HYPERAMMONEMIA IN NEONATES

Pushpendra Kumar Patel 1, Raj Rishav2, N. Niranjan3
1,2Chacha Nehru Bal Chikitsalya, New Delhi, 3Ram Manohar Lohiya, New Delhi

ABSTRACT

Hyperammonemia in critically ill newborn is a life-threatening condition that occur due to block at some point in the normal metabolic pathway caused by a genetic defect of a specific enzyme. Some of these disorders are potentially reversible; others are amenable to long-term therapy if early diagnosis and aggressive management in the neonatal period can prevent the catastrophic neurologic deterioration that accompanies massive hyperammonemia. Early recognition of these conditions is important for proper management.

AIM

The present study was undertaken with objective of detecting hyperammonemia by using basic laboratory investigations and specialized investigations followed by systemic sketch of protocol that is followed at our institute. We also attempt to chart a systemic approach to be followed for the early and exact diagnosis in newborn presenting with hyperammonemia.

KEY WORDS

Hyperammonemia, citrullinemia, IEMs

INTRODUCTION

Inborn errors of metabolism (IEM) are disorders in which there is a block at some point in the normal metabolic pathway caused by a genetic defect of a specific enzyme. A metabolic disorder should be strongly suspected in all term babies with ammonia>200 micromol/L. As treatment differ for different causes of hyperammonemia, it is important to reach the exact diagnosis in these cases as early as possible. Diagnosis is important not only for treatment and prognostication but also for genetic counselling and antenatal diagnosis in subsequent pregnancies. The outcome of treatment of many IEM especially those associated with hyperammonemia is directly related to the rapidity with which problems are detected and appropriate management instituted. In this retrospective analysis we determine the most common metabolic disorders associated with hyperammonemia. We also attempt to chart a systemic approach to be followed for the early and exact diagnosis in newborn presenting with hyperammonemia.

MATERIALS AND METHODS

This was a retrospective study conducted over a three year period in the pediatric Hospital, tertiary care Institute in Kamalaraja hospital Gwalior In the study we analyzed a total of 454 critically ill Newborn from Jan 2012 to 2015. Among these 53 patients presented chief with hyperammonemia. Basic laboratory investigations like blood glucose,ammonia, acid –base status, lactate and urinary ketones was followed by a series of specialized tests such as organic acids and orotic acid in urine, amino acids in plasma and urine and acyl carnitines in blood spots.

In the study we analyzed a total of 454 critically ill Newborn from Jan 2012 to 2015. Among these, 53 patients presented chief with hyperammonemia. Basic laboratory investigations like blood glucose,ammonia, acid –base status, lactate and urinary ketones was estimated followed by a series of specialized tests such as organic acids and orotic acid in urine, amino acids in plasma and urine and acyl carnitines in blood spots. A systemic sketch of the protocol followed at our institute to work-up hyperammonemia case is given below.
RESULTS

In our study out of 454 critically ill newborns 54 (11%) develop hyperammonemia. There were 62.9% male and 37.1% female neonates. Our result showed hyperammonemia to be a primary presenting symptom in various Urea cycle disorders among which citrullinemia constituted the principle differential. Organic aciduria and mitochondrial disorders also represented a major group of disorders.

Our result showed hyperammonemia to be a primary presenting symptom in various Urea cycle disorders among which citrullinemia constituted the principle differential. Organic aciduria and mitochondrial disorders also represented a major group of disorders.

<table>
<thead>
<tr>
<th>Metabolic Disorders</th>
<th>Scattered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrullinemia</td>
<td>N=12</td>
</tr>
<tr>
<td>Arginosuccinic aciduria</td>
<td>N=1</td>
</tr>
<tr>
<td>Mitochondrial disorders</td>
<td>N=7</td>
</tr>
<tr>
<td>MMA</td>
<td>N=10</td>
</tr>
</tbody>
</table>
MMA-methyl melonic aciduria, PA-propionic aciduria IVA- isovaleric aciduria, MSUD-mapple syrup urine disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>3</td>
</tr>
<tr>
<td>IVA</td>
<td>3</td>
</tr>
<tr>
<td>MSUD</td>
<td>2</td>
</tr>
<tr>
<td>LIVER DISORDER</td>
<td>3</td>
</tr>
<tr>
<td>NO IEM</td>
<td>12</td>
</tr>
</tbody>
</table>

**DISCUSSION**

It is essential to measure ammonia early in any sick child in whom a metabolic disorder may be the underlying diagnosis. Blood collected in heparinized or EDTA Vacutainers and kept on ice or analyzed immediately or deproteinized immediately (within 15-20mins) give accurate results. False elevation of ammonia may be seen otherwise. Also mild hyperammonemia is common and levels of 100-200 micromol/L are commonly seen in a sick child.

\[ \text{NH}_3 \text{ concentration} = \text{micromole/L} \times 0.59 \]

The most common cause of severe hyperammonemia in our cohort was found to be Urea cycle Disease (Citrullinaemia type I being the principal differential). These newborns presented with progressive or chronic encephalopathy. Respiratory alkalosis and metabolic alkalosis was also observed in some cases. The prognosis of urea cycle disorder is poor if there is prolonged coma (>36hrs) before specific therapy is started or if the concentration of ammonia remains elevated.

Emergency management of hyperammonemia by means of extra-corporeal detoxification must be promptly initiated after detection of hyperammonemia. Glucose infusion (6-10mg/kg/min) with appropriate electrolytes to reduce catabolism and sodium benzoate/sodium phenyl butyrate for detoxification of ammonia (dose of 250 mgm/kg/day) should be started at the earliest.
CONCLUSION

Hyperammonemia plays an important role in differential diagnosis of many IEMs. The outcome depends upon early and exact diagnosis and proper management and treatment. We therefore insist upon a systematic approach towards diagnosis in Hyperammonemia.

REFERENCES

3. Jalan A. Treatment of IEM in CINB. In inborn Error of Metabolism in critically Ill newborns 2011.