Effect of oral magnesium supplementation on serum magnesium levels in children recovering from severe acute malnutrition

***B Dakshayani**[1], **A V Keshav Murthy**[1], **Mallesh Kariyappa**[1]

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Abstract

Introduction: Children with severe acute malnutrition (SAM) have increased requirements for magnesium during recovery. World Health Organization recommends routine use of magnesium supplements in children with SAM. But, there is scanty knowledge about the effect of oral supplementation of magnesium sulphate on serum magnesium levels in children with SAM.

Objectives: To estimate the levels of serum magnesium in SAM children on admission, in transition phase and on discharge.

Method: Prospective observational study, measuring serum magnesium levels on admission, in transition phase and on discharge, in 1–59 month old children admitted with SAM and treated as per national guidelines. Fifty percent magnesium sulphate was given at 0.3ml/kg/day for 14 days.

Results: Of the 43 children studied, mean age was 11.54±7.90 months. The mean serum magnesium level was 2.49±0.55 mg/dl at admission, 2.34±0.48mg/dl at transition phase, and 2.36 ±0.47mg/dl at discharge. The decrease in mean serum magnesium at transition phase was not significant when compared to admission. Also the mean serum magnesium at discharge was not significantly decreased when compared to admission. Only one child had asymptomatic hypomagnesaemia at admission which recovered during treatment. 28 (65%) children responded well by gaining weight and the remaining 15 (35%) children did not respond. The study group had an average weight gain of 7.23±4.82 per kg per day.

Conclusions: The mean serum magnesium levels at admission, during transition and at discharge were within the normal range in children with SAM when supplemented with 50% magnesium sulphate as per national guidelines.

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(Key words: severe acute malnutrition, serum magnesium, oral magnesium sulphate supplementation)

Introduction

Nutritional factors contribute to around 45% deaths in under-5 year old children[1]. Deficiency of magnesium is common in children with severe acute malnutrition (SAM)[2]. Hypomagnesaemia is known to increase mortality in children with SAM[3]. Magnesium deficiency in malnourished children can be asymptomatic or can produce symptoms like loss of appetite, muscular weakness, lethargy, weight loss, tremor, seizures and psychomotor changes[4]. Magnesium therapy in SAM aids recovery and decreases the case fatality rate[5]. World Health Organisation (WHO)[6] and national guidelines[7] recommend the routine use of magnesium supplementation in children with SAM. Magnesium is supplemented in the form of 1) oral 50% magnesium sulphate solution or 2) in the form of standard mineral mix, used for local preparation of Formula 75 and Formula100 or 3) a pre-mix (Formula 75 and Formula 100) fortified with magnesium. Both standard mineral mix and pre-mix (Formula 75 and Formula100) are effective in improving serum magnesium levels in malnourished children[8,9,10]. However, they are not available in India. In India, magnesium is supplemented as 50% magnesium sulphate (intramuscular on day 1, and then orally for 14 days). Previous study[11] on efficacy of oral magnesium supplementation in SAM children was not conclusive due to high loss of follow up. Although concentration of serum magnesium might not sufficiently reflect body status, low levels can still indicate inadequate intake. Hence our aim was to assess the efficacy of oral magnesium supplementation by estimating serum magnesium levels during nutritional rehabilitation of SAM children.

Objectives

To estimate the levels of serum magnesium in SAM children on admission, in transition phase and on discharge.

[1]*Bangalore Medical College and Research Institute, Karnataka, India*
**Correspondence: dakshayani.sreeraghu@gmail.com*

https://orcid.org/0000-0003-4238-3006

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Method

A prospective observational cohort study was carried out in the nutritional rehabilitation centre attached to a tertiary care hospital from April to September 2019. SAM children admitted to Nutritional Rehabilitation Centre (NRC), aged between one month and 5 years, were enrolled in the study. SAM children with any underlying chronic illness as secondary cause of malnutrition were excluded from the study.

Anthropometry and clinical assessment were performed on admission. Body weight was measured to the nearest 10g utilising an electronic paediatric scale (Salter weighing machine). The recumbent length, to the nearest 0.1cm was measured using an infantometer for children 2 years old or younger. For children over 2 years old or longer than 87 cm, standing height was measured to the nearest 0.1 cm, utilising a stadiometer. Anthropometric Z-scores, based on the 2006 WHO child growth standards, were calculated. Mid upper arm circumference (MUAC) was measured to the nearest 0.1cm utilising a MUAC tape. Presence of bilateral pitting oedema was assessed by applying gentle pressure with the thumb for 10 seconds to the dorsal surface of both feet on admission.

Serum magnesium was measured at three time points during the children's stay in hospital - on admission, just before transition to F100 (end of stabilisation phase), and on discharge, in all children. At each time point, 1ml of blood was taken into a vacutainer and centrifuged using Beckman Coulter Au 480, and serum magnesium was estimated by the photometer method. According to the laboratory reference values and Nelson Textbook of Paediatrics[12], we defined normal plasma magnesium concentration as 1.5-2.3 mg/dl. After enrolment, all children were managed according to national SAM guidelines[7]. Children were given formula 75 diet on admission. Magnesium was supplemented as 0.3ml/kg/day of 50% magnesium sulphate (0.6 mmol/kg/day) for 14 days. It was given intramuscularly on day 1 and then orally diluted with feeds. After stabilization, children were given formula 100 in transition and rehabilitation phases and home based diet before discharge during rehabilitation phase.

Demographic features, clinical features, laboratory investigations, treatment aspects and outcome were recorded in a pretested proforma. The outcome indicators were defined as follows:

- Recovered – weight gain of more than 5g/kg/day on three consecutive days or 15% weight gain from base line before discharge.
- Non responder – no weight gain after completing treatment.
- Average weight gain (g/kg/day)
  Maximum weight in kg at discharge - minimum weight in kg x 1000 divided by *minimum weight × No. of days between minimum weight to maximum weight*
- Time for stabilization - The criteria for stabilization was according to WHO guidelines: Absence of any danger or emergency signs, decreasing oedema, tolerating and completing full prescribed volume of F75 feeds.
- Time to discharge - number of days taken to achieve a weight gain of 5g/kg/day on three consecutive days

Based on a previous study by Madhusudan K, *et al,* as serum magnesium increased by 0.2% from admission to discharge, and an alpha error of 5% and a power of 80 we arrived at a sample size of 40. As we had also planned to do serum calcium simultaneously, the sample size for serum calcium was estimated as 43, based on previous studies. Hence we decided to enrol 43 patients.

Ethical issues: Ethics Clearance was obtained from the Bangalore Medical College and Research Institute, Karnataka, India (ERC No. BMC/PGs/289/2017-178) and written informed consent from the parents of participating children

Statistical analysis: The data collected were entered into the Microsoft Excel sheet and analysed using SPSS version 20.0. Baseline data were presented using descriptive statistics namely mean, standard deviation, percentage. Independent t-test was used to determine significant difference between two groups and dependent t-test was used to determine significant difference between pre- and post-data, Chi Square test was used to determine association between qualitative variables.

Results

All 214 children admitted to Nutritional Rehabilitation Centre (NRC) during the study period were screened for eligibility. About 145 children were excluded as they did not meet inclusion criteria (spastic cerebral palsy, global developmental delay, congenital heart disease, renal disorders, postoperative surgical conditions, only on mother's milk etc.). Among remaining 69 children, 19 declined to participate. Remaining 50 children were enrolled on admission. But 4 were discharged early and only 46 were examined at transition phase. On discharge, as we could not get serum magnesium in 3 patients only 43 were examined. The flow chart of the participants in the study is shown in Figure 1.

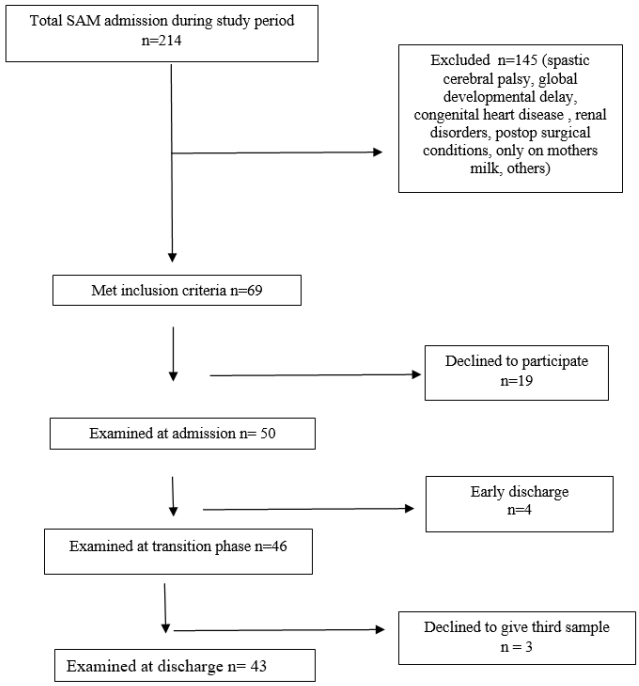

Figure 1: ***Flow chart of study participants***

The mean age on admission (Mean ± SD) was 11.54±7.90 months. The mean weight on admission was 5.12±1.68kg which increased significantly to 5.32±1.66kg on discharge (p=0.0001). The mean height was 64.77±9.80 cm on admission and 64.79±9.82 cm on discharge (p=0.323). The mean mid upper arm circumference (MUAC) was 9.77±2.47 cm on admission and 9.92±2.06 cm on discharge (p = 0.521). The baseline data of study population on admission are shown in Table 1.

The mean serum magnesium level was 2.49±0.55 mg/dl on admission, 2.34±0.48mg/dl in the transition phase and 2.36 ±0.47mg/dl on discharge (Figure 2).

Table 1: ***Baseline data of the study population on admission n=43***

Parameter	Number (%)
Age	
≤ 6 Months	11 (25.6)
6 months to 5 years	32 (74.4)
Gender	
Male	24 (55.8)
Female	19 (44.2)
Maturity	
Term	36 (83.7)
Preterm	07 (16.3)
Low birth weight	19 (44.2)
Neonatal intensive care unit graduate	15 (34.9)
Feeding	
Exclusively breast fed for 6 months	25 (58.2)
Top fed	24 (55.8)
Complementary feeding started at 6 months	25 (58.2)
Weight for length criteria (<3SD)	43 (100.0)
Mid upper arm circumference criteria (<11.5)	27 (62.8)
Pitting oedema	01 (02.3)
Comorbid condition (multiple)	
Anaemia	21 (48.8)
Pneumonia	13 (30.2)
Diarrhoea	13 (30.2)
Sepsis	04 (09.3)
Other	13 (30.3)

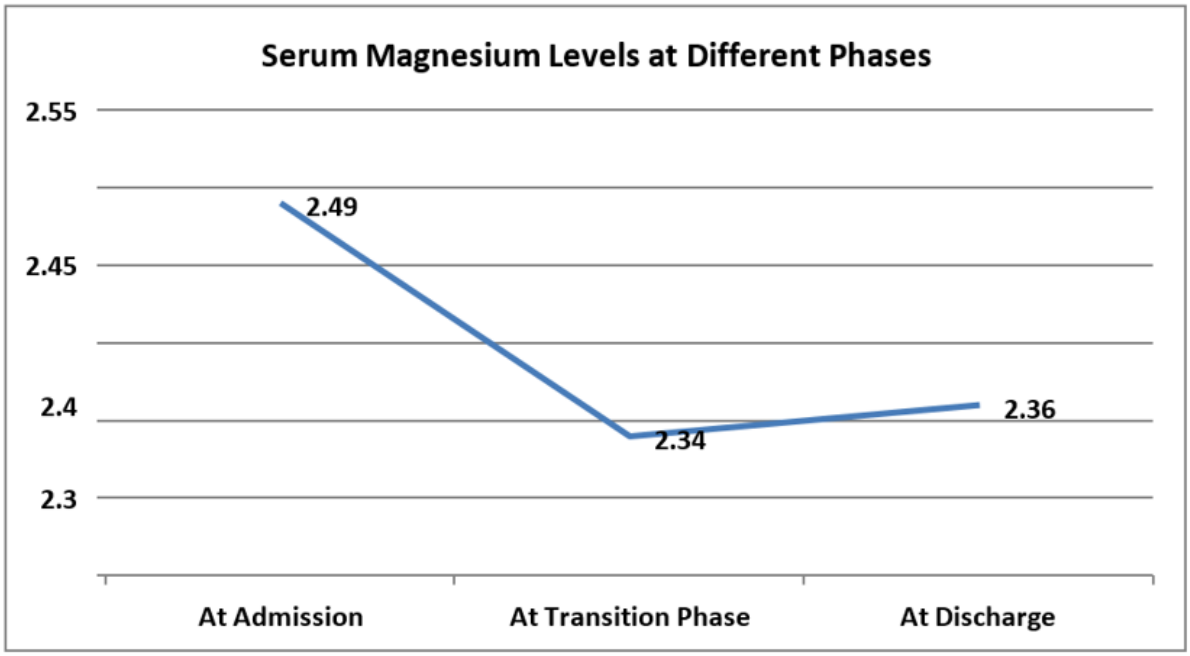

Figure 2: ***Mean serum magnesium at different phases of nutritional rehabilitation***

The decrease in mean serum magnesium at transition phase was not significant when compared to admission. Also the mean serum magnesium at discharge was not significantly decreased when compared to admission (Table 2).

Table 2: ***Comparison of serum magnesium (mg/dl) among study participants at various phases of the study***

Serum magnesium	Mean	Standard deviation	p-value
At admission	2.49	0.55	0.083
At transition phase	2.34	0.48	
At admission	2.49	0.55	0.082
At transition phase	2.36	0.47	

Only one child had hypomagnesaemia at admission which was asymptomatic and resolved with treatment. Among the 43 children in the study group, 28 (65.1%) responded well by gaining weight and the remaining 15 (34.9%) did not respond. There was no difference in mean serum magnesium levels at admission between non responders (2.42±0.51mg/dl) and responders (2.54±0.44mg/dl). There was no difference in mean serum magnesium levels at transition phase between non responders (2.4±0.7mg/dl) and responders (2.31±0.3mg/dl). The mean serum magnesium at discharge was significantly more (p=0.02) in non-responders (2.55±0.64mg/dl) when compared to responders (2.26±0.32 mg/dl). The study group had an average weight gain of 7.23 ±4.82 per kg per day. The mean duration of stabilization phase (time for stabilization) was 4.81±0.96 days and the mean duration of stay (time to discharge) was 13.40±2.61days (Table 3).

Table 3: ***Distribution of outcome among study participants (n=43)***

Outcome indicator	Result
Recovered n (%)	28 (65.1)
Non-responder n (%)	15 (34.9)
Average weight gain (g/kg/day) Mean ±SD	7.23±4.82
Duration of stabilization phase (in days) Mean ±SD	4.81±0.96
Duration of stay (in days) Mean ±SD	13.40±2.61

Discussion

In our study the mean serum magnesium at admission was 2.49±0.55 mg/dl which is similar to Madhusudan K, *et al*[11]. Others have reported lesser values (Zafar *et al* 1.11±0.24mg/dl)[13]. The lower values of serum magnesium in other studies could be due to variation in dietary intake of the study population. After supplementation with

0.6mmol/kg/day of magnesium orally, as 50% magnesium sulphate, serum magnesium decreased to 2.34±0.48 mg/dl at start of the transition phase in our study. Similarly, Mbethe *et al*[14] have reported a serum magnesium of 2.45±0.82mg/dl at admission which decreased to 2.31±0.65mg/dl on day 5 despite supplementing with magnesium sulphate 0.4–0.6mmol/kg/day orally. They have also reported that about 15% children developed re-feeding syndrome on day 5 and that serum magnesium was significantly lower in the re-feeding syndrome group when compared to those without re-feeding syndrome on day 5.

In our study the mean serum magnesium was 2.49±0.55mg/dl at admission and 2.36±0.47mg/dl at discharge after supplementing with 0.3 ml/kg of 50% MgSO4 for 14 days. Madhusudan K, *et al*[11] have reported a serum magnesium of 2.4±0.5mg/dl at admission which increased to 2.6±0.4mg/dl after supplementing with 0.3 ml/kg of 50% MgSO4 for 14 days. Madhusudan K has reported higher serum magnesium value at discharge when compared to our study probably because of 30% loss of follow up at discharge (including all three with hypomagnesaemia) in their study. Khalil *et al*[9] have reported a serum magnesium of 1.36±0.25mg/dl at admission which increased to 2.06±0.35mg/dl after supplementing with combined mineral vitamin mix which provides 0.3-0.6mmol/kg/day of magnesium. They have also reported better weight gain in magnesium supplemented group. Hence we can understand that a magnesium supplementation of 0.3-0.6mmol/kg/day either by combined mineral vitamin mix or by 50% magnesium sulphate is enough to maintain serum magnesium values and weight gain.

On the other hand, Hother *et al*[10] have treated children with pre-mixed F-75 and F-100 (Nutriset, Malaunay, France), containing 85mg/l (3.49 mmol/l) and 154 mg/L (6.32mmol/l) of magnesium respectively. This amounts to an intake of 0.44mmol/kg/day during F 75 and 0.94 to 1.39mmol/kg/day during F100 therapy. Hother *et al* have reported a mean serum magnesium of 2.31±0.55mg/dl at admission, which increased by 0.51mg/dl during transition and became 2.74 ± 0.41mg/dl at discharge. At discharge, majority had serum magnesium level above the normal range. Hence premix F75 and F100 are also effective in improving serum magnesium levels in SAM children. In our study, hypomagnesaemia was found in 1 (2.3%) child. The frequency of hypomagnesemia at admission has been reported as 36% by Karakelleoglu C *et al*[3], 13 % by Hother *et al*[10], 3.2% by Madhusudan K, *et al*[11]. This discrepancy can be due to variation in dietary intake of magnesium in the study population. The hypomagnesaemia in one child in our study was asymptomatic and improved with magnesium supplementation. Karakelleoglu C, *et al*[3] have reported that mortality was 7.5 times higher in the malnourished children with hypomagnesaemia than in the malnourished children without hypomagnesaemia.

Majority of children in our study responded with good weight gain. The higher serum magnesium at discharge in non-responders shows that magnesium was not a limiting factor in growth. The importance of supplementing malnourished children with magnesium has been appreciated for many years, due to its importance to lean tissue accretion, as well as for homeostasis of potassium, calcium and other nutrients. Ideally, evaluation of the adequacy of magnesium supplementation would require a trial of different doses, and with measurement of urinary excretion and growth.

The strength of our study is that this is one of the first studies to describe the levels of serum magnesium at different phases of nutritional rehabilitation of SAM children receiving oral magnesium sulphate supplementation. In addition, there was no loss of follow up in the three points of time at which serum magnesium was done. The limitations include observational design and modest sample size.

Conclusions

Mean serum magnesium levels at admission, during transition and at discharge were well within the normal range in severe acute malnourished children when supplemented with 50% magnesium sulphate as per national / WHO guidelines. We conclude that oral magnesium supplementation as per WHO /national guidelines during treatment of severe acute malnourished children is adequate.

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