EFFECTIVENESS OF ORAL IRON SUPPLEMENT ON BREATH-HOLDING SPELLS IN CHILDREN

Inayatullah Khan1, Taj Muhammad2, Muhammad Amjad Khan1
1Department of Pediatrics, Lady Reading Hospital Peshawar - Pakistan
2Department of Child Health, Khyber Teaching Hospital Peshawar - Pakistan

ABSTRACT

Objective: To evaluate the effectiveness of iron therapy in breath-holding spells.

Material and Methods: This was a prospective interventional study, which was conducted in the Department of Pediatrics, Lady Reading Hospital, Peshawar, from September 2010 to October 2011. A total of 43 children between the ages of 8 and 54 months, with breath holding spells (BHS) were included. Relevant data was recorded on specifically designed questionnaire. All patients were treated by an oral iron preparation for 12 weeks. Haemoglobin, mean corpuscular volume (MCV) and frequency of BHS were recorded at baseline and every 4 weeks for effectiveness of iron therapy.

Results: Twenty seven (62.8%) patients were male and 16 (37.2%) were female with male to female ratio of 1.6:1. Mean age at presentation was 21 months while age regarding onset of spells ranged between 3 to 28 months with mean age of 9.7 months. The cyanotic type of spell was detected in 34 (79.1%) children and the pallid type in 9 (20.9%) children. A positive family history of Breath-Holding (BH) was identified in 13(30.2%) children. There was a statistically significant fall in the frequency of breath holding spells with 12 weeks of iron therapy. At start of therapy, 25 patients were having more than 10 episodes per week while no patient was having such episodes at 12 weeks of therapy (p-value=0.000).

Conclusion: Iron therapy is effective in the treatment of BHS.

Key Words: Breath Holding, Children, Hemoglobin, Iron.

INTRODUCTION

Breath holding spells (BHS) is a common funny turn in children, well recognized, and is a common problem affecting approximately 5% of healthy children1. The diagnosis is based on a distinctive and stereotyped sequence of clinical events beginning with a provocation, resulting in crying or emotional upset that leads to a noiseless state of expiration accompanied by color change and ultimately loss of consciousness and postural tone2. Cerebral anoxia is the ultimate factor responsible for the loss of consciousness observed in the severe forms of breath- holding spells3. The spells are rare before age 6 months, peak around 2 years of age and abate by 5 years of age4. There are two major types of BHS: the more common cyanotic form and the pallid form. A cyanotic breath-holding spell is always provoked by upsetting or scolding an infant, the pallid spells are much less common than cyanotic breath-holding spells and they are typically initiated by a painful experience, or a sudden startle5. Many authors have proposed the presence of an underlying dysfunctional autonomic nervous system in children with BHS6,7.

BHS has also been associated with iron deficiency anaemia8,9. It has been documented that iron deficiency anemia may lead to adverse effects on oxygen uptake in the lungs and reduce available oxygen to the tissues, including central nervous system tissues10,11. Several studies have reported abatement of breath holding spells with iron treatment, which may suggest a relation between iron deficiency anemia and breath holding spells6,9. The aim of this study was to find out the effectiveness of iron therapy in breath holding spells.

MATERIAL AND METHODS

We enrolled 43 children (27 boys, 16 girls) with BHS diagnosed between October 2010 and September 2011. Their ages at diagnosis ranged from 8-54 months. Diagnosis of BHS was made clinically based on the history given by the mothers and observation of the spells. Spells were defined as the child’s breathing stopping in expiration after a deep inspiration during crying. The spells were classified into cyanotic and pallid type. Patients with hemoglobin level
of less than 5 gm/dl, a history of febrile convulsions or epilepsy, current treatment with anticonvulsant medications, a clinically identified mental disability were excluded from our study. A detailed medical and family history was taken. We recorded type and frequency of the attacks according to the information given by the mother. Hemoglobin concentration and mean corpuscular volume was determined for each patient initially and repeated 4 weekly during follow up. Other parameters of iron deficiency like serum iron, total iron binding capacity, ferritin and transferrin saturation could not be done due to financial restraints. Blood sugar and calcium concentrations were recorded and electro-encephalography (EEG), electrocardiography (ECG) was carried out. All affected children, regardless of their iron status were treated with oral iron (6 mg/kg daily in three divided doses for three months). The number of attacks was recorded at every 4 week interval. At the end of 3 months, response to treatment was evaluated by the change in frequency of BHS. Data was analyzed using SPSS software version 15.

RESULTS

Out of total 43 patients with breath holding spells, a higher percentage (27, 62.8%) were male as compared to female patients(16, 37.2%). Mean age of patients was 21.2 months compared to female patients(16, 37.2%). Mean age of a higher percentage (27, 62.8%) were male as compared to female patients(16, 37.2%). Mean age of female patients was 21.2 months compared to female patients(16, 37.2%). Mean age of female patients was 21.2 months, where as male patients was 21.2 months compared to female patients(16, 37.2%). Mean age of male patients was 21.2 months.

Table 1: Age of patients and frequency of BHS (N=43)

<table>
<thead>
<tr>
<th>Age of patients (in months)</th>
<th>&lt;20</th>
<th>21-40</th>
<th>&gt;40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of BHS</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>&lt;5/week</td>
<td>10(41.7)</td>
<td>2(12.5)</td>
<td>1(33.3)</td>
</tr>
<tr>
<td>5-10/week</td>
<td>4(16.7)</td>
<td>0(0)</td>
<td>1(33.3)</td>
</tr>
<tr>
<td>&gt;10/week</td>
<td>10(41.7)</td>
<td>14(87.5)</td>
<td>1(33.3)</td>
</tr>
<tr>
<td>Total</td>
<td>24(100)</td>
<td>16(100)</td>
<td>3(100)</td>
</tr>
</tbody>
</table>

P-value=0.03

Table 2: Comparison of Hb

<table>
<thead>
<tr>
<th>Hb</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9.8698</td>
<td>1.51572</td>
<td>-1.46630 to -0.55766</td>
<td>0.000</td>
</tr>
<tr>
<td>At 4 weeks</td>
<td>10.8767</td>
<td>2.09817</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>9.8698</td>
<td>1.51572</td>
<td>-1.90799 to -1.49626</td>
<td>0.000</td>
</tr>
<tr>
<td>At 8 weeks</td>
<td>11.5714</td>
<td>1.16136</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>9.8698</td>
<td>1.51572</td>
<td>-2.84807 to -2.24960</td>
<td>0.000</td>
</tr>
<tr>
<td>At 12 weeks</td>
<td>12.4186</td>
<td>0.96047</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Comparison of MCV

<table>
<thead>
<tr>
<th>MCV</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>66.38</td>
<td>±5.8</td>
</tr>
<tr>
<td>At 4 weeks</td>
<td>69.65</td>
<td>±4.9</td>
</tr>
<tr>
<td>At 8 weeks</td>
<td>71.6</td>
<td>±4.2</td>
</tr>
<tr>
<td>At 12 weeks</td>
<td>73.6</td>
<td>±3.4</td>
</tr>
</tbody>
</table>

Table 4: Comparison of frequency of BHS at start and 12 weeks of therapy (N=43)

<table>
<thead>
<tr>
<th>Frequency of BHS</th>
<th>&lt;5/week</th>
<th>5-10/week</th>
<th>&gt;10/week</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>N(%)</td>
<td>13(30.2)</td>
<td>5(11.6)</td>
<td>25(58.1)</td>
</tr>
<tr>
<td>Frequency at 12 weeks</td>
<td>N(%)</td>
<td>40(93.0)</td>
<td>3(7.0)</td>
<td>0(0)</td>
</tr>
</tbody>
</table>

P-value=0.000

DISCUSSION

The exact role of iron in BHS is not known, however abnormalities in catecholamine metabolism
and various neurotransmitters may explain association of BHS with iron deficiency anemia. The correction of spells with iron therapy may be related to the functional restoration of these neurotransmitters. Besides this, Mocan et al hypothesized that the clinical and hematological picture of BHS may be related to the interactions of cerebral erythropoietin, nitric oxide and interleukin 1. They postulated that increased brain erythropoietin production has a protective effect during BHS, but if this does not compensate for the severity of anoxic spells, then seizures may develop. Breath-holding spells have been reported to occur in approximately 0.1% to 4.6% of well children. The presence of an underlying dysfunctional autonomic nervous system in children with BHS has been proposed by some workers whereas others have reported their association with iron deficiency anemia. Holowach et al demonstrated that children with severe BHS had significantly lower hemoglobin values than children in a control group. They speculated that children with anemia have decreased cerebral oxygen tension at baseline making these children more susceptible to the chain of events leading to loss of consciousness during BHS. Bhatia et al also observed that children with BHS had significantly lower hemoglobin and serum iron values, a lower percentage of transferrin saturation, and higher total iron binding capacity (TIBC) than those of controls. Several other workers have studied the role of iron in resolution of BHS and reported significant benefit from iron treatment. Breath-holding spells are more common in males, the male to female ratio being around 1.3:1 as reported by many studies. In our study the ratio was found to be about 1.6:1. However in a study conducted in the Connecticut children’s hospital, no significant difference between genders was noted.

The onset age of BHS has been identified within the first 18 months of life in most studies addressing this issue. Bridge reported 66 of 83 patients having had their onset by age 18 months of age and Laxdal et al reported 87% of 150 patients having had their onset before age 18 months. In our study, age of onset was found to be under 18 months in 52.38% of patients. This difference may be due to poor socioeconomic conditions, lack of education, awareness and health facilities in our setup.

Several authors have identified a familial tendency for BHS spells. A range of 20% to 35% of all patients will have an identified family member who has suffered BHS at some time during their childhood. In our study positive family history was found to be 30.2% which is consistent with that reported by previous authors. Researchers believe that in areas with increased prevalence of iron deficiency, these spells are observed regardless of impact of family history.

There is a genetic basis identifiable in significant proportions of patients. An autosomal dominant trait with reduced penetrance has been demonstrated. In our study consanguinity was seen in 19 (44.2%) patients. Daoud and colleagues in a prospective study of iron therapy in children with BHS found that nearly 70% of their patients were products of consanguineous marriages. Although direct genetic transmission does not explain the occurrence of BHS in all children, a substantial proportion of cases may have a genetic predisposition.

CONCLUSION

We conclude that hypochromic anemia is often a part of clinical presentation of breath holding attacks in children, and iron therapy can stop these spells. Therefore, all children with BHS require investigations for iron deficiency anemia and treatment with iron where appropriate.

REFERENCES


ONLINE SUBMISSION OF MANUSCRIPT

It is mandatory to submit the manuscripts at the following website of JMS. It is quick, convenient, cheap, requirement of HEC and paperless.

Website: www.jmedsci.com

The intending writers are expected to first register themselves and then attach/submit the manuscript. If processing fee is not submitted before, it should be deposited with Managing Editor in cash or in the form of a Bank draft in the name of Editor JMS. Please follow the format and check list of the Journal. Author agreement can be easily downloaded from our website. A duly signed author agreement must accompany initial submission of the manuscript.