A Study of Oxidative Stress and Attenuation of Total Antioxidant Capacity in Severe Acute Malnutrition

ABSTRACT

Introduction: Malnutrition symbolizes one of the most harsh health problems in India. The free radicals take an important role in immunological response, which induces the oxidative burden in severe acute malnutrition (SAM). The aim of study was to scrutinize impact of oxidative stress in the form of serum malondialdehyde (MDA) as product of lipid peroxidation and total antioxidant capacity (TAC) in patients with SAM before and after supplementation of antioxidants for 12 weeks with diet and regular therapy. The data were compared with controls. Total 179 malnourished children were studied in between age group 6 to 60 months. After applying the inclusion and exclusion criteria, a total of 108 malnourished children were eligible for the study. The data were collected and compared with 108 age- and sex-matched healthy controls from the same age group. The statistical analysis was done using Statistical Package for the Social Science (SPSS) 16.0 software. All the patients were assessed for baseline parameters as per the criteria of World Health Organization (WHO). The serum MDA concentrations significantly increased (p < 0.001) in the patients when compared with controls, and significant depletions were found in the level of total protein, hemoglobin (Hb), and TAC (0.001) in patients with SAM when compared with controls.

After 12 weeks supplementation of antioxidants, the level of MDA was decreased significantly (p < 0.001), total protein concentration was increased marginally (p < 0.05), non-significant (p > 0.05) increase in Hb concentration, and TAC was increased significantly (p < 0.001) when compared with before supplementation results.

Conclusion: Unforgiving scarcity of various nutrients in SAM leads to generation of heavy oxidative stress. These effects may be minimized with supplementation of antioxidants with diet and regular therapy. Severe dietary deficiency of nutrients leads to increased oxidative stress in cellular compartments.

INTRODUCTION

Malnutrition characterizes one of the greatest serious health problems in India. According to World Health Organization (WHO), malnutrition is “the cellular imbalance between supply of nutrients and energy. The body’s demand for them to ensure growth, maintenance, and specific functions.” The WHO and United Nations Children’s Fund scheduled diagnostic standards for severe acute malnutrition (SAM) in children aged 6 to 60 months. Worldwide, nearly 20 million children are severe acute malnourished. There are about 132 million children under 5 present in total Indian population, of which about 8.1 million are assumed to be suffering from SAM.

Diarrhea and pneumonia contributes about half of the under 5 deaths. It assumed to contribute about 61% of the diarrheal and 53% pneumonia deaths. Malnutrition occurs principally due to scarce intake and absorption of essential nutrients to grow up normally. It is associated with anemia, pneumonia, failure to thrive, decreased activity, irritability, severe infections, diarrhea, stunning, and wasting. Today, different studies indicate that there is vast generation of free radical ions and reactive oxygen species (ROS) occur within the erythrocytes. These are superoxide anion (O$_2^-$), hydroxyl radical (OH$^-$), singlet oxygen and hydrogen peroxide (H$_2$O$_2$), etc. Induced oxygen free radicals and peroxidative tissue injury accompany severe anemia and lots of complications, which accelerate the multiple abnormalities, such as edema, wasting, growth retardation. Several studies in which it is founded that malondialdehyde (MDA) a product of lipid peroxidation is formed in excess quantities. This oxidative stress and a possible consequential accelerated apoptosis may contribute to pathophysiology of malnutrition.


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The antioxidants in the body are first line of defense against free radical damage. Also, it is serious for sustaining optimum health and well-being. They scavenge free radicals and other ROS. In the body, antioxidant acts simultaneously, and it may not be possible to determine the antioxidant potential of individuals. This made researcher to think on determining total antioxidant potential of the samples, which will measure all the antioxidants in it. Therefore, the total antioxidant potential is the test giving general idea about body’s defense status against ROS by all known and unknown antioxidants. In malnutrition, the total antioxidant capacity (TAC) level is reduced because of increased oxidative stress. The prevalence of malnutrition is high in tribal and non-tribal population in Maharashtra. With this background knowledge, the present study intends to scrutinize the knowledge concerning the oxidative biochemistry and its contribution in the malnutrition.

MATERIALS AND METHODS

The present work was carried out in the Department of Biochemistry at ACPM Medical College, Dhule, Maharashtra, and Department of Biochemistry at Dr. Vithalrao Vikhe Patil Foundation’s Medical College and Hospital, Ahmednagar, Maharashtra, India. Prior to the study, the Institutional Ethical Committee clearance was obtained, and utmost care was taken during experimental procedure according to the Declaration of Helsinki 1975.

Total 179 malnourished children were studied in between age group 6 to 60 months. After applying the inclusion and exclusion criteria, a total of 108 malnourished children were eligible for the study. The data were collected and compared with 108 age- and sex-matched healthy controls from the same age group. All patients were under the strict supervision of medical professionals during the study period. All the patients having history of cardiovascular diseases, hypertension, thyroid dysfunction, diabetes mellitus, which induce oxidative stress were excluded from the study.

After obtaining a written consent from all the participants who were included in the study, total 3 mL blood was withdrawn aseptically from the antecubital vein from each subject, out of this approximately 1 mL blood in ethylenediaminetetraacetic acid (EDTA) (0.47 mol/L K3-EDTA) container and 2 mL blood in plain bulb. The samples were centrifuged at 3000 rpm for 10 minutes to separate serum and red blood cells respectively. The separated serum was collected in polythene tube with cork and stored at –20°C. The serum with no sign of hemolysis was used for analysis of following parameters:

- Serum total protein
- Blood hemoglobin (Hb)
- Serum MDA
- Plasma TAC

The analysis of all parameters was done manually using the chemicals of Qualigens Fine Chemicals Co., Mumbai. The parameters were run on ultraviolet visible spectrophotometer (Systronics). The assessment of the above parameters in baseline except controls was conducted before and after 12 weeks of antioxidant supplementation in the form of an antioxidants syrup A-Z 5 mL twice a day, which was composed of predominantly antioxidants vitamins and trace elements. The supplementation was given with diet and regular treatment.

The statistical analysis was carried out by using the SYSTAT software, version 16.0 for Windows. The Student’s “Z” test was applied for the statistical analysis, and the results expressed in mean ± SD, p-values (p < 0.001) were considered as highly significant.

RESULTS

Table 1 shows significant depleted levels of serum total protein, Hb, TAC (p<0.001) and significantly increased levels of MDA (p<0.001) in SAM (group I) than healthy controls. After 12 weeks supplementation of antioxidant (group II), it was observed that significant increase in the levels of serum protein (p<0.05) and TAC (p<0.001), while nonsignificant increase in Hb (p>0.05), also significant decrease level of MDA (p<0.001) than SAM (group I).

DISCUSSION

There is a drastic rate of mortality among the preschool going children with severe protein-energy malnutrition (PEM). There are severe metabolic disturbances and

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (n = 108) Mean ± SD</th>
<th>SAM patients (n = 108) before supplementation of antioxidants (group I) Mean ± SD</th>
<th>p-value</th>
<th>SAM patients after 12 weeks supplementation of antioxidants (group II) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum total protein</td>
<td>7.01 ± 0.31</td>
<td>3.83 ± 0.46</td>
<td>p&lt;0.001</td>
<td>4.45 ± 0.54**</td>
<td>p&lt;0.05</td>
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<tr>
<td>Blood Hb (gm/dL)</td>
<td>10.8 ± 2.9</td>
<td>3.9 ± 1.3</td>
<td>p&lt;0.001</td>
<td>4.7 ± 1.4*</td>
<td>p&gt;0.05</td>
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<tr>
<td>Serum MDA (nmols/mL)</td>
<td>135.47 ± 21.99</td>
<td>284.51 ± 37.6</td>
<td>p&lt;0.001</td>
<td>179.64 ± 17.30*</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Plasma TAC (µmol/L)</td>
<td>857.05 ± 78.4</td>
<td>385.63 ± 29.3</td>
<td>p&lt;0.001</td>
<td>553.62 ± 52.98**</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
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*p>0.05 (nonsignificant); **p<0.05 (significant); ***p<0.001 (highly significant); n=number of subjects
systemic and intestinal infections. Various protein-energy-malnourished children suffer from severe childhood infection like pneumonia, diarrhea, septicemia, malaria, and measles.

Our results are in accordance with the research by Shaheen et al. in which significantly diminished levels of total protein and albumin were found. According to their study, the level of serum protein and albumin were decreased due to decreased protein intake and reduced hepatic biosynthesis of protein. After supplementation of A-Z antioxidant syrup, there was a marginal (p < 0.05) increase in concentration of total protein after 12 weeks of supplementation of antioxidants to patients group when compared to baseline levels. As per the study of Ashour et al., observed diminished concentration of Hb, hematocrit values in PEM children were compared with healthy controls.

Our results are in collaboration with Mizumoto et al. The total Hb concentration was drastically reduced before supplementation of antioxidants in both the groups of PEM. After supplementation of A-Z antioxidant syrup, there was a nonsignificant (p > 0.05) increase in concentration of Hb after 12 weeks of supplementation of antioxidants to patients group when compared to baseline levels. This slight elevation may be observed due to enhanced immune system followed by reduction in infections in both the groups.

As per the study of Jain et al. and Bosnak et al., MDA was generated in excess in SAM when compared with controls. It may be due to decreased antioxidant defense concentration which results in the enhanced membrane lipid peroxidation in malnutrition. One of the main reasons behind the increase in MDA could be due to scarcity of trace elements. It leads toward the depleted antioxidant status, and it may be one of the contributing factors for the pathogenesis of PEM. They also suggested that supplementation of trace element could be helpful in the management of PEM. These results are in accordance with our results that antioxidant therapy can affect positively on malnourished children.

Our results are in accordance with Jain et al. that due to the enhanced oxidative stress and disturbed immune system it leads toward the reduced TAC level in malnutrition. They further described that the low superoxide dismutase (SOD) level might be reason for decreased TAC activity in the malnutrition. Because SOD nullifies $O_2^-$ and forms $H_2O_2$, and thus it acts as a primary quencher of superoxide. In addition, the trace element zinc (Zn) plays an important role as a nutritional antioxidant cofactor. As there is severe deficiency of Zn, which further leads to reduced concentration of TAC in malnutrition, 12 weeks supplementation of antioxidants with diet and regular treatment to severe acute malnourished children, it was observed that the serum MDA was significantly reduced (p < 0.001), and highly significant elevation in plasma TAC concentration were found when compared with before supplementation results. It may be due to antioxidants, such as Vitamin E, which is an essential component of cell membranes, and which also protects the cell integrity. Vitamins E and C are chain-breaking antioxidants, which act as potent peroxyl radical scavenger. This ultimately may be useful in tumbling the oxidative stress generated in malnourished children.

CONCLUSION

The soul of the existing study lies in the fact that because of hypoalbuminemia, i.e., chronic diarrhea due to deficiency of trace elements, malnourished children are subjected to peroxidative tissue injury. The enhanced oxidative stress occurs in the form of MDA, hypoalbuminemia, and depleted levels of total antioxidant capacity to cope up the peroxidative injury in malnutrition. To handle this situation, the nutritional professionals suggested to focus on giving interventions especially micronutrient supplementation.

The regular antioxidant supplementation (A-Z syrup) with regular treatment as an adjunct therapy improves the redox potential status in erythrocytes as well as plasma and reduces the oxidative tissue injury. The antioxidant supplementation may minimize diarrheal episodes and other severe infections.

REFERENCES


