Assessment of the Effective Piracetam Oral Iron for Children with Breath Holding Spell in Tertiary Care Hospitals

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ABSTRACT
BHS (breath holding spell) are very successive & significant demonstrative difficulties in pediatric medicine. The obviously terrifying functions are generally basic in youngsters. Yet, at times BHS (breath holding spell) can be extremely upsetting by the guardians & the strategies on your own may not be adequate. Strong enhancements and piracetam are the two distinctive pharmacologic techniques those were utilized for giving BHS in kids. That go through such kind of study is driven in our assessment site and it is speculated to give a couple of results to investigate two healing schedules that are typically suggested for BHS in kids. An aggregate of 70 BHS (breath holding spell) cases are chosen into the examination of the 35 patients (A) stayed specified iron alone and 35 patients (B) that gives piracetam and oral iron. The examination gives the data to differentiate the ampleness of using piracetam and oral iron versus iron alone in kids with BHS (breath holding spell) in the outpatient division of PVS Hospital (P) Ltd, Calicut. The assessment contemplated that piracetam has all the reserves of being ensured and reasonable medicine for BHS. Piracetam despite oral iron in adolescents with BHS can reduce the repeat and earnestness of attacks than using iron alone, henceforth diminishing the difficulty of the agitated watchmen and misery by children.

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INTRODUCTION
BHS (breath holding spell) are the event of wordy apnea in youngsters, potentially connected with a loss of cognizance and vagaries in postural tone. These are brief periods when little youngsters quit breathing as long as one moment (Bernstein and Shelov, 2003; Breukels et al., 2002). On uncommon events, a seizure may be seen following the youngster passed out. These are not intentional and are caused from involuntary reflux and the child has no ability to control them. On the basis of severity, BHS (breath holding spell) can be simple or severe. In simple BHS, the event resolves with no associated syncope or postural change, whereas in severe BHS, there is a subsequent loss of awareness and changes in postural tone do happen. These episodes are terrifying to parents subsequent in nervousness and recurrent appointments to health care amenities. Breath holding incidents are infrequently real-
ized under six months of age. Peak occurrence of episodes occurs at 2-3 years, and they develop rare by 5-6 years. Some children have severe spells. Children can have BHS (breath holding spell) when they are responding to fear, pain, traumatic event and being startled or confronted. They are more common in children with genetic conditions such as rett syndrome, iron deficiency anemia and family history of BHS (Rao, 2015). A breath holding spell is terrifying to parents and to those experiencing it for the first time. Parents of children with recurrent episodes will anticipate future episodes and are able to react calmly. Blowing air forcefully on the face of the child will usually terminate the episode early on, but not for all children. Differentiating the episode of BHS from seizure or from an apparent life threatening event might be difficult. The clinical description by the family is an important and detailed family history, a detailed description of the spell and account of an initial cry with lack of postictal phase of lethargy are all factors that help in the diagnosis (Goldman, 2015).

Figure 1: Types of attacks (Group A).

Drugs are not usually designated in BHS. In simple bags by connected bradycardia or systole or in patients by numerous daily episodes, a 0.01 mg/kg/24hr in divided doses by a maximum daily dose of 0.4mg of oral atropine three times daily is effective in preventing BHS. An iron supplement is significant in reducing the number of spells, Piracetam, a cyclic imitative of GABA, is also extremely effective in the controller of BHS, oral theophylline, transdermal scopolamine and pacemakers also have been used (Allsman, 2008). Piracetam also known as 'Smart drug' is a plagiaristic form of Gama Amino Butyric Acid. Piracetam collaborates with the polar heads in the phospholipids film and the subsequent portable medication lipid edifices are thought to revamp the lipids and impact layer capacity and smoothness. Through reestablished film ease, piracetam advances Neuro transmission, for example, glutamatergic and cholinergic frameworks, upgrades neuropilancy and intervenes neurodefensive and anticonvulsant impacts at the neuronal level. Iron is modest, simple to control and has no genuine results. It might be critical in the treatment of BHS (breath holding spell) since iron lack frailty might be the fundamental basic imperfection. Anyway, iron insufficiency isn’t the main factor answerable for BHS on the grounds that not all youngsters with BHS were iron lacking at standard (Winnicka et al., 2005).

Figure 2: Types of attacks (Group B).

BHS include the part of iron in catecholamine digestion and the working of compounds and synapses in the focal sensory system. The adjustment of spells during treatment with iron might be identified with the useful reclamation of these synapses. Standard dose of iron in pediatrics: 3-6 mg/kg/day.

Figure 3: Average attacks/month throughout the study period in the two groups.

MATERIALS AND METHODS

The point of the study is to compare the efficiency of utilizing piracetam and oral iron and iron treatment alone in kids with BHS. The examination was led in the pediatric outpatient unit of PVS Hospital (P) Ltd; a 350 had relations with a multi-strength clinic in Calicut, Kerala. A planned observational investigation configuration was followed for the examination (Rathore et al., 2013). The study was done in six months from November 2017 to April 2018 using the medical records during this duration. Each patient was studied for a span of three months. Apart from the baseline 15th day, 30th day, 60th and 90th day were the follow-ups of the study. Children of the age group between 6 months to 6 years with a
Table 1: Comparison between the two studied groups according to demographic data.

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Group A (n = 35) (N%)</th>
<th>Group B (n = 35) (N%)</th>
<th>Test of significance</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>19 (54.29)</td>
<td>28 (80)</td>
<td>X²= 5.24</td>
<td>0.0221(s)</td>
</tr>
<tr>
<td>Girls</td>
<td>16 (45.71)</td>
<td>07 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (Years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>20 (57.14)</td>
<td>28 (80)</td>
<td>X²=5.905</td>
<td>0.052(ns)</td>
</tr>
<tr>
<td>&gt;1-2</td>
<td>04 (11.43)</td>
<td>4 (11.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2</td>
<td>11 (31.43)</td>
<td>3 (8.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age of onset of attacks (Years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>22 (62.86)</td>
<td>30 (85.72)</td>
<td>X²=4.82</td>
<td>0.089(ns)</td>
</tr>
<tr>
<td>&gt;1-2</td>
<td>07 (20)</td>
<td>03 (8.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2</td>
<td>06 (17.14)</td>
<td>02 (5.71)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison between the frequency of attacks (/month) in both groups before and after treatment.

<table>
<thead>
<tr>
<th>Frequency of attacks (/month)</th>
<th>Group A (n=10)</th>
<th>Group B (n=10)</th>
<th>Test of significance</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min.-Max.</td>
<td>2-16</td>
<td>2-16</td>
<td>Z=5.391</td>
<td>&lt;0.00001(s)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>7.46±3.69</td>
<td>8.03±4.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min.-Max.</td>
<td>0-8</td>
<td>0-3</td>
<td>Z=6.971</td>
<td>&lt;0.00001(s)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>3±1.99</td>
<td>0.68±0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

breath holding spell (BHS) and children with normal psychomotor development are included for study (Abbaskhanian et al., 2012). Children diagnosed with epilepsy and children who are receiving drugs other than piracetam and oral iron for the treatment of BHS are excluded. Prescriptions and medical cards of the study cases collected from the Pediatric Department (Winblad, 2006).

Systematically prepared data collection form. Study Drugs Syrup Ferrous sulphate 3-6 mg/kg/day (Brands: Hems-PD, Feris) and Syrup Piracetam 40 mg/kg/day (syrup) (Brands: Pirapil, Neuromin M) are used. The study Procedure was a prospective observational study on children with BHS (breath holding spell) referred to Pediatric Department, PVS Hospital (P) Ltd, Calicut in the age range of 6 months to 6 years from November 2017 to April 2018. Physical Examinations of the patients with BHS were performed (Mocan, 1999).

Diagnosis of BHS was based on the history that was revealed by the parents. This may arise by crying to the point of noiselessness and accompanying change of color (cyanotic or pallid) and ultimately a loss of consciousness with associated alterations in body tone. Children with the diagnosis of epilepsy or/and those who are receiving drugs other than piracetam and oral iron for BHS (breath holding spell) were excluded from the study. The children among six months and six years of age by a diagnosis of BHS were divided into Group A and Group B. In group A, children were given with iron therapy alone at a dose of 3-6mg/kg/day and whereas in group B they were given with iron therapy at the same dose along with piracetam at a dose of 40 mg/kg/day. Follow up assessment of the cases were done after 2 weeks of performance with more than half of them presenting above the age of less than or equal to 1 year in both the groups. These results are consistent with the findings of (Ghareib et al., 2017; Mocan, 1999; Abbaskhanian et al., 2012).

The age of onset of BHS in most of the studies is in the first 12 months of life. The event of BHS is uncommon in the initial a half year of life and faulty in the neonatal period as seen in (Donma, 1998).
Table 3: Response to treatments.

<table>
<thead>
<tr>
<th>Response Group</th>
<th>Two weeks</th>
<th>1 month</th>
<th>2 months</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C(%)</td>
<td>P(%)</td>
<td>N(%)</td>
<td>C(%)</td>
</tr>
<tr>
<td>Group A (Iron)</td>
<td>A</td>
<td>6</td>
<td>54</td>
<td>40</td>
</tr>
<tr>
<td>Group B (Iron+ Piracetam)</td>
<td>B</td>
<td>20</td>
<td>77</td>
<td>3</td>
</tr>
</tbody>
</table>

C - Complete response, P - Partial response, N - No response.

Similar results were found in our study that most of the cases in both groups had their age of onset of attacks in less than or equal to one year. Among the 70 patients, the types of BHS (breath holding spell) were studied. The commonly seen types are cyanotic, pallid and mixed.

1. Cyanotic spells are produced by a change in the child’s usual breathing pattern usually in reply to feeling angry or frustrated.

2. Pallid spell is produced by a slowing of the child’s heart rate, usually in response to pain.

3. Mixed type is a rare condition where both cyanotic and pallid spell occurs in the same child.

In our study, in group A, 19 patients (54%) had the cyanotic type; 15 (43%) and 1 (3%) had the pallid and mixed type respectively. In group B, 28 patients (80%) had the cyanotic type, 6 (17%) and 1 (3%) had the pallid and mixed type respectively. So in general, our study had 47 patients (67%) was of cyanotic type; 21 (30%) and 2 (3%) had the pallid and mixed type respectively.

In our study, the majority of patients presented with the cyanotic type of BHS (breath holding spell) followed by the pallid and mixed type. These results were consistent with the findings of (Winicka et al., 2005) (88.5% cyanotic, 8.5% pallid and 3% mixed type), Shabbir Hussain et al., (66.7% cyanotic, 26.7% pallid and 6.7% mixed type), Inayatullah Khan et al., (79.1% cyanotic and 20.9% pallid), Mostafa M Abosdera et al., (71.88% cyanotic and 28.12% pallid type) and Bahaa Abd Al Hussein Ahmed et al., (47.8% cyanotic, 34.7% pallid and 17.3% mixed type). Whereas in the study conducted by (Azab et al., 2015) they had a majority of pallid spells (35.7% pallid and 31.3% cyanotic spells) which was different from our study. These differences may be attributed to behavioral and social factors of the children like anger, frustration and response to pain. The improvement in the frequency of attacks in the two groups before and after the treatment was studied in Figure 1. The frequency of spells did not vary widely before treatment. In both the group’s A and B, it was found that the frequency of attacks were 2-16 per month with a median frequency of 8 episodes of BHS (breath holding spell) per month. In our study, before treatment group A had a mean episode of 7.46 and a standard deviation of 3.69 whereas, group B had a mean episode of 8.03 and a standard deviation of 4.01 in Table 1.

RESULTS AND DISCUSSION

After treatment, the mean episode of group A was reduced to 3 with a standard deviation of 1.99 and in group B mean episodes was reduced to 0.68 with standard deviation of 0.82. The frequency of attacks after treatment with iron therapy in group A was reduced to range from a minimum of zero attack to a maximum of eight attacks with a median frequency of 3 attacks per month in Figure 3. Two weeks after treatment in Group A, response to treatment was 6% complete response, 54% partial response and 40% no response. In group B, response to treatment was 20% complete response, 77% partial response and 3% no response. One month after treatment in group A, response to treatment was 10% complete response, 77% partial response and in 13% there was no response. In group B, response to treatment was 24% complete response and 76% partial response in Table 2.

Two months after treatment in Group A, response to treatment was 91% partial response and 9% there was no response. In group B, response to treatment was 63% complete response and 37% partial response. Three months after treatment in group A, response to treatment was 100% partial response. In group B, response to treatment was 0% (complete response was shown by all the patients within a maximum of 2 months duration). In our study, the majority of children 63% showed a complete response when treated with both iron and piracetam by the end of two months in Table 3.
study by (Winnicka et al., 2005) there was a majority of 68.6% children with a complete response when given with iron and piracetam, which was in agreement with our study. Similarly, in a study by Abbaskhanian et al. majority of the children (77%) given with iron and piracetam had a complete response.

In our study, the average attacks in two weeks and monthly for a span of three months in both the groups, group A (Iron) and group B (Iron and Piracetam) was compared. It was found that though the average attacks before treatment in group B were found to be more than compared to group A, in the further treatment, there was a decline in the average number of attacks in group B. From Figure 2, it is also seen that in group B the number of attacks after three months was found to be zero. In our study, it was found that there was a decrease in the quantity of assaults in the wake of treating with iron and piracetam (bunch B) contrasted with iron alone (bunch A). These results were consistent with the findings of Ali Abbaskhanian et. al. their study also stated that there is a decline in the number of attacks in the iron and piracetam group following the treatment.

CONCLUSIONS

The examination gives the information to contrast the viability of utilizing piracetam and oral iron versus iron alone in kids with BHS in the patient branch of PVS Hospital (P) Ltd, Calicut. An aggregate of 70 patients with breath-holding spell cases was contemplated. Of these 70 patients, 35 patients were remembered for bunch A, given with iron alone and 35 in bunch B given iron alongside piracetam. It was observed in our study that the number of boys was higher than the number of girls in both the groups and the patients ages ranged from 6 months to 6 years at the time of presentation with more than half of them presenting above the age of less than or equal to 1 year in both the groups. It was also observed that most of the cases in both groups had their age of onset of attacks in less than or equal to one year. Majority of the patients presented with the cyanotic type of BHS (breath-holding spell) followed by the pallid and mixed type. The frequency of attacks before treatment was similar in both the groups, whereas after the treatment, the frequency was decreased in patients prescribed with iron and piracetam than when iron was given alone. The response to treatment in the 70 patients was studied and observed that the majority of complete response was seen in patients given with iron and piracetam. When average attacks/month was studied, it was observed that there was a decline in the attacks when given with iron and piracetam and the average attacks were reduced to zero by the third month. But the decline in the patients given with iron alone was not profound. In this manner, the examination presumed that piracetam seems, by all accounts, to be sheltered and compelling medication for BHS (breath-holding spell). Piracetam notwithstanding oral iron in youngsters with BHS can diminish the recurrence and seriousness of assaults than utilizing steely on your own, subsequently lessening the misery of the upset guardians and enduring of their kids.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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