

MAGNESIUM SUPPLEMENTATION ON CHILDREN WITH SEVERE PROTEIN ENERGY MALNUTRITION

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Abstract

This hospital based prospective case control study was designed to determine the clinical outcome of magnesium supplementation in severely malnourished Bangladeshi children. The study was conducted at Paediatric department of Bangabandhu Sheikh Mujib Medical University (BSMMU) and Ad-din Hospital, Dhaka from June 2006 to December 2006. Total sixty children, divided into two equal groups, were included in the study. Group-I patients were given standard treatment of Protein Energy Malnutrition (PEM) and group-II children were given magnesium supplementation in addition. Serum magnesium level was measured on day-1 and day-12 of admission. Pre-treatment clinical parameters of both groups were comparable. Principal clinical findings were diarrhoea, vomiting, poor appetite, irritability, hypotonia and oedema. Serum magnesium level was low in severely malnourished children. Magnesium supplemented group of patients showed better improvement of appetite, reduction of vomiting and hypotonia. The rate of weight gain was 8.87 ± 3.51 gm/kg/day in group-I and 12.16 ± 6.32 gm/kg/day in group-II, which was significant. Serum magnesium level significantly improved in supplemented group of patients. So, magnesium may be routinely used in the management of malnourished children to hasten recovery.

Introduction

Magnesium depletion has been reported to occur in Protein Energy Malnutrition (PEM) which is evidenced by reduced concentration of magnesium in serum and tissue¹⁻⁵. Diets in populations are frequently deficient in macronutrients, micronutrients or both⁶. Magnesium, a common cation in the body plays an essential role in numerous cellular reactions including oxidative phosphorylation, enzymatic reactions, nucleic acid metabolism and protein synthesis^{7,8}.

Magnesium depletion in malnourished children may be asymptomatic or may produce symptoms like anorexia, nausea, muscular weakness, lethargy, tremors, atetoid

movement, seizures and psychomotor changes^{1,9}. Deficiency of magnesium is known to compromise primary and secondary immune response and increase tissue susceptibility to lipid peroxidation^{5,10-12}. Magnesium deficiency rises when demands increase markedly with the resumption of tissue growth during rehabilitation from malnutrition^{3,4}. The catch-up growth associated with recovery from PEM is achieved only if magnesium supply is increased substantially³. The measurement of serum magnesium is a useful test to detect magnesium deficiency in routine clinical practice¹. No study was carried out recently in Bangladesh to determine the beneficial effect of magnesium supplementation in malnourished children and magnesium is sporadically given in the management of malnutrition. So, this study was conducted to determine the outcome of magnesium supplementation in severely malnourished children.

Methodology

This hospital based prospective case-control study was carried out in the Departments of Paediatrics, BSMMU, Dhaka and Ad-din Hospital, Magbazar, Dhaka, from June 2006 to December 2006. Purposively consecutive sixty hospitalized children between 6 to 59 months age, with severe malnutrition were enrolled in the study. Severe malnutrition were defined as per WHO criteria of PEM. After admission detail history, through physical examinations and relevant investigations were collected on a pre-designed semi-structured questionnaire. In physical examination emphasis was given on weight, height and clinical evidence of disturbances in magnesium deficiency. Children were divided randomly into two equal groups, group-I (control) and group-II (case). Group-I patients were treated with F-75/F-100 formula¹⁴ along with vitamins and minerals without any magnesium supplementation. Group-II children were treated with F-75/F-100 formula and CMV (combined mineral & vitamins) containing magnesium. One scoop of CMV contains 146 mg of magnesium along with other minerals and vitamins. One scoop of CMV was dissolved in 40 ml of water and then 20 ml of the prepared solution was added to each liter of F-75/F-100 formula. So, each

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100 ml and 130 ml of F-75/F-100 formula contained 7.3 mg and 9.49 mg of magnesium respectively. Thus an average intake of magnesium was 7.3-14.6 mg/kg/day (0.3-0.6 mmol/kg/day) throughout the initial 12 days of treatment. Each patient of both the groups was daily followed-up to observe the clinical response.

Table-I: Demographic features of studied subjects

Parameters		Group-I (n=30)	Group-II (n=30)	p value
Age (months)		22.14 ± 12.03	23.15 ± 11.60	> 0.50
Height (cm)		72.32 ± 7.80	70.21 ± 7.82	> 0.50
Sex	Male (%)	13 (43.33)	16 (53.33)	> 0.50
	Female (%)	17 (56.67)	14 (46.67)	

Note: For Age & Height Unpaired 't' test and for Sex Chi square test were done.

After taking informed written consent from the guardians, under all aseptic precaution 2.5 ml of venous blood sample was collected at admission and 12th day of treatment from each patient of both groups. Serum was separated and preserved at -35°C in different vials until analysis. Serum magnesium was measured in the

Table-II: Clinical profile of patients on Day-1 and Day-12 of treatment

Clinical profile		Group-I (n=30)		Group-II (n=30)		p value*
		Frequency	(%)	Frequency	(%)	
Diarrhoea	Day 1	16	(53.33)	22	(73.33)	> 0.05
	Day 12	2	(6.67)	1	(3.33)	> 0.05
Vomiting	Day 1	21	(70.00)	15	(50.00)	> 0.05
	Day 12	7	(23.30)	0	(00)	< 0.01
Irritability	Day 1	22	(73.33)	25	(83.33)	> 0.50
	Day 12	3	(10.0)	0	0	> 0.05
Poor appetite	Day 1	24	(80.00)	22	(73.33)	> 0.05
	Day 12	7	(23.33)	1	(3.33)	< 0.01
Hypotonia	Day 1	30	(100.0)	30	(100.0)	> 0.05
	Day 12	15	(50.0)	2	(6.67)	< 0.001
Symmetrical oedema	Day 1	17	(56.67)	16	(53.33)	> 0.50
	Day 12	0	0	0	0	
Tremor	Day 1	6	(20.00)	8	(26.67)	> 0.50
	Day 12	0	0	0	0	
Skin changes	Day 1	6	(20.00)	5	(16.67)	> 0.05
	Day 12	1	(3.33)	0	(0)	> 0.05

Note: Chi square test was done.

Biochemistry Laboratory of BSMMU by auto-analyzer. Statistical analysis was done by using SPSS 10.0. All the continuous data were expressed as mean ± SD and categorical data were expressed in frequency &

percentage (%). Statistical analyses were performed by Chi-square and paired & unpaired 't' test and 95% confidence level was taken as level of significance.

Result

Age range of the children was 6-56 months. Almost equal number of children of either sex was studied in both groups. Age, height and sex distribution of studied children were not significantly ($p > 0.05$) different (table I).

Clinical profile of studied children was shown in table-II. Before treatment diarrhoea was found in 16 (53%) and 22 (73%) children of group-I & II respectively and the difference was not significant ($p > 0.05$). Vomiting was seen in 21(70%) and 15 (50%) children of group-I & II respectively. After treatment, this was improved completely (100%) in group-II but only 76% cases improved in group-I ($p < 0.01$). In both the groups, majority of the patients showed irritability which was improved after treatment and magnesium supplemented group showed better improvement.

Poor appetite was noted in 24 (80%) in group-I and 22 (73%) in group-II patients before treatment, which were not significantly ($p > 0.05$) different. After treatment appetite was improved significantly ($p < 0.01$) in magnesium supplemented group. Hypotonia was found in all the patients in both the groups before treatment. After magnesium supplementation, hypotonia was improved in most of the cases, 28 (93%) in group-II and only 15 (50%) cases in group-I ($p < 0.001$). Symmetrical oedema was seen in 17 (56%) patients of group-I and 16(53%) patients of group-II which disappeared completely after treatment and magnesium supplementation showed no change in subsiding oedema. Gastroenteritis was found as the commonest infection in malnourished children, 10 (33%) in group-I and 11 (36%) in group-II followed by pneumonia, oral candidiasis and tuberculosis. Infections were improved after treatment.

Pre-treatment magnesium levels were not significantly ($p > 0.05$) different between the groups. Post-treatment magnesium values were significantly ($p < 0.001$) different between the groups

(table-III). Magnesium level was significantly improved in group II on 12th day of treatment ($p < 0.001$).

Before treatment weight was not significantly ($p > 0.05$)

Table-III: Serum Magnesium level before and after supplementation

Serum Magnesium (mg/dL)	Group-I (n=30)	Group-II (n=30)	p value
Day 1	1.46 ± 0.25	1.36 ± 0.25	> 0.50
Day 12	1.63 ± 0.26	2.06 ± 0.35	< 0.001
p value (Day 1 vs. Day 12)	> 0.50	< 0.001	

Note: Group-I vs. group-II by unpaired 't' test and day-1 vs. day- 12 by paired 't' test.

Table-IV: Effect of Magnesium supplementation on weight of the children

Weight (kg)	Group-I (n = 30)	Group-II (n = 30)	p value*
Day I	7.3 ± 1.63	7.2 ± 1.5	> 0.50
After oedema subsided	7.2 ± 1.6	7.1 ± 1.4	> 0.50
Day 12	7.7 ± 1.9	9.6 ± 1.7	< 0.05
Rate of weight gain (g/kg/day)	8.9 ± 3.5	12.2 ± 6.3	< 0.01

Note: Oedema was completely subsided on different days of treatment. Rate of weight gain was calculated by taking weight after edema completely subsided and weight on day 12. Unpaired 't' test between groups and paired 't' test between days.

different between the groups i.e. 7.3 ± 1.63 kg vs 7.21 ± 1.50 kg. After treatment weight was 7.72 ± 1.87 kg vs 9.61 ± 1.71 kg in group-I and group-II respectively. The weight was significantly ($p < 0.05$) different after treatment in both the groups. The rate of weight gain (g/kg/day) was significantly different in group-I and group-II which were 8.87 ± 3.51 and 12.16 ± 6.32 respectively. Athetoid movement, seizures or convulsion were not observed in any studied child.

Discussion

Diets in population are frequently deficient in micronutrients and magnesium is gaining recognition as a clinically important electrolyte⁶. Mean age of the studied children was 22.14 ± 12.03 months (group I) and 23.15 ± 11.60 months (group II). There was a female preponderance and male female ratio 1:1.06. Similar observation was mentioned by others¹³⁻¹⁵.

Vomiting is associated with hypomagnesemia⁹. It was improved in all cases of magnesium supplementation (76% vs 100% in group I and group II respectively; and $p < 0.01$). Similar finding was reported by Caddell of Nigeria¹⁶.

In general, magnesium treated children rapidly acquired a

good appetite¹⁶. In this study, magnesium supplemented children showed significant improvement of appetite. Similar findings were noted by other authors^{17, 18}.

Deficiency of magnesium causes generalized hypotonia^{9,19}. Hypotonia was found in all cases of studied children. Significant improvement was observed in magnesium supplemented group. This improvement of tone may be due to replenishment of muscle magnesium pool. Similar observation was reported by others^{16, 17}. Nichols et al mentioned that magnesium may play a role in promoting recovery of muscle composition³.

Symmetrical oedema was found in about half of the patients of both the groups. Reported study could not find any correlation between magnesium supplemented and non-supplemented group as oedema subsided in PEM children between 4 to 10 days of treatment¹³. Tremor is associated with hypomagnesemia^{17,20}. In this series, tremor was found in 14(23%) which was improved on 12 day of treatment. No correlation was observed with magnesium supplementation.

Mean serum magnesium levels were 1.46 ± 0.25 mg/dL in group I and 1.36 ± 0.25 mg/dL in group II on day 1 before

starting treatment. These levels were below normal value of 1.56 mg/dL¹. After treatment on day 12 these were 1.63 ± 0.26 mg/dL and 2.06 ± 0.35 mg/dL in group I and group II respectively; much improved in magnesium supplemented group. Karla et al²¹ found serum magnesium level 1.92 mg/dL before supplementation and 2.23 mg/dL after supplementation. In this series magnesium was as low as 0.8mg/dL but Montgomery reported serum magnesium levels as low as 1.2 mg/dL²².

Before treatment weight was not significantly different between the groups. After treatment, weight gain occurred significantly in both the groups of children. Rate of weight gain was accelerated after magnesium supplementation³. In this series, rate of weight gain was 8.87 ± 3.51 gm/kg/day in group-I and 12.16 ± 6.32 gm/kg/day in group-II. This difference was statistically significant. Similar observation was noted by Montgomery²².

Conclusion

In this study serum magnesium level was lower than normal in severely malnourished children. Magnesium supplemented group of patients showed better improvement of appetite, reduction of vomiting and hypotonia. The rate of weight gain was highly significant ($p < .001$) in magnesium supplementation group. So, magnesium may be routinely used in the management of malnourished children to hasten recovery.

References

1. Singla PN, Chand P, Kumar A, Kanchhwaha JS. Serum magnesium levels in protein energy malnutrition. *J Trop Paed* 1998; 44:117-19.

2. Deshmukh CT, Rane SA, Gurav MN. Hypomagnesaemia in pediatric population in an intensive care unit. *J Postgraduate Med* 2000; 46(3): 179-80.
3. Nichols BL, Alvarado J, Hazelwood CF, Viteri F. Magnesium supplementation in protein calorie malnutrition. *Am J Clin Nutr* 1978; 31: 176-78.
4. Pretorius PJ, Wehmeyer AS, Theron JJ. Magnesium balance studies in South African Bantu children with kwashiorkor. *Am J Clin Nutr* 1963; 13: 331-39.
5. Gueux E, Azais-Braesco V, Bussiere L, Grolier P, Mazur A, Rayssiguier Y. Effect of magnesium deficiency on triglycerol rich lipoprotein and tissue susceptibility to per-oxidation in relation to E content. *Br J Nutr* 1995;74: 849-56
6. Muller O, Krawinkel M. Malnutrition and health in developing countries. *CMAJ* 2005; 2(3): 173 -75.
7. Greenbaum LA. Pathophysiology of body fluids and fluid therapy. In: Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson Textbook of Pediatrics* 17th ed. Philadelphia: Saunders, 2004. p. 191-242.
8. Logan RW. Fluid, electrolytes and acid-base disturbance. In: Campbell AG, MacIntosh N editors. *Forfar and Arneil's Textbook of Paediatrics*, 5th ed. USA: Churchill Livingstone Company; 1998. p. 409.
9. WHO/FAO, Human vitamins and Mineral requirements: Magnesium. Report of a joint FAO/WHO expert consultation. Bangkok, Thailand, 2002.
- 10 McCoy JH, Kenny MA. Depressed immune response in the magnesium deficient rat. *J Nutr* 1975; 105:791-97.
11. Guenounou M, Armier J, Gaudin-Harding F. Effect of magnesium deficiency and food restriction on the immune response in the young mice. *Int J Vit Nutr Res* 1978: 290-95.
- 12 Rayssiguier Y, Gueux E, Bussiere L, Burlach J, Mazur A. Dietary magnesium affects susceptibility to lipoproteins and tissues to per - oxidation in rats. *J Am Coll Nutr* 1993; 12: 133-37.
13. World Health Organization. Management of the child with a serious infection or severe malnutrition: Guidelines for care at the first referral level in developing countries. Geneva: WHO 1999.
14. World Health Organization. Guidelines for the inpatient treatment of severely malnourished children. WHO 2003, SEARO Technical publication no-24.
15. Roy NC. Use of MUAC for evaluation of nutritional status of children and for identification of high-risk groups for malnutrition in rural Bangladesh. *J Health Popul Nutr* 2000; 18(3): 171-80.
16. Caddell JJ. A double-blind clinical trial to assay magnesium therapy. *New Eng J Med* 1967; 276 (10):535-40
17. Shills ME. Experimental human magnesium depletion. *Medicine* 1969; 48: 61-85.
- 18 Caddell JJ, Goddard DR. Studies in protein-calorie malnutrition. I. Chemical evidence for magnesium deficiency. *New Eng J Med* 1967; 276(10):533-535.
19. Weisinger JR, Font EB. Magnesium and Phosphorus. *Lancet* 1998; 352: 391-396.
20. Gupta. *The Short Textbook of Pediatrics*. 10th edn. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd. 2004 .p. 125-66.
21. Karla K, Mital VP, Pal R, Goyal RK, Dayal RS. Serum electrolytes studies in malnutrition. *Indian Pediatr* 1975;12 (11):1135-40.
22. Montgomery RD. Magnesium metabolism in infantile protein malnutrition. *Lancet* 1960; 2:74-75.