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Serum and Stool Levels of Zinc, Copper and Vitamin A in Children aged 6 - 24 Months with Diarrhoea

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Abstract

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Background: Diarrhoea is one of the major causes of morbidity and mortality among infants and young children in developing countries. More than half of the deaths due to diarrhoea results from dehydration and/or excessive loss of essential nutrients including micronutrients such as zinc, copper and vitamin A. These micronutrients are essential for immunological protection, as well as the proper growth and development of children.

Objective: To determine the serum and stool levels of zinc, copper and vitamin A in children presenting with diarrhoea.

Methods: This was a comparative cross-sectional study. Thirty consecutive infants with diarrhoea from the Diarrhoea Training Unit (subjects) and thirty without diarrhoea (controls) from the Infant Welfare clinic of the Jos University Teaching Hospital [JUTH], were studied. The feeding practices, diarrhoeal history, and anthropometric measurements of the study and control groups were noted. Their sera and stool samples were analyzed for zinc and copper using *Vernox Elmer* Atomic Absorption spectrophotometer and for Vitamin A using spectrophotometer *Pye Unicain PU 8600*. The data obtained were analysed statistically.

Results: The age, body mass index [BMI], mid upper arm circumference [MUAC] and sex distribution of children in the two groups were similar but their mean weight, and length/height were significantly different [$p < 0.05$]. The subjects had significantly lower serum zinc [$2.32 \pm 0.72 \mu g/ml$ vs 2.67 ± 0.43] and vitamin A [$1.94 \pm 0.47 \mu mol/l$ vs. 2.48 ± 0.46] levels but significantly higher serum copper [$2.80 \pm 0.93 \mu g/ml$ vs 1.83 ± 0.42] and stool zinc [$0.67 \pm 0.03 \mu g/mol$ vs 0.45 ± 0.01 levels.

Conclusion: The results of our study highlights the impact of diarrhoea which results in excessive faecal loss of zinc and vitamin A with parallel increase in the serum copper concentration. This finding supports the WHO recommendation that children with diarrhoea should have vitamin A and zinc supplements in their diet.

Key words: Zinc, Copper, Vitamin A, Children, Diarrhoea

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Introduction

DIARRHOEA is one of the commonest reasons for paediatric consultation or hospitalization throughout developing countries in the tropics. Despite widespread access to oral rehydration solution, diarrhoea has contributed over five million deaths per year in children under five years in developing countries.[1] More than half of such deaths are caused by associated dehydration and/or excessive loss of essential nutrients including micronutrients such as zinc, copper and vitamin A.[2] Episodes of diarrhoea which usually resolve within a few days in a healthy child, persist longer in children

with risk factors such as malnutrition and impaired cellular immunity.[3]

Zinc, copper and vitamin A are indispensable and essential micronutrients for the normal growth, development and maintenance of normal immune function of the infant.[4] Zinc plays a vital role in the transportation of vitamin A across biological membranes,[5] while zinc and vitamin A which are available in the breastmilk, have also been shown to have a significant inter-relationship in a wide variety of clinico-pathological conditions. Zinc is an essential trace element that is required for normal intestinal mucosal integrity, skeletal growth, sodium and water transport and immune function.[6] Deficiency of this trace element results in growth retardation, poor overall immune function and resistance to infection.[6] On its part, copper is important for normal haemoglobin function, and its deficiency results in microcytic hypochromic anaemia, osteoporosis and neurological abnormalities.[7] Vitamin A plays a vital role in vision, bone growth and maintenance of integrity of membrane linings.[4] Diarrhoea has been reported to cause a negative balance of these elements by way of high faecal losses of zinc and copper, and impaired absorption of Vitamin A.

The present study was undertaken to determine the serum levels of these essential nutrients in children with diarrhoea especially now that Vitamin A has been introduced along with the National Programme of Immunization.

Patients and Methods

This comparative cross sectional study was carried out in Jos, a town situated in the North Central Zone. Thirty consecutive infants with acute diarrhoea from the Diarrhoea Training Unit (subjects) and 30 age and sex- matched well nourished controls [who were diarrhoea free for two months] from the Infant Welfare Clinic of Jos University Teaching Hospital [JUTH] were recruited for the study with the written consent of the parents. The protocol was approved by the ethical committee of the hospital.

The feeding practices, 'diarrhoea histories' and anthropometric measurements of the study and control groups were noted. The length of each child was determined to the nearest 0.1cm using an infantometer, weight was measured to the nearest 0.01kg using basinate scale and the mid-upper arm circumference [MUAC] was measured to the nearest 0.1cm (at the mid-point between the acromium and olecranon process) using a fibreglass tape measure.

Sera and stool samples were then obtained from each child and analyzed for zinc and copper using *Vernox Elmer Atomic* absorption spectrophotometer and for serum vitamin A, using spectrophotometer *Pye Unicam PU 8600*. The instructions supplied in the manuals were carefully followed. Calibration and validation of the spectrophotometer were carried out, using stock standards. Standard solutions of varying concentrations were prepared from the stock solution. A blank solution containing deionized water was used to determine the zero baseline of the spectrophotometer. The sera were aspirated into the nebulizer for the estimation of the elements, and the results were expressed as μg/ml for zinc and copper and μmol/l for vitamin A. The data were analysed for mean, standard deviation and the student's "t" test where applicable, and the strength of association between the variables was tested.

Results

The age, body mass index [BMI], mid-upper arm circumference [MUAC] and sex distribution of children in the two groups were similar but the mean weight and height were significantly different, the controls being significantly heavier and taller than the subjects [$p < 0.05$; Table 1].

Table I

Characteristics of the Subjects and Controls

	Subjects		*Controls*		
	Mean	*SD*	*Mean*	*SD*	*P value*
Age [months]	12.56	9.69	14.57	9.21	>0.05
Weight [kg]	9.00	2.86	10.57	2.37	<0.05
Length [cm]	72.90	11.37	79.22	14.10	<0.05
BMI [kg/m^2]	16.98	1.00	16.80	1.10	>0.05
MUAC [cm]	12.35	0.61	12.42	1.20	>0.05
Male/female ratio	1:1		1:0.81		

The duration of diarrhoea before enrollment of the subjects ranged from 3-9 days (mean, 3.40±1.75), the frequency of stooling per day from 2–8 (mean, 4.60±1.65) and episodes of diarrhoea per year from 0-8 (mean, 1.97±2.41). Thirty percent of the subjects were exclusively breast-fed compared with a significantly higher percentage (80 percent) of the controls [$p < 0.05$].

The subjects had significantly lower serum zinc [2.32±0.72μg/ml vs 2.67±0.43μg/ml], and vitamin A [1.94 ±0.47μmol/l vs 2.48±0.46 μg/ml] levels and significantly higher serum copper [2.80±0.93μg/ml vs 1.83±0.42μg/ml] [Table II], and stool zinc [0.67±0.03μg/ml vs 0.45 ±0.01 μg/ml] levels than the control group t $p < 0.05$ [Table III].

populations[9] including infants.[10] Studies in Malawian children have shown unusually high intestinal losses of endogenous zinc even among apparently healthy children.[11,12] A Brazilian study[13] also noted similar low serum levels of zinc in under fives with acute diarrhoea, which was also associated with the duration of diarrhoea. These increased losses of endogenous zinc may deplete the level of body zinc and may further trigger another cycle of diarrhoea. The possible risk of continued diarrhoea may exacerbate the loss of these nutrients. This could lead to their deficiencies with concomitant effects on the nutritional and immunological status as well as the general health of the patients resulting in a substantial risk of death. Thus, there may be a need

Table II

Mean Serum Levels of Zinc, Copper and Vitamin A

	Subjects		*Controls*		
	Mean	*SD*	*Mean*	*SD*	*P value*
Zinc [μg/ml]	2.32	0.72	2.67	0.43	<0.05
Copper [μg/ml]	2.80	0.93	1.83	0.42	<0.05
Vitamin A [μmol/l]	1.94	0.47	2.48	0.46	<0.05

Table III

Mean Stool Levels of Zinc and Copper

	Subjects		*Controls*		
	Mean	*SD*	*Mean*	*SD*	*P value*
Copper [μg/ml]	1.10	0.38	1.56	0.31	<0.05
Zinc [μg/ml]	0.67	0.03	0.45	0.01	<0.05

Discussion

The present study, which was conducted in Jos, documented the sera and stool levels of zinc, copper and vitamin A in children with diarrhoea. Diarrhoea was associated with clinically important and statistically reduced serum levels of zinc and vitamin A, and increased stool levels of zinc and copper. This conforms with the results obtained by Rahman *et al*[8] and Castillo-Duran *et al*.[2] The increased faecal loss of zinc might have resulted from the unabsorbed dietary zinc and endogenous zinc. This in turn, may be attributed to the poor intestinal health and permeability commonly seen in lower income

to give these children supplements of these nutrients to enhance their survival.

Also associated with diarrhoea was a significantly increased serum and decreased stool levels of copper. The reason for this cannot be conclusively explained at the present time. However, it could be due to the acute phase action of interleukin-1 in infectious or inflammatory diseases.[4] Whatever the explanation, we recommend that zinc and vitamin A supplements for these children should not contain copper as recommended by some workers.[1] The frequency of diarrhoea in the children is a crucial factor. The children in our study suffered from 0-8 episodes of

diarrhoea per year and each episode lasted for an average of 3-9 days with 2-8 frequencies of stooling per day. This cycle of diarrhoea with reduced nutritional status and faecal nutrient losses may substantially reduce the zinc and vitamin A stores, which could result in growth faltering and increased morbidity, especially in malnourished children.

Significantly, most of the children without diarrhoea were at the time of the study being exclusively breastfed or were exclusively breastfed in their first 4-6 months of life. This was contrary to the case of children with diarrhoea who, although breastfed, were not exclusively so. Several workers[14-15] have reported the protective effects of breastfeeding especially exclusive breastfeeding on diarrhoea. This they attributed to its anti-infective/ immunological properties. Exclusive breastfeeding for the first six months of life therefore continues to be an effective strategy for curbing the incidence and frequency of diarrhoea in children.

Conclusion

The results of our study highlight the impact of diarrhoea on the faecal loss of zinc and vitamin A with parallel increase in the serum copper concentration. Therefore, there may be a need to supplement these infants with dietary or synthetic zinc and vitamin A without copper. This finding further supports WHO recommendation that children with diarrhoea should have vitamin A and zinc supplements in their diet. We therefore suggest that further studies on this topic be carried out.

References

1. Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bull World Health Orgn* 1992; 70: 705-14.
2. Castillo-Duran C, Vial P, Uauy R. Trace mineral balance during acute diarrhea in infants. *J Pediatr* 1988; 113: 452-7.
3. Tomkins A. Nutritional status and severity of diarrhoea among pre-school children in rural Nigeria. *Lancet* 1981; 1:860-2.
4. Solomons NW, Russell RM. The interaction of vitamin A and zinc: implications for human nutrition. *Am J Clin Nutr* 1980; 33:2031-40.
5. Christian P, West KP Jr. Interactions between zinc and vitamin A: an update. *Am J Clin Nutr* 1998; 68 (2 Suppl): S355-S415.
6. Roy SK, Tomkins AM, Haider R, Behren RH, Akramuzzamau SM, Mahalanabis D, Fuchs GJ. Impact of zinc supplementation on subsequent growth and morbidity in Bangladesh children with acute diarrhoea. *Eur J Clin Nutr* 1999; 53: 529-34.
7. Krebs NF, Primak LF. Vitamin and Mineral Deficiencies. In: Kliegman RM, Marcdante KJ, Jenson HB, Behrman RE, eds. Nelson's Essentials of Pediatrics. Philadelphia: Elsevier Saunders (Publishers), 2006:156.
8. Rahman MM, Vermund SH, Wahed MA, *et al.* Simultaneous zinc and vitamin A supplementation in Bangladeshi children: randomised double blind controlled trial. *BMJ* 2001; 323: 314-8.
9. Menzies IS, Zuckerman MJ, Nukajam WS, Somasundaram SG, Murphy B, Jenkins AP, Crane RS, Gregory GG. Geography of intestinal permeability and absorption. *Gut* 1999; 44: 483-9.
10. Goto K, Chew F, Torun B, Peerson JM, Brown KH. Epidemiology of altered intestinal permeability to lactose and mannitol in Guatemalan infants. *J Pediatr Gastroenterol Nutr* 1999; 28: 282-90.
11. Manary MJ, Hotz C, Krebs NF, Gibson RS, Westcott JE, Arnold T, Broadhead RL, Hambidge KM. Dietary phytate reduction improves zinc absorption in Malawian children recovering from tuberculosis but not in well children. *J Nutr* 2000; 130: 2959-64.
12. Manary MJ, Hotz C, Krebs NF, Gibson RS, Westcott JE, Arnold T, Broadhead RL, Hambidge KM. Zinc homeostasis in Malawian children consuming a high-phytate, maize-based diet. *Am J Clin Nutr* 2002; 75: 1057-61.
13. Al-Sonboli N, Gurgel RQ, Shenkin A, Hart CA, Cuevas LE. Zinc supplementation in Brazillian children with acute diarrhoea. *Ann Trop Paediatr* 2003; 23: 3-8.
14. Haider R, Islam A, Hamadani J, *et al.* Breast-feeding counselling in a diarrhoeal disease hospital. *Bull World Health Organ* 1996; 74: 173-9.
15. Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. *Pediatrics* 2001; 108: E67.