INTRODUCTION

In institutional practice, we often come across several patients presented with fever and altered sensorium. This is not a specific disease entity rather a group of diseases with varied clinical manifestations, caused by different etiological agents and they commonly come under the terminology of “Acute Febrile Encephalopathy” (AFE) which is a major health problem in rural and urban areas of India. Early diagnosis of the disease with co-morbid conditions and its proper management irrespective of etiology may reduce the mortality and morbidity caused by it. AFE is used to describe patients with condition in which altered mental status either accompanies or follows a short febrile illness (Anga et al., 2010). It includes mainly meningitis, meningoencephalitis or encephalitis and also enteric fever, cerebral malaria, sepsis (Chaudhari et al., 2002). AFE is a common condition leading to hospital admissions in both adults and children in India (Bansal et al., 2005; Bhalla et al. 2010). It may result from the pathogenic mechanism directly affecting the nervous system or may be due to the metabolic complications. Acute encephalitis, a major cause of AFE is a severe illness in both pediatric and adult age group, with an incidence of 10 cases per 100000 child-years (Kennedy, 2004; Koskiniemi et al., 1997). Apart from common clinical manifestations like headache, vomiting, convulsion, the child may present with different complications like dyselectrolytemia, respiratory acidosis due to CNS depression accompanied by metabolic acidosis if there is shock (Kothari et al., 2006). The present study was conducted to establish the electrolyte and metabolic status of these patients apart from clinico-etiological and epidemiological aspect of the disease in a rural tertiary care centre so as to get an idea regarding initial fluid therapy.

MATERIALS AND METHODS

A hospital based observational prospective study involving 120 children between 1 to 12 years of age who were admitted in the department of Pediatrics of Burdwan Medical College and Hospital during the period of March 2014 to February 2015 was conducted after taking proper ethical clearance from the institutional ethical committee.

ARTICLE INFO

Article History:
Received 16th December, 2016
Received in revised form 25th January, 2017
Accepted 23rd February, 2017
Published online 28th March, 2017

Key Words:
Acute febrile encephalopathy, serum electrolytes, sodium, bicarbonate.

ABSTRACT

Objectives: To study the changes in serum electrolytes with special emphasis on serum sodium status in children admitted with acute febrile encephalopathy.

Material and Methods: A hospital based observational prospective study involving 120 children between 1 to 12 years of age group who were admitted with fever and altered sensorium with or without convulsion, headache or vomiting, and whose total duration of illness was less than 2 weeks; was conducted in the department of Pediatrics of Burdwan Medical College and Hospital, over a period of one year.

Results: The mean age of the children included in the study was 72.4 months. 20% children were in the age group of 1 to 3 years, 34.16% in the age group of 3 to 6 years and rest (45.84%) were in the age group of 6 to 12 years. 58.33% were male, 41.66% were female. Hyponatremia and low bicarbonate were the predominantly noticeable electrolyte changes on admission. Mean serum sodium on admission was 133.39 ± 5.63 mEq/L and after 48 hours was 139.60 ± 3.24 mEq/L. Mean bicarbonate on admission and after 48 hours were 21.59 ± 1.72 and 23.94 ± 1.81 mEq/L, respectively. Both these differences were statistically significant (p=0.000 in both cases). However serum level of potassium, calcium and chloride were not significantly changed.

Conclusion: An idea of serum electrolyte changes in children with acute febrile encephalopathy can help us to initiate appropriate fluid therapy early in the course of management and thus can prevent or reduce mortality and morbidity.
The inclusion criteria were: 1. Fever with or without convulsion, headache or vomiting; and altered sensorium and 2. Total duration of illness less than 2 weeks. Those who had febrile convulsion, seizure disorder precipitated by fever, history of head injury or poisoning, known case of metabolic disorder or those who died within 48 hours were excluded from the study.

Children whose parents gave informed consent were included. After hemodynamic stabilization, particulars of patients (name, age, sex, religion) epidemiological data were obtained. Detail history was taken, through clinical examinations were performed and data were put in the pre-designed proforma. Serum electrolytes [sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺), chloride (Cl⁻) and bicarbonate (HCO₃⁻)] level on admission were measured. While doing intravenous cannulation, blood samples were drawn and sent to laboratory for necessary investigations. CSF was also drawn before starting first dose of antibiotic. Patients were placed on isotonic fluid (normal saline/DNS), appropriate supportive, and presumptive treatment (antibiotics/antiviral/anti-malarial) depending upon the merit of the cases. Interpretation of the probable etiology like bacterial, viral, tubercular or non-specified was done from CSF study. Some of the etiological diagnoses were made using Dengue MAC ELISA, JE serology, blood for Malarial Parasite (MP), MP Dual Antigen (MPDA), and Widal test. Neuroimaging was also done to see the extent of involvement. A repeat value after 48 hours was also measured to compare it with the previous one. The data obtained were analyzed using SPSS software version 20.0 applying appropriate statistical methods (Chi-square test, paired T-test and ANOVA test) to determine the significant changes in electrolyte composition so that we could assess the effectiveness of fluid therapy.

RESULTS

The study comprised of 120 children with mean age of 72.4 months. 24 (20%) children were in the age group of 1 to 3 years, 41 (34.16%) in the age group of 3 to 6 years and rest 55 (45.84%) were in the age group of 6 to 12 years. 70 (58.33%) were male, 50 (41.66%) were female. Majority of the children were Hindu and belong to lower upper or lower socioeconomic class. CSF findings suggestive of bacterial etiology were in 35 (29.16%) cases, viral etiology in 58 (48.33%) cases, 3 (2.5%) were tubercular and in 24 (20%) cases no etiology could be determined. In children of age group 1 to 3 years, bacterial etiology was more common than viral where as in 3 to 6 years and 6 to 12 years age group and for both male and female viral etiology was commoner. Table 1 shows minimum, maximum and mean values of different electrolytes on admission and after 48 hours.

The difference was statistically significant for serum sodium (p=0.000) and bicarbonate (p=0.000) but not for potassium, calcium or chloride (p values are 0.187, 0.374 and 0.296 respectively. Frequency of different grades of hyponatremia on admission and after 48 hours has been listed in Table 2 as follows:-

On admission, hyponatremia was present in 16 (66.66%) children of age group between 1 to 3 years; 29 (70.73%) children of age group between 3 to 6 years and 29 (52.72%) children of age group between 6 to 12 years. Age wise distribution of hyponatremia was not statistically significant (p=0.025). Mean Na⁺ on admission in this three different age groups were (132.8±5.84), (132.79±5.78) and (134.09±5.49) mEq/L which were not statistically significant (p=0.526). Mean Na⁺ after 48 hours in this three different age groups were (139.75±2.34), (139.94±3.14) and (139.28±3.67) mEq/L which were also not statistically significant (p=0.656) [Table 3].

Hyponatremia was present in 43 (61.42%) male and 31 (62%) of female. Sex wise distribution of hyponatremia was not statistically significant. (p=0.875). Mean Na⁺ on admission in male and female were (133.22±5.97) and (133.62±5.20) mEq/L which were not statistically significant (p=0.731). Mean Na⁺ after 48 hours in male and female were (139.41±3.60) and (139.86±2.70) mEq/L, respectively which were not statistically significant (p=0.503) [Table 3].

On admission, hyponatremia was present in 22 cases (62.85%) of bacterial etiology and 34 cases (58.62%) of viral etiology. The difference was not statistically significant. (p=0.746). After 48 hours, hyponatremia was present in 4 cases (29.16%) cases, viral etiology and 1 case (1.72%) of bacterial meningitis. The difference was not statistically significant (p=0.119). Mean Na⁺ on admission in bacterial meningitis and viral meningitis were (133.07±5.21) and (133.48±4.94) mEq/L which were not statistically significant (p=0.238). Mean Na⁺ after 48 hours in bacterial meningitis and viral meningitis were (139±2.95) and (140.92±2.10) mEq/L which were statistically significant (p=0.001) (Figure 1) and (Table 1).

Mean HCO₃⁻ on admission in age group between 1 to 3 years, 3 to 6 years and 6 to 12 years were (21.15±1.57), (21.88±1.92) and (21.57±1.63) mEq/L, respectively which were not statistically significant (p=0.321). Mean HCO₃⁻ after 48 hours in this age groups were (24.10±1.55), (23.62±1.69) and (24.11±2.01) mEq/L, respectively which were not statistically significant (p=0.450). Mean HCO₃⁻ on admission in male and female were (21.60±1.57) and (21.57±1.94) mEq/L, respectively which were not statistically significant (p=0.928). Mean HCO₃⁻ after 48 hours in male and female were (23.67±1.77) and (24.31±1.84) mEq/L which were not statistically significant (p=0.360). Mean HCO₃⁻ on admission in bacterial and viral etiology were (21.55±1.86) and (21.63±1.68) mEq/L, respectively which were not statistically significant (p=0.859). Mean HCO₃⁻ after 48 hours in these cases were (24.38±1.64) and (24.02±1.67) mEq/L, respectively which were not statistically significant (p=0.360) (Table 3).

Serum K⁺, Ca²⁺, Cl⁻ values however among different age groups, among male-female or among bacterial or viral etiology were also statistically insignificant.

DISCUSSION

Acute Febrile Encephalopathy is a clinical term used to describe altered mental state that either accompanies or follows a short febrile illness (less than 2 weeks) and is characterized by a diffuse and nonspecific brain insult manifested by a combination of CNS manifestations (Bansal et al, 2005). CNS infection is the most common identifiable etiology in acute febrile encephalopathy among which viral encephalitides constitutes around 1/3 rd cases (Glaser et al, 2006; Karmarkar...
Sepsis, enteric encephalopathy, cerebral malaria, endemic typhus are also some other common etiologies of AFE.

The study was conducted among 120 children between age group 1 to 12 years where males were predominant (58.33%). Most of the children were between 6 years to 12 years (45.83%). Mean age was 72.4 months. With the help of CSF finding and other supportive investigations, viral encephalitis was found in most cases (48.33%), followed by bacterial (29.16%) as seen in some other studies (Glaser et al, 2006; Karmarkar et al, 2008; Singh et al, 2009). Apart from fever and altered sensorium, convulsion (48%), vomiting (39%) and headache (28%) were the common symptoms. Dyselektrolytemia is a common complication of AFE.

In this study, serum Na \(^+\) on admission ranged from 123 to 144 with mean value of \((133.39\pm5.63)\) mEq/L and after 48 hours ranging from 128 to 145 with mean value of \((139.60\pm3.25)\) mEq/L (Table 1).

### Table 1 Change of Serum electrolyte levels in febrile encephalopathy patients (n = 120)

<table>
<thead>
<tr>
<th>Electrolytes</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na(^+)</td>
<td>On admission</td>
<td>123</td>
<td>144</td>
<td>133.39</td>
</tr>
<tr>
<td></td>
<td>After 48 hrs</td>
<td>128</td>
<td>145</td>
<td>139.60</td>
</tr>
<tr>
<td>Serum K(^+)</td>
<td>On admission</td>
<td>3.3</td>
<td>4.7</td>
<td>4.08</td>
</tr>
<tr>
<td></td>
<td>After 48 hrs</td>
<td>3.6</td>
<td>4.8</td>
<td>4.11</td>
</tr>
<tr>
<td>Serum Ca(^++)</td>
<td>On admission</td>
<td>8.8</td>
<td>10.9</td>
<td>9.82</td>
</tr>
<tr>
<td></td>
<td>After 48 hrs</td>
<td>8.9</td>
<td>10.7</td>
<td>9.87</td>
</tr>
<tr>
<td>Serum Cl(^-)</td>
<td>On admission</td>
<td>99</td>
<td>106</td>
<td>103.19</td>
</tr>
<tr>
<td></td>
<td>After 48 hrs</td>
<td>98</td>
<td>106</td>
<td>102.87</td>
</tr>
<tr>
<td>Serum HCO(_3)</td>
<td>On admission</td>
<td>18</td>
<td>26</td>
<td>21.59</td>
</tr>
<tr>
<td></td>
<td>After 48 hrs</td>
<td>20</td>
<td>28</td>
<td>23.94</td>
</tr>
</tbody>
</table>

The difference was statistically significant (p=0.000). Similar finding was observed in a study by Glaser et al where mean serum Na at the time of admission was 128.6 mEq/L which became133.4 mEq/L after 48 hours of admission (Glaser CA et al, 2006). Another study by Singh et al showed that mean serum Na levels (130.5 ± 8.15 mEq/L) were significantly lower in children with acute bacterial meningitis in comparison to controls (p<0.001) (Singh et al, 1993). In the present study (Table 2), only 38.33% cases had normal sodium on admission, 34.16% had mild (130 to 134), 23.33% had moderate (125 to 129) and 4.16% had severe (<125) hyponatremia (Moritz et al, 2010;[12,13]).

### Table 2 Grades of hyponatremia on admission and after 48 hours (n=120)

<table>
<thead>
<tr>
<th>% of cases</th>
<th>Mean serum Na(^+) on admission with SD</th>
<th>Mean serum Na(^+) 48 hrs after admission with SD</th>
<th>Mean serum HCO(_3) on admission with SD</th>
<th>Mean serum HCO(_3) 48 hrs after admission with SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt;135)</td>
<td>46 (38.33)</td>
<td>108 (90)</td>
<td>132.8±5.84</td>
<td>139.75±2.34</td>
</tr>
<tr>
<td>Mild (130 to 134)</td>
<td>41 (34.16)</td>
<td>10 (8.33)</td>
<td>134.09±4.9</td>
<td>139.28±3.37</td>
</tr>
<tr>
<td>Moderate (125 to 129)</td>
<td>28 (23.33)</td>
<td>2 (1.66)</td>
<td>133.22±5.97</td>
<td>139.4±3.14</td>
</tr>
<tr>
<td>Severe (&lt;125)</td>
<td>5 (4.16)</td>
<td>0</td>
<td>133.62±5.97</td>
<td>139±2.95</td>
</tr>
</tbody>
</table>

The scenario was changed when measured after 48 hours (after giving isotonic fluid, NS or DNS). 108 cases (90%) had normal sodium after 48 hours. Hyponatremia in patients with AFE can result from syndrome of inappropriate ADH secretion (SIADH), cerebral salt wasting (CSW) and excessive fluid administration (Albanese et al, 2001; Jayakumar et al, 2006; Palmar, 2003). Acute severe hyponatremia is usually associated with neurological symptoms such as seizures, altered sensorium etc. and should be treated urgently because of the high risk of cerebral edema and hyponatremic encephalopathy which may further complicate the outcome of AFE children (Moritz et al, 2011). It has been documented that acute correction of hyponatremia and hypoosmolality reduces the incidence of seizure and cerebral edema (Liamis et al, 2000; Peng, 2004; Michael et al, 2010). It has been observed that in children who are on parenteral fluids, administration of isotonic saline as the maintenance therapy is the most important prophylactic measure to prevent the development of hyponatremia (Moritz ML et al, 2005) as seen in our study.

In our study serum HCO\(_3\) level on admission ranges from 18 to 26 with mean value of (21.59±1.72) mEq/L and after 48 hours ranges from 20 to 28 with mean value of (23.94±1.82) mEq/L (Table 3). The difference was statistically significant (p=0.000). Shock is a cause of metabolic acidosis. In acute febrile encephalopathy, CNS involvement gives rise to myocardial depression; and also there is circulatory compromise leading to shock and metabolic acidosis. With advancement of fluid bolus, ionotropes and correction of shock, metabolic acidosis gets corrected. Rise of serum bicarbonate in the later part of the disease process was due also to metabolic compensation of respiratory acidosis that results from cerebral depression and hypercapnoea.

### Table 3 Comparison of serum sodium and bicarbonate levels (mEq/L) among different age group, sex and etiology on admission and after 48 hours (n=120)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean serum Na(^+) on admission with SD</th>
<th>Mean serum Na(^+) 48 hrs after admission with SD</th>
<th>Mean serum HCO(_3) on admission with SD</th>
<th>Mean serum HCO(_3) 48 hrs after admission with SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 3 years</td>
<td>132.8±5.84</td>
<td>139.75±2.34</td>
<td>132.22±5.97</td>
<td>139.4±3.14</td>
</tr>
<tr>
<td>3 to 6 years</td>
<td>134.09±4.9</td>
<td>139.28±3.37</td>
<td>133.62±5.97</td>
<td>139±2.95</td>
</tr>
<tr>
<td>6 to 12 years</td>
<td>134.09±4.9</td>
<td>139.28±3.37</td>
<td>133.62±5.97</td>
<td>139±2.95</td>
</tr>
<tr>
<td>Male</td>
<td>132.8±5.84</td>
<td>139.75±2.34</td>
<td>132.22±5.97</td>
<td>139.4±3.14</td>
</tr>
<tr>
<td>Female</td>
<td>134.09±4.9</td>
<td>139.28±3.37</td>
<td>133.62±5.97</td>
<td>139±2.95</td>
</tr>
<tr>
<td>Bacterial</td>
<td>133.07±5.21</td>
<td>139±2.95</td>
<td>133.48±4.94</td>
<td>140.92±2.10</td>
</tr>
<tr>
<td>Viral</td>
<td>133.48±4.94</td>
<td>140.92±2.10</td>
<td>133.07±5.21</td>
<td>139±2.95</td>
</tr>
</tbody>
</table>

However, there was no significant association found in serum sodium or bicarbonate level among different age group, male-female and bacterial and viral etiology on admission as well as 48 hours after admission. While comparing the serum potassium, calcium and chloride level on admission and after 48 hours, no significant change has been found.

With the help of this study, an idea of serum electrolyte changes in acute febrile encephalopathy can be obtained which helps us to formulate the treatment plan, particularly fluid therapy. In future, larger studies can be undertaken involving greater number of cases, so that initial choice of fluid can be specifically recommended and the neurological morbidity resulting from inappropriate fluid therapy in children with AFE can be prevented, thus reducing the burden of the disease sequelae in our community.
Acknowledgements

We are especially thankful to Dr. Asok Kumar Datta, Professors and Head of our Department, Professor (Dr.) Kaustav Nayek and Professor (Dr.) Kanaial Barik for enlightening us with their vast knowledge and their continuous motivation in writing the manuscript.

References


How to cite this article: