Effectiveness of zinc supplementation plus oral rehydration salts for diarrhoea in infants aged less than 6 months in Haryana state, India

Sarmila Mazumder,[a] Sunita Taneja,[a] Nita Bhandari,[a] Brinda Dube,[a] RC Agarwal,[b] Dilip Mahalanabis,[c] Olivier Fontaine[d] & Robert E Black[e]

Objective To determine if educating caregivers in providing zinc supplements to infants < 6 months old with acute diarrhoea is effective in treating diarrhoea and preventing acute lower respiratory infections (ALRIs), and whether it leads to a decrease in the use of oral rehydration salts (ORS).

Methods In this retrospective subgroup analysis of infants aged < 6 months, six clusters were randomly assigned to intervention or control sites. Care providers were trained to give zinc and ORS to children with acute diarrhoea at intervention sites, and only ORS at control sites. Surveys were conducted at 3 and 6 months to assess outcomes. Differences between intervention and control sites in episodes of diarrhoea and ALRI in the preceding 24 hours or 14 days and of hospitalizations in the preceding 3 months were analysed by logistic regression.

Findings Compared with control sites, intervention sites had lower rates of acute diarrhoea in the preceding 14 days at 3 months (odds ratio, OR: 0.60; 95% confidence interval, CI: 0.43–0.84) and 6 months (OR: 0.72; 95% CI: 0.54–0.94); lower rates of acute diarrhoea in the preceding 24 hours at 3 months (0.66; 95% CI: 0.50–0.87) and of ALRI in the preceding 24 hours at 6 months (OR: 0.59; 95% CI: 0.37–0.93); and lower rates of hospitalization at 6 months for all causes (OR: 0.40; 95% CI: 0.34–0.49), diarrhoea (OR: 0.34; 0.18–0.63) and *pasli chalna* or *pneumonia* (OR: 0.36; 95% CI: 0.24–0.55).

Conclusion Educating caregivers in zinc supplementation and providing zinc to infants < 6 months old can reduce diarrhoea and ALRI. More studies are needed to confirm these findings as these data are from a subgroup analysis.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Studies on the effect of zinc supplementation on diarrhoeal episodes in children have yielded varying results depending on age, with a clear beneficial effect in infants older than 6 months[1–4] but no effect before that age.[5,6] The effect of treatment in younger infants is important to document because of high death rates. It is plausible that zinc administered to children during acute diarrhoea may reduce the overall incidence and severity of diarrhoea and pneumonia in subsequent months.[7]

Evidence from several clinical trials has established zinc deficiency as a public health problem.[8,9] Zinc supplementation has been shown to be effective for preventing diarrhoea and pneumonia in children.[7,10] When used as a therapy for acute or persistent diarrhoea, zinc reduces the duration of the episode as well as its severity and complications.[2] The results are more limited with regard to zinc supplementation as an adjuvant to pneumonia treatment. A significant reduction in the duration of pneumonia was seen in children in Bangladesh[11] and India but only in boys.[12] Another study in Tamil Nadu, India showed no benefits.[13]

Zinc supplementation can prevent diarrhoea and pneumonia through several mechanisms, notably through its ability to restore immunity in children who have zinc deficiency.[14–16]

Zinc deficiency reduces the number of B and T lymphocytes (CD4+ lymphocytes in particular) through increased apoptosis, and reduces their functional capacity. This element stabilizes the cell membrane, and zinc deficiency disrupts the intestinal mucosa, reduces brush border enzymes and increases mucosal permeability and the intestinal secretion of water.[17,18] Zinc also acts as a potassium channel blocker, inhibiting cyclic adenosine monophosphate-mediated chlorine secretion.[19] Zinc supplementation during diarrhoea can therefore reduce the severity and duration of the episode.

In an earlier cluster-randomized trial, we compared the effectiveness of community-based education of caregivers on how to provide zinc plus oral rehydration salts (ORS) with the effectiveness of administering ORS alone to treat acute diarrhoea in children aged 1 month to 4 years.[20] That trial was designed to explore the impact, under real-life conditions, of implementing the World Health Organization (WHO) and United Nations Children's Fund recommendation to use zinc.[21] We did not give placebo to children at control sites because we also wanted to determine whether using zinc led to a decrease in the use of ORS. That trial showed a reduction in the prevalence of diarrhoea and acute lower respiratory infections (ALRI), and fewer hospitalizations for diarrhoea and pneumonia in the intervention sites compared with the control sites.[20] We concluded that diarrhoea was

[a] Society for Applied Studies, 45 Kalu Sarai, New Delhi, 110016, India.
[b] Badshah Khan Hospital, Faridabad, Haryana, India.
[c] Society for Applied Studies, Kolkata, India.
[d] Department of Child and Adolescent Health and Development, World Health Organization, Geneva, Switzerland.
[e] Bloomberg School of Public Health, Johns Hopkins University, Baltimore, United States of America.
Correspondence to Nita Bhandari (e-mail: community.research@cih.uib.no).

more effectively treated when caregivers received education about the usefulness of zinc and had easy access to supplies of zinc and ORS, and that this approach did not adversely affect the use of ORS, but rather greatly increased their use.

An important issue, and one for which data are limited, is whether the impact of zinc and ORS on diarrhoea as seen in that trial is also observed in infants aged less than 6 months. We report here the findings of a retrospective subgroup analysis restricted to infants younger than 6 months of age who were studied in the previously published trial.[20] As in the larger trial, the primary objective was to explore the effectiveness of caregiver education and the provision of zinc supplements to infants for the treatment and prevention of acute diarrhoeal episodes. Additional objectives were to find out whether the use of zinc lowered the rate of ALRI and whether it led to a decrease in the use of ORS.

Methods

The methods for the original cluster-randomized trial were published previously.[20] Briefly, the trial was conducted between January 2005 and September 2006 in 6 primary health centre areas in Faridabad district in the state of Haryana, India. Each primary health centre served a population of approximately 30 000 inhabitants. Verbal permission to work in the areas was sought from community leaders. Written informed consent was obtained from caregivers. The study was approved by the human subjects ethics review committees of the Society for Applied Studies and WHO.

A baseline cross-sectional survey was conducted in a randomly-selected sample of households in each of the 6 primary health centre areas. Information was collected on sociodemographic characteristics, prevalence of diarrhoea, ORS use rates and care-seeking for diarrhoea. A score was computed for each primary health centre based on socioeconomic indicators such as population size, farmland ownership, caste, water supply, sanitation facilities, literacy rates, diarrhoea rates, care-seeking rates for diarrhoea and hospitalization rates. Centres with similar scores were paired and one centre from each pair was randomly allocated to the intervention or control group.[20]

The intervention had three components. (i) Training was given to care providers including physicians, auxiliary nurse midwives, *anganwadi* workers, private medical practitioners (with and without qualifications in allopathic medicine), practitioners of indigenous medicine and other providers with no formal medical training. These participants were trained in diarrhoea management based on the WHO treatment package plus zinc treatment.[21] (ii) The availability of ORS and zinc was ensured at primary health centres, subcentres, *anganwadi* centres and private provider clinics. (iii) Diarrhoea treatment was promoted through the primary health-care system in the community to generate awareness. At control sites, treatment with ORS alone was promoted in the community and the availability of supplies was ensured.

The channels for delivery of the intervention were chosen in partnership with the local government.[22] These channels included government health-care providers (physicians with a medical degree and auxiliary nurse midwives at primary health centres) and integrated community development scheme *anganwadi* workers. These workers reside in the community, and there is one for every 1000 residents. They are involved primarily in growth monitoring, nutritional supplementation and preschool education for children less than 6 years old and are expected to provide ORS to treat diarrhoea. Private medical practitioners, over 90% of whom do not possess a medical degree but practice indigenous systems of medicine, were also included as channels because they are commonly used by the study population. All channels in the intervention communities received standard training in diarrhoea management, the appropriate use of zinc, how stocks of zinc and ORS would be provided and referral criteria. At control sites, the training content was identical except that zinc was not mentioned. The duration of training and persons deployed as trainers were the same in the intervention and control areas.

In each pair of primary health centres, intervention and control training activities were completed concurrently in 1 month. Government physicians and private providers were trained for half a day and *anganwadi* workers for one full day. Private providers were given the option of referring patients to *anganwadi* workers to obtain ORS packets. After training, the project staff had no further role in patient treatment.[20]

The strategy in the intervention sites was to give 1 blister strip containing 14 dispersible zinc tablets (20 mg each) along with 2 ORS packets (to mix in 1 litre of water each) to all infants aged 1 to 5 months with diarrhoea. Infants were to receive half a tablet in a teaspoon of breast milk each day. At control sites, infants were given only ORS.

Zinc supplies were replenished monthly by supply officers from the study team. Uninterrupted availability and supplies of zinc and ORS packets at the intervention sites and of ORS packets alone at control sites were ensured by strengthening logistics in the local health system. At intervention sites, activities to generate awareness of the new treatment with zinc and ORS (posters and announcements) were targeted to the community. Posters were displayed at clinics, *anganwadi* centres and subcentres, primary health care centres and other strategic locations such as bus stops, market places and shops. Announcements about the availability of zinc and ORS as treatment for diarrhoea were made in the village. At control sites ORS (but not zinc supplementation) was promoted verbally by care providers at facilities and in the community.

Definitions

In infants aged < 2 months, diarrhoea was defined based on the caregiver's report of a recent change in the consistency or frequency of stools. For children 2 months of age or older, the caregiver's report of ≥ 3 loose or watery stools in a 24-hour period was considered to indicate diarrhoeal illness. If a child had more than 1 diarrhoeal episode in the previous 4 weeks, information was collected on the most recent episode, i.e. only 1 episode per child was included in the analysis.

We defined ALRI as the caregiver's report of cough or difficulty in breathing along with rapid breathing.[23] In this article severe respiratory illness is referred to as *pasli chalna* or *pneumonia*, both of which are local terms used by caregivers for severe respiratory illness. It should be noted that *pneumonia* as used in the community we studied does not necessarily indicate that a diagnosis of pneumonia was confirmed by a physician. If a child had more than one episode of ALRI in the previous 4 weeks, information was collected on the most recent episode, i.e. only one episode per child was included in the analysis.

Sources of care were categorized as *anganwadi* worker, private provider and "other." The latter included the primary health centre physicians, auxiliary nurse midwives and pharmacies. A hospitalization was defined as an inpatient admission to a government or private facility irrespective of the length of stay.

Outcome measures

Outcome data were obtained by means of two cross-sectional surveys conducted 3 months (survey 2) and 6 months (survey 3) after the start of the intervention. In each of these surveys, households with children aged < 4 years were visited and caregivers were interviewed to collect information on socioeconomic factors, history of diarrhoea, cough, rapid or difficult breathing (in the preceding 24 hours and 2 weeks) and hospitalizations during the preceding 3 months. If the child had diarrhoea in the preceding 2 weeks, information was collected on the type of health-care provider visited, the prescription and actual use of zinc, ORS, syrups, tablets or powders of unknown identity.[20] If there were two or more children in the household, information was obtained for the youngest child.

The outcomes recorded were ascertained by independent reviewers who were unaware of the intervention. The recall period was restricted to 2 weeks to reduce recall bias. However, the study was not blinded, hence reporting bias cannot be ruled out.
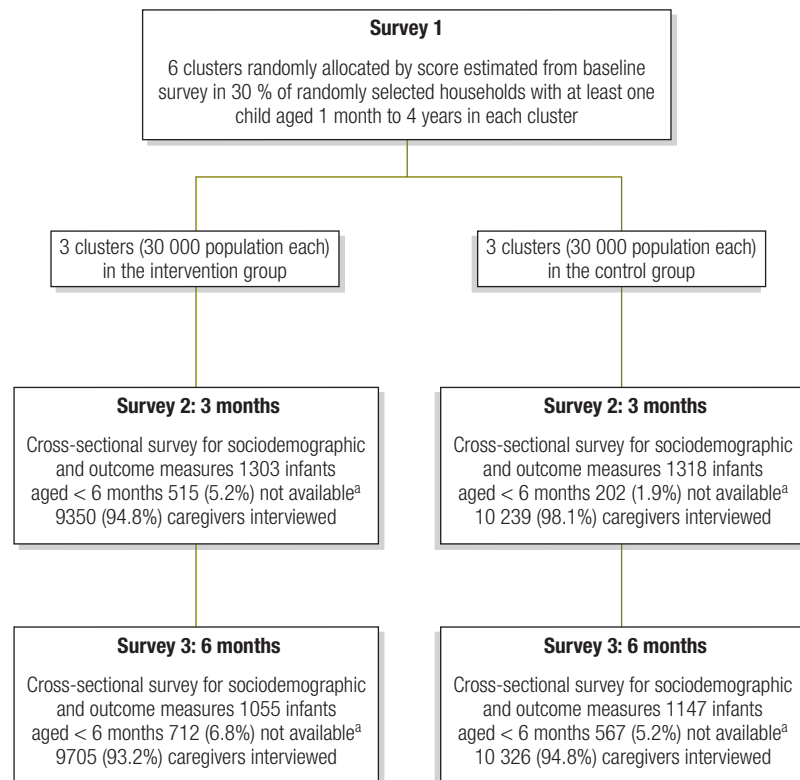
Statistical analysis

Forms with built-in range and consistency checks were created with Fox Pro software (Microsoft Corp., Redmond, United States of America). Files were merged into the main database daily after double data entry and validation. The data were analysed with Stata 8 software (Stata Corp., College Station, USA). Because this was a community randomized trial, adjustment for cluster randomization was done.

The subgroup analysis reported here was not planned a priori and hence not powered for the group of infants younger than 6 months. Sample size was estimated for the main trial.[20]

The proportions of infants at intervention and control sites with diarrhoea or ALRI in the previous 24 hours or hospitalization in the previous 3 months were analysed by logistic regression. The differences in proportions between the intervention and control groups are presented after adjustment for cluster in the logistic regression model. Analyses of ORS and zinc use were based on the most recent episode of diarrhoea within the 2-week interval preceding the date of the interview.

Results

Fig. 1 shows the numbers of infants aged less than 6 months seen at the intervention and control sites for which data were obtained for the present analysis. The sociodemographic characteristics of the sample households with at least one child aged less than 6 months in the baseline survey were similar at the intervention and control sites (Table 1).

Table 2 shows the odds ratios (OR) obtained with logistic regression. When compared with control sites, intervention sites had 40% fewer diarrhoeal episodes within the 14 days before survey 2, and 28% fewer episodes before survey 3. Intervention sites also had 34% fewer diarrhoeal episodes in the 24 hours before survey 2, and 41% fewer ALRI episodes before survey 3. The differences between intervention and control sites were all statistically significant.

All-cause hospitalizations in the 3-month period preceding survey 3 were 60% fewer at the intervention sites. Hospitalizations associated with diarrhoea and *pasli chalna* or *pneumonia* also occurred at significantly lower rates (66% and 64% lower, respectively) in survey 3 at intervention sites compared with control sites (Table 2).

Use of zinc and ORS

ORS use rates were significantly lower at control sites compared with intervention sites. In survey 2 the use rate was 3.9% at control sites versus 29.7% at intervention sites (odds ratio, OR: 10.5 (adjusted for cluster randomization); 95% confidence interval, CI: 4.38–25.12). In survey 3 the use rate was 8.3% at control sites versus 60.4% at intervention sites (OR: 16.75; 95% CI: 6.82–41.12). At intervention sites the use of zinc increased from 38.4% in survey 2 to 60.4% in survey 3.

As observed earlier in the overall analysis, the prescription of syrups, tablets or powders of unknown identity for the most recent episode of diarrhoea in the preceding 4 weeks was 33% lower (95% CI: 6–51) in survey 2 and 80% lower

Fig. 1. **Cluster participants in a controlled trial of the effect of zinc supplementation on childhood morbidity and mortality from diarrhoea and acute lower respiratory infection, Haryana state, India, 2005–2006**

a Not available at home at time of scheduled visit or at visits made daily for 1 week.

(95% CI: 65–88) in survey 3 at intervention sites compared with control sites.

Discussion

The principal findings of this subgroup analysis in infants aged less than 6 months are similar to the overall findings of the trial published earlier for children 1 to 4 years of age in Haryana state, India.[20] An intervention to treat acute diarrhoea, based on the education of caregivers and the provision of zinc and ORS delivered through both government and private providers at the village level, was beneficial in terms of reducing the burden of diarrhoea and ALRI. The benefits included reductions in the incidence or severity of episodes of diarrhoea and ALRI in subsequent months. The effect of the intervention in young infants was substantial and of public health importance.

Previous studies of this age group suggest that in infants < 6 months of age, treatment of acute diarrhoea with zinc does not reduce the duration or severity of the treated episode.[5,6] This contrasts with findings in children ≥ 6 months of age, in whom zinc given with ORS during an episode of acute diarrhoea has been shown to reduce the mean duration and severity of the treated episode.[1,2] These earlier results make it more likely that the current findings reflect a reduction in the incidence or severity of diarrhoea and

Table 1. Distribution of baseline characteristics in households in intervention[a] and control[b] sites, Haryana state, India, 2005–2006

Characteristic	Intervention (n = 414)	Control (n = 410)
Socioeconomic status		
Household residents, median no. (IQR)	6 (5–9)	6 (5–9)
Household income per yr (in US$[c]), median (IQR)	750 (500–1250)	750 (500–1375)
Caregivers not working outside home, no. (%)	403 (97.3)	398 (97.1)
Mothers who never attended school, no. (%)	203 (49.0)	188 (45.8)
Mother's years of schooling, mean (SD)	4.1 (4.6)	4.2 (4.5)
Morbidity (in children aged 1–5 months)		
Diarrhoea in preceding 24 h,[d] no. (%)	32 (7.7)	40 (9.8)
ALRI in preceding 24 h,[e] no. (%)	7 (1.7)	6 (1.5)
Pasli chalna or *pneumonia* in preceding 24 h,[f] no. (%)	1 (2.2)	8 (1.9)
Hospitalization in preceding 3 mo, no. (%)	21 (5.1)	21 (5.1)

ALRI, acute lower respiratory infection; IQR, interquartile range; SD, standard deviation; US$, United States dollars.
[a] Zinc supplementation plus oral rehydration salts.
[b] Oral rehydration salts only.
[c] At the time this study was conducted, 1 US$ was worth 48 Indian rupees.
[d] For infants aged < 2 months, caregiver's report of recent change in consistency or frequency of stools or both; for older infants, caregiver's report of ≥ 3 loose or watery stools in a 24-hour period.
[e] Presence of cough or difficult breathing along with fast breathing as reported by the caregiver.
[f] Based on caregiver's use of the local terms *pasli chalna* or *pneumonia*.

Table 2. Comparison of illness episodes and hospitalizations among children in intervention[a] and control[b] sites, Haryana state, India, 2005–2006

	Survey 2 (at 3 mo)				OR[c]	95% CI	Survey 3 (at 6 mo)				OR[c]	95% CI
	Intervention		Control				Intervention		Control			
	No.	%	No.	%			No.	%	No.	%		
Caregivers interviewed	1303	–	1318	–			1055	–	1147	–		
Episode in preceding 24 h												
Diarrhoea[d]	93	7.1	138	10.5	0.66	0.50–0.87	98	9.3	106	9.2	1.00	0.87–1.16
Pasli chalna or *pneumonia*[e]	38	2.9	44	3.3	0.87	0.46–1.62	12	1.1	24	2.1	0.54	0.27–1.06
ALRI[f]	32	2.5	39	3.0	0.82	0.42–1.60	12	1.1	22	1.9	0.59	0.37–0.93
Episode in preceding 14 d[g]												
Diarrhoea	198	15.2	304	23.1	0.60	0.43–0.84	200	18.9	282	24.6	0.72	0.54–0.94
Pasli chalna or *pneumonia*	107	8.2	128	9.7	0.83	0.47–1.47	44	4.2	76	6.6	0.61	0.30–1.23
ALRI	81	6.2	95	7.2	0.85	0.45–1.60	38	3.6	71	6.2	0.57	0.30–1.07
Hospital admissions												
All causes	59	4.5	102	7.7	0.56	0.31–1.02	41	3.9	104	9.1	0.40	0.34–0.49
Diarrhoea	9	0.7	16	1.2	0.56	0.23–1.40	7	0.7	22	1.9	0.34	0.18–0.63
Pasli chalna or *pneumonia*	39	3.0	80	6.1	0.48	0.20–1.18	25	2.4	72	6.3	0.36	0.24–0.55

ALRI, acute lower respiratory infection; CI, confidence interval; OR, odds ratio.
[a] Zinc supplementation plus oral rehydration salts.
[b] Oral rehydration salts only.
[c] Adjusted for cluster randomization.
[d] For infants aged < 2 months, caregiver's report of recent change in consistency, frequency of stools or both; for children 2 months of age or older, caregiver's report of ≥ 3 loose or watery stools in a 24-hour period.
[e] Based on caregiver's use of the local terms *pasli chalna* or *pneumonia*.
[f] Presence of cough or difficult breathing along with fast breathing as reported by caregiver.
[g] If a child had multiple episodes in the specified window period, information was collected on the most recent one, i.e. only 1 episode per child was included in the analysis.

ALRI in the months after treatment of an initial acute episode with zinc.

Studies in children 6 months to 4 years of age have suggested reduced morbidity from diarrhoea and respiratory infections during the 2 to 3 month window after treatment of acute diarrhoea with zinc.[7] A community-based trial similar to ours reported a reduction in hospitalizations for diarrhoea and a trend towards a similar reduction in hospitalizations for ALRI.[24] It should be noted, however, that a study of the effect of treatment with zinc for diarrhoea in infants < 6 months old on subsequent diarrhoeal and respiratory morbidity failed to document any benefit.[25] A subgroup analysis of a trial in Bangladesh[24] also suggested that zinc reduced the duration of diarrhoea and subsequent morbidity and mortality in infants < 6 months of age, although the sample sizes were small in the age-stratified subgroups.[26]

We defined ALRI as a caregiver's report of the presence of cough or difficulty in breathing along with rapid breathing. In this article severe respiratory illness is referred to as *pasli chalna* or *pneumonia*, both of which are local terms used by caregivers for serious respiratory illness. The term ALRI denotes probable pneumonia as defined by WHO and may include genuine pneumonia and in some cases conditions such as bronchitis and bronchiolitis. We recorded pneumonia when the local terms *pneumonia* or *pasli chalna* were mentioned by the caregiver, anticipating that this would identify serious, lower respiratory tract infection more accurately than asking caregivers to recall severe respiratory illness described according to the WHO criteria. Because of these definitions, there may be overlap between ALRI and *pasli chalna* or *pneumonia* as recorded in our survey.

Our findings should be considered preliminary and need to be interpreted with caution because they are derived from a subgroup analysis of the larger trial.[20] They indicate the need for further studies of the effects of zinc in addition to ORS in the treatment of acute diarrhoea in the first 6 months of life as a strategy to reduce the overall burden of diarrhoea and ALRI. Several important limitations of the study need to be considered. The effect of the intervention may not be attributable entirely to zinc. The possibility of reporting bias cannot be ruled out although it seems unlikely because zinc was promoted for diarrhoea alone, yet impact was observed on both diarrhoea and ALRI. Contamination was likely due to geographical proximity and movement between clusters. However, none of the control sites reported having used zinc. Since the subgroup analysis was not planned a priori and the sample was not powered for this, our analysis is subject to the problems inherent in retrospective subgroup analysis.

The current WHO recommendations are to offer zinc and ORS to children with acute diarrhoea who are 2 months to 4 years of age.[21] Although these recommendations have been adopted by most countries, some experts question the adequacy of the data that support them for the group of infants aged 2 to 6 months.[4,27] Our data are consistent with the WHO recommendations. If confirmed, our findings would have important public health implications because a high proportion of childhood deaths from diarrhoea and ALRI occur in the first 6 months of life, so even a moderately efficacious intervention would have substantial benefits in reducing this high mortality. ∎

ملخص

فعالية مكملات الزنك مع أملاح تعويض السوائل بطريق الفم بين الرضّع الأصغر من ستة أشهر في ولاية هاريانا الهندية

الغرض اكتشاف ما إذا كان تعليم مقدمي الرعاية إعطاء مكملات الزنك للرضّع الأصغر من ستة أشهر مع علاج الإسهال سيكون فعالاً في معالجة الإسهال والوقاية من عداوى الجهاز التنفسي السفلي الحادة، وما إذا كان ذلك سيقلل من استعمال أملاح تعويض السوائل بطريق الفم.

الطريقة في هذا التحليل الاسترجاعي للفئات الفرعية للرضّع الأصغر من ستة أشهر، أدرجت ست مجموعات عشوائية في مواقع أجري فيها التدخل ومواقع اختيرت كشواهد. ودُرِّب مقدمو الرعاية في مواقع إجراء التدخل على إعطاء الزنك وأملاح تعويض السوائل عن طريق الفم للأطفال المصابين بالإسهال الحاد، بينما أعطيت أملاح تعويض السوائل عن طريق الفم في مواقع الشواهد. وأجريت مسوح في الشهرين الثالث والسادس لتقييم النتائج. وأجري تحليل التحوّف اللوجستي للفروق بين مواقع التدخل ومواقع الشواهد من حيث نوبات الإسهال وعداوى الجهاز التنفسي السفلي الحادة خلال الأربع والعشرين ساعة أو الأربعة عشر يوماً السابقين والإدخال للمستشفى خلال الثلاثة أشهر السابقة.

الموجودات بالمقارنة مع مواقع الشواهد، كانت مواقع التدخل أقل من حيث معدلات الإسهال الحاد خلال الأربعة عشر يوماً في الشهور الثلاثة (نسبة الأرجحية: 0.60، فاصلة الثقة 95%، حد الثقة: 0.84-0.43) وفي الشهور الستة (نسبة الأرجحية: 0.72؛ فاصل الثقة 95%: حد الثقة 0.94 0.54-)؛ وكانت معدلات الإسهال الحاد خلال الأربع والعشرين ساعة السابقة أقل في الشهور الثلاثة (نسبة الأرجحية: 0.66 ؛ فاصل الثقة 95%، حد الثقة 0.50-0.87) وعداوى الجهاز التنفسي السفلي الحادة خلال الأربع والعشرين ساعة السابقة في الشهور الستة (نسبة الأرجحية 0.59؛ فاصل الثقة 95%: حد الثقة 0.93-0.37)؛ وكانت معدلات الإدخال للمستشفى لجميع الأسباب أقل (نسبة الأرجحية: 0.40؛ فاصل الثقة 95%: 0.34 حدا الثقة 0.49-) وكذلك الإسهال (نسبة الأرجحية: 0.34؛ 0.18 حدا الثقة0.63-)، والالتهاب الرئوي (نسبة الأرجحية: 0.36؛ فاصل الثقة 95%: حد الثقة 0.24-0.55).

الاستنتاج يمكن لتعليم مقدمي الرعاية إعطاء مكملات الزنك للرضّع الأصغر من ستة أشهر أن يقلل الإسهال، وعداوى الجهاز التنفسي السفلي الحادة.

وهناك حاجة لمزيد من الدراسات للتأكد من هذه النتائج لأن هذه المعطيات مستقاة من تحليل لفئات فرعية.

Résumé

Efficacité de la supplémentation en zinc associée aux solutés de réhydratation orale dans le traitement de la diarrhée chez les nourrissons de moins de 6 mois, dans l'état d'Haryana, en Inde

Objectif Déterminer si le fait de former le personnel soignant à la prescription de supplémentation en zinc aux nourrissons âgés de < 6 mois et atteints de diarrhée aiguë est efficace pour traiter la diarrhée et prévenir des infections aiguës des voies respiratoires inférieures (IAVRI), et si cela permet une réduction de l'utilisation des solutés de réhydratation orale (SRO).

Méthodes Dans cette analyse rétrospective de sous-groupe de nourrissons âgés de < 6 mois, six groupes ont été répartis au hasard entre sites d'intervention et sites de contrôle. Le personnel soignant a été formé pour administrer du zinc et des SRO aux enfants ayant une diarrhée aiguë sur les sites d'intervention, et uniquement des SRO aux enfants atteints de diarrhée aiguë sur les sites de contrôle. Des enquêtes ont été effectuées à 3 et 6 mois pour évaluer les résultats. Les différences entre sites d'intervention et sites de contrôle durant les épisodes diarrhéiques et d'IAVRI dans les 24 heures ou 14 jours précédant l'enquête, et durant les épisodes d'hospitalisations dans les 3 mois précédents ont été analysées par régression logistique.

Résultats En comparaison avec les sites de contrôle, les sites d'intervention présentaient des taux de diarrhée aiguë inférieurs dans les 14 jours précédents, à 3 mois (risque relatif approché, RRA : 0,60 ; intervalle de confiance 95%, IC : 0,43–0,84) et à 6 mois (RRA : 0,72 ; IC 95% : 0,54–0,94) ; taux de diarrhée aiguë inférieurs dans les 24 heures précédentes, à 3 mois (0,66 ; IC 95% : 0,50–0,87) et des taux d'IAVRI inférieurs dans les 24 heures précédentes, à 6 mois (RRA : 0,59 ; IC 95% : 0,37–0,93) ; et des taux d'hospitalisation inférieurs, à 6 mois, toutes causes confondues (RRA : 0,40 ; IC 95% : 0,34–0,49), diarrhée (RRA : 0,34 ; 0,18–0,63) et fièvre et difficultés respiratoires ou pneumonie (RRA : 0,36 ; IC 95% : 0,24–0,55).

Conclusion Le fait de former le personnel soignant à la prescription d'une supplémentation en zinc et à l'administration de zinc aux nourrissons âgés de < 6 mois peut réduire les diarrhées et les IAVRI. Des études supplémentaires seront nécessaires pour confirmer ces conclusions, car ces données proviennent d'une analyse de sous-groupe.

Resumen

Eficacia de los suplementos de cinc más sales de rehidratación oral para la diarrea en bebés menores de 6 meses en el estado de Haryana (India)

Objetivo Determinar la eficacia de la educación del personal sanitario en la administración de suplementos de cinc a bebés menores de 6 meses con diarrea aguda, en el tratamiento de la diarrea y en la prevención de infecciones agudas de las vías respiratorias inferiores (IAVRI), y si puede ayudar a disminuir el uso de sales de rehidratación oral (SRO).

Métodos En este análisis retrospectivo de subgrupos de lactantes menores de 6 meses, se asignaron aleatoriamente 6 grupos a centros de intervención o de control. Se formó al personal sanitario en la administración de cinc y SRO a niños con diarrea aguda en los centros de intervención y sólo de SRO en los centros de control. Las encuestas se realizaron a los 3 y 6 meses para evaluar los resultados. Se analizaron, mediante regresión logística, las diferencias existentes entre los centros de intervención y los de control respecto a los episodios de diarrea y de infecciones agudas de las vías respiratorias inferiores en las últimas 24 horas o 14 días, así como respecto a las hospitalizaciones de los últimos 3 meses.

Resultados A los 3 meses, los centros de intervención, en comparación con los centros de control, registraron tasas menores de diarrea aguda en los últimos 14 días (cociente de probabilidades, CP: 0,60; intervalo de confianza [IC] 95%: 0,43–0,84), y a los 6 meses (CP: 0,72; IC 95%: 0,54-0,94); a los 3 meses, tasas menores de diarrea aguda en las últimas 24 horas (0,66; IC 95%: 0,50-0,87) y, a los 6 meses, de IAVRI en las últimas 24 horas (CP: 0,59; IC 95%: 0,37-0,93); y tasas menores de hospitalización por cualquier causa a los 6 meses (CP: 0,40; IC 95%: 0,34-0,49), diarrea (IC: 0,34; 0,18-0,63) y tiraje o neumonía (CP: 0,36; IC 95%: 0,24-0,55).

Conclusión La formación del personal sanitario en suplementos de cinc y la administración de dichos suplementos a lactantes menores de 6 meses puede reducir la diarrea y las IAVRI. Se precisan más estudios para confirmar estos resultados, ya que estos datos proceden de un análisis de subgrupos.

References

1. Fontaine O. Effect of zinc supplementation on clinical course of acute diarrhoea. *J Health Popul Nutr* 2001;19:339–46. PMID:11855358

2. Bhutta ZA, Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *Am J Clin Nutr* 2000;72:1516–22. PMID:11101480

3. Trivedi SS, Chudasama RK, Patel N. Effect of zinc supplementation in children with acute diarrhea: randomized double blind controlled trial. *Gastroenterol Res* 2009;2:168–74. doi:10.4021/gr2009.06.1298

4. Haider BA, Bhutta ZA. The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence. *Food Nutr Bull* 2009;30(Suppl):S41–59. PMID:19472601

5. Fischer Walker CL, Bhutta ZA, Bhandari N, Teka T, Shahid F, Taneja S et al.; Zinc Study Group. Zinc supplementation for the treatment of diarrhea in infants in Pakistan, India and Ethiopia. *J Pediatr Gastroenterol Nutr* 2006;43:357–63. doi:10.1097/01.mpg.0000232018.40907.00 PMID:16954960

6. Brooks WA, Santosham M, Roy SK, Faruque AS, Wahed MA, Nahar K et al. Efficacy of zinc in young infants with acute watery diarrhea. *Am J Clin Nutr* 2005;82:605–10. PMID:16155274

7. Bhutta ZA, Black RE, Brown KH, Gardner JM, Gore S, Hidayat A et al. Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: pooled analysis of randomized controlled trials. Zinc Investigators' Collaborative Group. *J Pediatr* 1999;135:689–97. doi:10.1016/S0022-3476(99)70086-7 PMID:10586170

8.   Hambidge KM. Zinc and pneumonia. *Am J Clin Nutr* 2006;83:991–2. PMID:16685039

9.   Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS; Bellagio Child Survival Study Group. How many child deaths can we prevent this year? *Lancet* 2003;362:65–71. doi:10.1016/S0140-6736(03)13811-1 PMID:12853204

10. Brooks WA, Santosham M, Naheed A, Goswami D, Wahed MA, Diener-West M et al. Effect of weekly zinc supplements on incidence of pneumonia and diarrhoea in children younger than 2 years in an urban, low-income population in Bangladesh: randomised controlled trial. *Lancet* 2005;366:999–1004. doi:10.1016/S0140-6736(05)67109-7 PMID:16168782

11. Brooks WA, Yunus M, Santosham M, Wahed MA, Nahar K, Yeasmin S et al. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *Lancet* 2004;363:1683–8. doi:10.1016/S0140-6736(04)16252-1 PMID:15158629

12. Mahalanabis D, Lahiri M, Paul D, Gupta S, Gupta A, Wahed MA et al. Randomized, double-blind, placebo-controlled clinical trial of the efficacy of treatment with zinc or vitamin A in infants and young children with severe acute lower respiratory infection. *Am J Clin Nutr* 2004;79:430–6. PMID:14985218

13. Bose A, Coles CL, Gunavathi , John H, Moses P, Raghupathy P et al. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old. *Am J Clin Nutr* 2006;83:1089–96, quiz 1207. PMID:16685051

14. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr* 1998;68(Suppl):447S–63S. PMID:9701160

15. Prasad AS. Zinc and immunity. *Mol Cell Biochem* 1998;188:63–9. doi:10.1023/A:1006868305749 PMID:9823012

16. Overbeck S, Rink L, Haase H. Modulating the immune response by oral zinc supplementation: a single approach for multiple diseases. *Arch Immunol Ther Exp (Warsz)* 2008;56:15–30. doi:10.1007/s00005-008-0003-8 PMID:18250973

17. Penny ME, Lanata CF. Zinc in the management of diarrhea in young children. *N Engl J Med* 1995;333:873–4. doi:10.1056/NEJM199509283331311 PMID:7651481

18. Roy SK, Tomkins AM, Akramuzzaman SM, Behrens RH, Haider R, Mahalanabis D et al. Randomised controlled trial of zinc supplementation in malnourished Bangladeshi children with acute diarrhoea. *Arch Dis Child* 1997;77:196–200. doi:10.1136/adc.77.3.196 PMID:9370894

19. Hoque KM, Binder HJ. Zinc in the treatment of acute diarrhea: current status and assessment. *Gastroenterology* 2006;130:2201–5. doi:10.1053/j.gastro.2006.02.062 PMID:16762641

20. Bhandari N, Mazumder S, Taneja S, Dube B, Agarwal RC, Mahalanabis D et al. Effectiveness of zinc supplementation plus oral rehydration salts compared with oral rehydration salts alone as a treatment for acute diarrhea in a primary care setting: a cluster randomized trial. *Pediatrics* 2008;121:e1279–85. doi:10.1542/peds.2007-1939 PMID:18450870

21. World Health Organization & United Nations Children's Fund. *WHO/UNICEF Joint Statement: clinical management of acute diarrhea*. New York: WHO & UNICEF; 2004 (WHO/FCH/CAH/04.7). Available from: http://www.afro.who.int/cah/documents/intervention/acute_diarrhoea_joint_statement.pdf, http://www.unicef.org/nutrition/files/ENAcute_Diarrhoea_reprint.pdf [accessed 15 April 2010].

22. Bhandari N, Mazumder S, Taneja S, Dube B, Black RE, Fontaine O et al. A pilot test of the addition of zinc to the current case management package of diarrhea in a primary health care setting. *J Pediatr Gastroenterol Nutr* 2005;41:685–7. doi:10.1097/01.mpg.0000182799.69675.92 PMID:16254536

23. World Health Organization, Division of Child Health and Development. *Integrated management of childhood illness.* Geneva: World Health Organization, 1997 (WHO/CHD/97.3E).

24. Baqui AH, Black RE, El Arifeen S, Yunus M, Chakraborty J, Ahmed S et al. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomised trial. *BMJ* 2002;325:1059. doi:10.1136/bmj.325.7372.1059 PMID:12424162

25. Walker CL, Bhutta ZA, Bhandari N, Teka T, Shahid F, Taneja S et al. Zinc during and in convalescence from diarrhea has no demonstrable effect on subsequent morbidity and anthropometric status among infants <6 mo of age. *Am J Clin Nutr* 2007;85:887–94. PMID:17344513

26. Fischer Walker CL, Black RE, Baqui AH. Does age affect the response to zinc therapy for diarrhoea in Bangladeshi infants? *J Health Popul Nutr* 2008;26:105–9. PMID:18637534

27. Saleem T, Khalid U. Zinc supplementation in infants less than 6 months of age. *Indian Pediatr* 2009;46:268. PMID:19346582