Comparison of electrolyte and electrocardiographic changes in patients with protein–energy malnutrition at admission and after 2 weeks of nutritional rehabilitation therapy: A prospective study

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ABSTRACT

Introduction: Protein–energy malnutrition (PEM) in children is associated with several biochemical and electrocardiographic changes, which if left untreated may result in increased morbidity and mortality. **Objective:** This study compared the various biochemical and electrocardiographic changes present in patients with PEM on admission and after 2 weeks of nutritional rehabilitation therapy. **Methods:** This was prospective analytical study conducted at tertiary care pediatric hospital in North India. A total of 75 patients were enrolled with PEM. The electrolyte and electrocardiogram findings were recorded at the time of admission and after 2 weeks of nutritional rehabilitation therapy. **Results:** The mean age of patients was 2.2±1.2 years. The mean weight on admission was 7.2±2.1 kg. There were a total of 42 males and 33 females. There were significant improvements ($p<0.05$) in serum sodium, serum potassium, serum calcium levels, PR interval, and QTc interval after 2 weeks of therapy in most of the patients with PEM. The improvement may be less obvious in the PEM Category IV due to less number of patients. **Conclusion:** Among the several biochemical and electrocardiographic changes present in these patients with PEM, the majority showed significant improvement and reverts back to normal after nutritional therapy.

Key words: *Changes, Electrocardiographic, Electrolyte, Malnutrition*

Protein–energy malnutrition (PEM) is still a major challenge in low- and middle-income countries like India. It mainly involves population ranging from 6 months to <5 years of age. This includes stunting, wasting, and kwashiorkor, of which kwashiorkor and severe wasting are referred as severe acute malnutrition (SAM) [1]. As per the National Family Health Survey-4, it was found that the proportion of under-five children suffering from SAM weight for height Z (WHZ) score <−3 as per the WHO criteria has increased from 6.4% to 7.5% over the past 10 years [2]. Although the prevalence of SAM is lower in northern India (2.2%) as compared to the national average (around 7.5%), still it is a major cause of morbidity and mortality [3]. Younger age, small nuclear families, poor parental education, and occupation of family head were risk factors, which predispose the child to SAM [3].

PEM has the potential to involve multiple organ systems. Biochemical changes such as hyponatremia and hypokalemia are common and add to the severity of disease [4]. It was established that the mortality increases with increase in the severity of malnutrition, and it increases to 10 times–20 times for children with WHZ score <−3 and WHZ score <−4, respectively [5]. Similarly, these patients have myocardial involvement presenting commonly with congestive heart failure. Cardiac changes are more common with moderate-to-severe malnutrition patients, and these changes may correlate well with body mass index and to a lesser extent with electrolyte abnormalities like serum calcium levels [6]. Cardiac changes in such patients can be picked up by electrocardiogram (ECG) done at admission, and appropriate interventions can be started as soon as possible [7].

These biochemical and electrocardiographic changes have the potential to revert back to normal with standard management of SAM. With this objective, this study compared the various biochemical and electrocardiographic changes present in these patients on admission and after 2 weeks of nutritional rehabilitation therapy.

MATERIALS AND METHODS

This was a prospective analytical study done at a tertiary care pediatric center in North India from over a period of 1 year after getting approval from the institutional ethics committee. Patients with the age range of 6 months–5 years with diagnosis of PEM were enrolled in the study after taking informed consent from the parents. The patients of this age group were classified

as per the Indian Academy of Pediatric classification of PEM into four categories (Grade I PEM=weight/age 70–80% of expected; Grade II PEM=weight/age 60–70% of expected; Grade III PEM=weight/age 50–60% of expected; and Grade IV PEM=weight/age <50% of expected).

After recruitment, detailed history and examination were performed. The anthropometric indices including weight were recorded in all patients to assess the severity of PEM. The weight was recorded using the electronic weighing scale with precision of ±5 g. Soon after admission, 2-ml blood was collected in plain Vacutainer for serum electrolytes estimation (sodium, potassium, and calcium levels), and ECG was carried out using 12-lead Clarity electronic ECG machine (with small chest leads with recording speed of 25 mm/s), and results were analyzed by the principal investigator. In ECG, heart rate, QRS axis, PR interval, QTc interval, and ST segment changes were noted. The patients were managed as per the WHO guideline for managing SAM [8]. ECG and the serum electrolytes were repeated after 2 weeks of nutritional rehabilitation therapy.

All the collected data were filled in the pre-designed pro forma for the analysis. The quantitative variables were presented as mean±SD, and nominal variables were presented as number (percentages). The pre- and post-difference in the continuous variables such as serum electrolytes and ECG changes having the normal distribution was analyzed using the Student's paired t-test, whereas the qualitative variables were analyzed using the McNemar Chi-square test. $p<0.05$ was considered statistically significant.

RESULTS

A total of 75 patients were enrolled at the time of admission, of which PEM Grade I was 17, PEM Grade II was 28, PEM Grade III was 21, and PEM Grade IV was 9 patients. There were a total of 42 males and 33 females. The mean age of patients was 2.2±1.2 years, and the mean weight on admission was 7.2±2.1 kg. The most common presenting complaints of the admitted patient were fever for PEM Grade I (78%), PEM Grade II (79%), loose motions for PEM Grade III (56%), and poor feeding and lethargy for PEM Grade IV (79%) at the time of admission. Common diagnosis with which the patient was admitted was acute watery diarrhea with dehydration in 12 (16%), marasmus in 13 (17.3%), malaria in 12 (16%), meningitis in 12 (16%), and marasmic kwashiorkor in 10 (13.3%) patients. A total of five patients died before day 14 of admission, two in PEM Grade III and three in PEM Grade IV category.

In PEM Grade I category, there were a total of 17 pairs for comparison. There was a significant increase in the serum sodium (p=0.03), serum potassium (p=0.02), and serum calcium (p=0.002) in the patients after 14 days of nutritional rehabilitation. The QTc interval significantly decreased (p=0.001) after therapy from mean of 0.33±0.07 to 0.31±0.07 s. There was no statistically significant improvement in the weight (p=0.18), heart rate (p=0.8), QRS axis (p=0.4), and PR interval (p=0.15). There were no ST segment changes in either of the two groups in PEM Grade I patients (Table 1).

In PEM Grade II, there were a total of 28 pairs for comparison. There was statistically significant improvement in serum sodium (p=0.002), serum potassium (p=0.01), serum calcium (p=<0.001), and QTc interval (p=0.001) after 14 days of nutritional rehabilitation. There was no significant improvement in the weight (p=0.08), heart rate (p=0.25), QRS axis (p=0.65), PR interval (p=0.1), and ST-segment changes after the 14 days of therapy (Table 1).

In PEM Grade III, there were a total of 19 pairs for comparison as two patients died before day 14 of admission. There was statistically significant improvement in serum sodium (p=0.02), serum potassium (p=0.01), serum calcium (p=0.01), heart rate (p=0.01), and QTc interval (p=0.001) after 14 days of nutritional rehabilitation. There was no significant improvement in the QRS axis (p=0.81) although there was borderline improvement in the weight (p=0.05) after therapy. There were two ST-segment changes at admission in the group which were absent in the group after the therapy (Table 1).

In PEM Grade IV, there were a total of six pairs for comparison as three patients died before completion of the study. There was statistically significant improvement in the serum calcium (p=0.03) and QTc interval (p<0.01) after 14 days of nutritional rehabilitation. There was no significant improvement in the serum sodium (p =1.0), serum potassium (p=0.19), heart rate (p=0.54), QRS axis (p=0.46), and PR interval (p=0.08). There was improvement in ST-segment changes, but it was not statistically significant (p=1.0) (Table 1).

DISCUSSION

The present study showed that there were significant biochemical changes such as hyponatremia, hypokalemia, and hypocalcemia and ECG abnormalities such as tachycardia and prolongation of PR and QTc interval in patients with PEM at the time of admission which improved significantly after 2 weeks of nutritional rehabilitation. Although there was not much improvement in the weight gain, there is a definite improvement in serum electrolytes such as serum sodium, serum potassium, and serum calcium levels post-nutritional rehabilitation therapy. There was also significant improvement seen with ECG changes such as shortening of PR and QTc interval with nutritional therapy. There was not much effect on ST-segment changes which may be due to decrease incidence of these abnormalities in the present study. This study provides strong evidence suggesting that many of the biochemical changes and ECG changes can be improved significantly after appropriate management of PEM.

Moderate-to-severe malnutrition has definite effect on cardiac volume, muscle mass as well as the electrical properties of the myocardium. Systolic functions are affected more than the diastolic functions [9]. A study was conducted by Srivastava *et al.* [4] from Meerut, India, who enrolled 20 patients of malnutrition also showed hypokalemia, hypocalcemia, and prolongation of QTc interval in malnourished patients. The prolong QTc interval was attributed to the hypocalcemic changes in these patients by the

Table 1: Comparison of serum electrolytes and ECG changes at the time of admission and 14 days after the nutritional rehabilitation therapy

Variables	Mean±SD/n (%)		p value
	At admission	After 14 days	
PEM Grade I			
Weight in kg	8.7±2.0	8.8±2.0	0.18
Sodium (in meq/L)	131±7.3	132±6.8	0.03*
Potassium (in meq/L)	3.7±0.7	3.8±0.6	0.02*
Calcium (mg/dL)	8.8±0.8	9.0±0.7	0.002*
Heart rate	117±20.9	117±18.2	0.80
QRS axis (degrees)	80.0±20.9	82.3±15.6	0.41
PR interval (in seconds)	0.08±0.03	0.07±0.03	0.15
QTC interval (in seconds)	0.33±0.07	0.31±0.07	0.001*
ST-segment changes	0 (0%)	0 (0%)	-
PEM Grade II			
Weight in kg	7.6±1.8	7.6±1.8	0.08
Sodium (in meq/L)	128.7±4.6	130.0±4.3	0.002*
Potassium (in meq/L)	3.6±0.96	3.8±0.82	0.01*
Calcium (mg/dL)	8.6±1.1	8.8±1.01	<0.001*
Heart rate	119.7±11.4	118.2±12.3	0.25
QRS axis (degrees)	79.3±22.3	80.3±24.1	0.65
PR interval (in seconds)	0.08±0.03	0.08±0.02	0.10
QTC interval (in seconds)	0.38±0.07	0.37±0.06	0.002*
ST-segment changes	1 (3.6%)	1 (3.6%)	1.0
PEM Grade III			
Weight in kg	6.4±1.5	6.6±1.5	0.05
Sodium (in meq/L)	126.4±7.2	128.4±4.8	0.02*
Potassium (in meq/L)	3.6±0.9	3.8±0.8	0.01*
Calcium (mg/dL)	8.3±1.1	8.4±1.1	0.01*
Heart rate	121.2±18.7	116.8±17.2	0.01*
QRS axis (degrees)	86.8±42.2	87.4±37.7	0.81
PR interval (in seconds)	0.07±0.03	0.07±0.02	0.06*
QTC interval (in seconds)	0.36±0.09	0.34±0.07	<0.01*
ST-segment changes	2 (10.5%)	0 (0%)	-
PEM Grade IV			
Weight in kg	4.3±1.6	4.6±1.7	0.3
Sodium (in meq/L)	124.0±8.0	124.0±8.7	1.0
Potassium (in meq/L)	2.8±0.8	2.9±0.8	0.19
Calcium (mg/dL)	6.4±1.0	6.6±1.0	0.03*
Heart rate	133.5±9.1	131.7±5.6	0.54
QRS axis (degrees)	71.7±43.1	76.7±40.8	0.46
PR interval (in seconds)	0.12±0.05	0.09±0.03	0.08
QTC interval (in seconds)	0.47±0.04	0.42±0.02	<0.01*
ST-segment changes	2 (33.3%)	1 (16.7%)	1.0

Variable presented as mean±SD/n (%). *p<0.05 is considered statistically significant. SD: Standard deviation

author. Olowonyo *et al.* suggested that the myocardial atrophy in patients with kwashiorkor as the cause of ECG changes [10].

Olivares *et al.* [7] also found hypokalemia and hypocalcemia in patients with malnutrition as compared to controls. They also found prolonged QTc interval in the patients with PEM as compared to control (QTc: 445.9±31.4 vs. 400.9±17.7 ms, p<0.001). The QTC interval in their study was comparable to QTc interval of 0.47 seconds in PEM Grade IV patient in the present study. Most of the ECG abnormalities found in our study at admission like prolongation of PR and QTc interval were significantly improved after nutritional rehabilitation as shown by other authors from Egypt and India [9,11,12].

Gopalan *et al.* [11] did the study where he compared ECG changes, pre- and post-nutritional therapy similar to our study. He found increased QT interval and diminution in amplitudes of all the deflections in ECG. There were no changes in the PR interval and ST-segment changes unlike our study. He was able to demonstrate normalization of few of the recorded ECG changes after high-protein diet in such patients. The ECG changes found in these patients were assigned to multifactorial etiology and were not attributed to electrolyte disturbance solely as suggested by Gopalan *et al*.

In a study from Nigeria, Taiwo *et al*. [13] demonstrated significant improvement in the serum sodium and potassium after treatment similar to our study, but serum calcium levels did not improve much despite treatment. The other parameters which were measured in Taiwo *et al.* study were serum albumin, chloride, and bicarbonate which were not measured in our study. Etukudo *et al.* [14] and Said *et al.* [15] also demonstrated similar biochemical derangements of sodium and potassium similar to our study.

The strengths of the study include double verification of patient weight on electronic weighing scale with high precision ±5 g and ECG changes recorded by the principal investigator, were cross-verified by the cardiologist in cases of doubt. The limitations of the study were that it was not blinded though the outcome measures were objective, and there are less chances of bias in the analysis. We did not calculate QT dispersion in ECG and also could not do the echocardiogram of these patients in view of the limitation of resources which was done in earlier studies. We could not collect the data on long-term follow-up for these patients.

CONCLUSION

Patients with moderate-to-severe PEM present with several biochemical (e.g., hyponatremia, hypokalemia, and hypocalcemia) and electrocardiographic changes (e.g., tachycardia and prolongation of PR and QTc interval). These changes can improve significantly and revert back to normal on appropriate nutritional rehabilitation of such patients.

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