family income mo^{-1} (rupees)			
<2000	83.7%	79.5%	80.4%
2000–5000	14.1%	18.2%	14.9%
>5000	2.2%	2.3%	4.6%
Occupation of head of household			
Daily labour	54.3%	56.8%	52.9%
Other	45.6%	43.2%	47.1%
Literacy of father			
Illiterate	28.8%	28.4%	27.6%
Literate	71.7%	71.6%	72.4%
Literacy of mother			
Illiterate	45.7%	56.8%	56.3%
Literate	54.3%	43.2%	43.7%

occurred in each of the zinc-supplemented groups (either daily or weekly), and 44 episodes occurred in the placebo group. The outcome variables on diarrhoeal morbidity in the three groups are presented in Table 2. It is evident from the Table 2 that 15.8% and 16.5% of children suffered from diarrhoea who received zinc supplementation either daily or weekly, respectively, compared with the children (30.8%) who received placebo, and the differences between the supplemented and placebo children were statistically significant. The overall incidence of diarrhoea in the daily and weekly supplemented groups was 0.68 and 0.69 episodes child^{-1} y^{-1} respectively, whereas the incidence in the placebo group was 1.67 episodes child^{-1} y^{-1} (RR 0.41, 95% CI 0.24–0.70).

The incidence of diarrhoeal episodes child^{-1} y^{-1} among children <2 y of age were significantly less: 1.09 and 0.62 in the zinc-supplemented groups, compared with 2.71 in the placebo group (RR 0.39, 95% CI 0.18–0.84 and RR 0.23, 95% CI 0.10–0.51). In contrast, the incidence among children aged ≥2 y was not significant different in the daily and weekly zinc-supplemented groups compared with placebo group.

The risk of developing watery as well as mucoid

Table 2. Efficacy of zinc supplementation in reducing diarrhoea with 10 mg (daily) or 50 mg (weekly) dosage schedule compared with placebo.

Parameter	Daily ($n=95$)	Weekly ($n=91$)	Placebo ($n=94$)	Daily vs placebo			Weekly vs placebo			Daily vs weekly		
				p	RR	95% CI	p	RR	95% CI	p	RR	95% CI
Proportion of children suffering												
	15.8%	16.5%	30.8%	0.014	0.51	0.29–0.89	0.022	0.53	0.31–0.93	0.897	0.96	0.50–1.84
Incidence (episodes child^{-1} y^{-1})												
Overall	0.68 (1370)	0.69 (1364)	1.67 (1369)	<0.001	0.41	0.24–0.70	<0.001	0.41	0.24–0.71	0.989	1.00	0.52–1.91
Age (y)												
<2	1.09 (477)	0.62 (589)	2.71 (575)	<0.001	0.40	0.20–0.81	<0.001	0.23	0.10–0.51	0.239	1.76	0.68–4.60
≥2	0.46 (893)	0.74 (775)	0.92 (794)	0.117	0.51	0.21–1.20	0.586	0.80	0.37–1.76	0.315	0.63	0.26–1.56
Gender												
Male	0.52 (606)	0.52 (597)	1.06 (687)	0.127	0.49	0.19–1.26	0.136	0.49	0.19–1.28	0.979	0.99	0.32–3.04
Female	0.82 (764)	0.81 (767)	2.29 (682)	0.001	0.36	0.18–0.69	0.001	0.36	0.18–0.69	0.992	1	0.45–2.22
Family income mo^{-1} (rupees)												
≤2000	0.63 (1147)	0.38 (1078)	1.40 (1112)	0.011	0.45	0.24–0.85	<0.001	0.28	0.13–0.60	0.254	1.64	0.69–3.91
>2000	0.70 (223)	1.38 (286)	1.01 (257)	0.442	0.69†	0.17–2.86	0.691	1.26	0.40–3.91	0.289	0.55†	0.14–2.10
Incidence (type of episode)												
Watery	0.11	0.19	0.53	0.007	0.21‡	0.06–0.74	0.039	0.36	0.13–0.99	0.360	0.60†	0.14–2.49
Mucoid	0.42	0.42	0.95	0.018	0.44	0.22–0.89	0.019	0.44	0.22–0.89	0.991	1.00	0.43–2.29
Bloody	0.15	0.08	0.19	0.499	0.80†	0.22–2.97	0.227	0.40†	0.08–2.07	0.345	1.99†	0.37–10.85
Incidence (duration of episode, d)												
1–3	0.15	0.19	0.57	0.021	0.27	0.09–0.8	0.025	0.33	0.12–0.92	0.497	0.80†	0.21–2.96
4–7	0.38	0.50	0.95	0.010	0.40	0.19–0.83	0.051	0.52	0.27–1.02	0.523	0.77	0.34–1.74
>7	0.15	–	0.15	0.636	1.00†	0.25–3.99	0.062	–	–	0.062	–	

Figure in parentheses indicate child week of observation.
RR: relative risk; 95% CI: 95% confidence interval.
† Fisher's Exact test; ‡ Yates' correction.

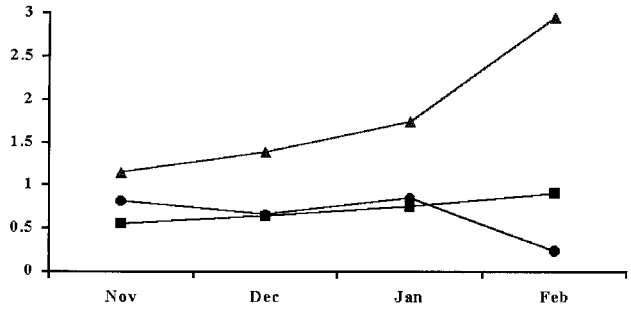

Fig. 1. Monthly incidence of diarrhoea in zinc-supplemented and control children from November 1999 to February 2000. ●: Daily; ■: weekly; ▲: placebo.

diarrhoea was much lower in both zinc-supplemented groups than in the placebo group (Table 2). The relative risk for the occurrence of watery diarrhoea was 0.21 (95% CI 0.06–0.74) and 0.36 (95% CI 0.13–0.99) in the daily and weekly supplemented groups, respectively, and that of mucoid diarrhoea was 0.44 (95% CI 0.22–0.89) in both supplemented groups. However, zinc supplementation did not have any impact on the incidence of bloody diarrhoea.

Table 2 also shows that children in both the daily and weekly zinc-supplemented groups had significantly less chance of developing a shorter duration (1–3 d) of diarrhoea (incidence 0.15 and 0.19, respectively) than did children in the placebo group (incidence 0.57) (RR 0.27, 95% CI 0.09–0.8 and RR 0.33, 95% CI 0.12–0.92). The incidence of diarrhoea with a duration of 4–7 d was significantly less (RR 0.40, 95% CI 0.19–0.83) in the daily supplemented group, but weekly supplementation did not show any effect compared with placebo group. The outcome variables did not show significant difference between the daily and weekly supplemented groups.

The overall incidence of diarrhoea in girls was significantly greater than in boys (RR 1.77, 95% CI 1.12–2.83). The reduction in the incidence in girls was significantly higher (RR 0.36, 95% CI 0.18–0.69) in the daily and weekly supplemented group. This impact was not reflected in the boys. The incidence of diarrhoea in lower income group ($\leq$Rs 2000) was 0.64 and 0.38 in the daily and weekly supplemented groups compared with 1.44 in the placebo group. These differences were significant in the daily (RR 0.45, 95% CI 0.24–0.85) and the weekly (RR 0.27, 95% CI 0.13–0.60) supplemented groups. No such differences in reduction was observed in the income group of >Rs 2000.

Monthly differences in the incidence of diarrhoea in the three groups are shown in Fig. 1. During the first month of supplementation no significant differences in the incidence of diarrhoea were observed in the three groups. However, an increasing trend towards a difference in the incidence of diarrhoea in both zinc-supplemented groups was observed compared with the placebo group. The difference was significant (RR 0.08, 95% CI 0.01–0.60) in the daily supplemented group and (RR 0.3, 95% CI 0.1–0.93) in the weekly supplemented group in the last month of the study.

No adverse effects were detected in the zinc-supplemented groups.

Discussion

This double-blind, randomized, placebo-controlled, community-based study was designed to compare the efficacy of zinc supplementation in daily and single weekly doses in children aged 6–41 mo. The results confirmed that zinc supplementation (in both daily and weekly doses) in young children can substantially decrease the incidence of diarrhoea. The overall reduction of diarrhoeal episodes was 59% among zinc-supplemented children.

The findings of the study are in accordance with other community-based studies of zinc supplementation in children, particularly in developing countries (15, 17). Pooled data analysis of zinc-supplemented trials in developing countries also indicated an overall reduction of 25% prevalence and an 18% reduction in the incidence of diarrhoea (21). In those published trial zinc supplementation was given on a daily basis. A greater impact of zinc on diarrhoeal morbidity was found in the current study than in other studies. However, the discrepancies between the findings of this study and other published studies may be due to variations in sample size and the shorter duration of the present study. Zinc deficiency is quite common in people in developing countries, because of the low consumption of foods of animal origin and because people live mainly on a cereal-based diet (8) containing high levels of fibre and phytate, which hamper zinc absorption. Zinc supplementation in an already zinc-deficient community may have had a greater impact.

There are gender differences in childcare practice in India. Girls are likely to be more malnourished than boys (22). Boys are given a better share of the food, leading to more malnutrition in females (23). In the present study, there was a greater incidence of diarrhoea in girls than in boys in the non-supplemented group. The supervised administration as free supplementation of zinc meant that there was no sharing, which may have led to a greater impact of zinc on female children. A review article also showed that females tended to benefit more than boys from zinc supplementation, although this difference was not significant (24). An effect on boys were also reported in children >11 mo of age (16).

A study in Bangladesh reported that zinc supplementation was associated with a 43% reduced rate of prolonged diarrhoea in the 6–23 mo age group (25). In the present observation the impact of zinc supplementation was reflected much more in children below 2 y of

age, and the zinc-supplemented groups had significantly less short-duration (1–3 d) diarrhoea. However, the power of the tests was inadequate, which may be due to the small number of diarrhoeal episodes during 16 wk of observation.

In this study, the overall incidence of diarrhoea in daily and weekly zinc-supplemented groups was 0.68 and 0.69 episodes child^{-1} y^{-1}, respectively, compared with 1.67 episodes child^{-1} y^{-1} in the placebo group. However, after 4 mo of supplementation it was noticed that there may be a greater effect on diarrhoeal morbidity of daily supplementation than weekly supplementation in the long run.

In the present study no effect of zinc was observed on the incidence of bloody diarrhoea in either the daily or weekly dosing schedule. In contrast, a study conducted in India reported a reduction in the incidence of dysentery in boys receiving zinc supplementation (26). Studies conducted in developing countries also showed other beneficial effects of zinc (27–29), including a reduction in the incidence (15–17) and clinical course of acute diarrhoea (30).

The findings of the present study suggest that weekly and daily zinc supplementation has similar beneficial effects in reducing the incidence of diarrhoea among children in the rural community in West Bengal, India. If zinc supplementation is included in the diarrhoeal diseases control programme for reducing diarrhoeal incidence, weekly supplementation of zinc will be suitable, sustainable and cost-effective to the public health programme in developing countries such as India, through village-level workers. Despite the advantages of weekly supplementation, one disadvantage is that if it is missed for 1 or 2 wk there would be a long gap until the next supplementation. A major drawback of daily zinc supplementation is that the dose must be administered daily, which may place an extra burden to the mothers or health workers. Moreover, daily zinc supplementation may be difficult to supervise if introduced in public-health programmes.

In conclusion, weekly supplementation of zinc had a significant impact on diarrhoeal morbidity. On the basis of this study and studies conducted in other developing countries, a general recommendation is made that zinc supplementation is beneficial for the reduction of diarrhoeal morbidity, after taking into account other host and environmental factors.

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