



A STUDY OF THE ROLE OF DIAZEPAM AND PIRACETAM IN THE MANAGEMENT OF BREATH-HOLDING SPELLS IN CHILDREN

Paediatrics

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ABSTRACT

Breath holding spells are dramatic, involuntary episodes that occur in otherwise healthy children. The role of diazepam or piracetam in the sub group of children with severe breath holding spells has to be studied. There was a significant reduction in the frequency of spells in each group following treatment, but there was no statistically significant difference between the groups. The cure rate following treatment was also comparable among the three groups. Neither diazepam nor piracetam was found to produce a statistically significant maximum spell-free interval more than the control group. The mean haemoglobin levels, pre- and post- treatment were comparable in all three groups. From this study, we conclude that the role of diazepam and piracetam was not found to be significant as compared to the control group, though there are reports to the contrary.

KEYWORDS

Breath holding spells, Diazepam, Piracetam.

INTRODUCTION

Breath holding spells are dramatic, involuntary episodes that occur in otherwise healthy children.

Cyanotic Attacks-

This is the most common type of BHS. Anger, frustration and painful stimuli such as a fall are common triggers. After such a stimulus, the child cries, stops breathing in expiration, and becomes cyanosed, limp and unconscious.

Pallid Attacks- These are termed 'reflex anoxic seizures' by Stephenson (1978).

Aetiopathogenesis-

The aetiology of BHS is not yet clear. Some workers have related its origin to the child's temperament, parental attitudes, iron deficiency, or constitutional hyperventilation.

Mechanisms Postulated-

Emotional factors are certainly involved. The attacks are most frequent during normal developmental phase of negativism. Many of the affected children are described by their parents as being demanding and rather stubborn children. Hereditary and familial factors are also important. Previous observations have noted that perhaps 20–30 % of children with benign BHS have family members who are affected during their childhood. In addition, data from detailed analysis suggest an autosomal dominant mode of inheritance in some cases of severe BHS. Vulliamy (1956) suggested that the basic mechanism was an acute reduction in cerebral blood flow produced by a sharp rise in intrathoracic pressure or valsalva like maneuver caused by breath holding in expiratory phase. The initial hyperventilation caused hypocapnia and this caused cerebral vasoconstriction.

Study Justification-

Breath holding spells are often benign, but fairly common disorders affecting children. Various underlying autonomic nervous system abnormalities and brain stem dysfunction have been implicated recently in the pathogenesis of these spells. Rarely, life-threatening events such as status epilepticus and prolonged bradycardia or asystole may occur. But till date, research into available drug therapy has remained inadequate. Various drugs such as diazepam, sodium valproate, carbamazepine and phenobarbitone have been used based on sporadic reports of usefulness or for their anticonvulsant effect. Iron therapy has been found to reduce the frequency of spells in anaemic children with BHS. Piracetam is a new drug on the horizon. Few studies have been conducted in India. This study has been undertaken to study the clinical profile of BHS in the children attending our outpatient department, and to assess the role of diazepam and

piracetam in the management of BHS. This study has been undertaken after obtaining the approval of the institutional review board in our hospital.

MATERIAL AND METHODS

It is a Randomized controlled trial conducted on Children attending the OPD or the Child Guidance Clinic and diagnosed as breath holding spell by history.

Inclusion criteria-

Children aged 1 month to 5 years with history suggestive of breath holding spell as follows:-Antecedent provocative event (anger/frustration/pain/fear) crying, progressively increasing in intensity @ point of noiselessness @ colour change (cyanosis/pallor) @ resolution of features or loss of consciousness with or without seizure-like activity followed by resolution.

Exclusion criteria-

Underlying cardiac disease, Underlying CNS pathology, Primary lung pathology.

Sample size-

Assuming an improvement of at least 40% in the study groups as compared to the control group, and the power of the study to be 85%, sample size was calculated to be 30 per group, with a total of 90 cases. 90 children diagnosed to have breath holding spells by history and satisfying the study criteria were included in the study after obtaining written parental consent. A structured interview was conducted at the time of enrolment into the study (Proforma included in the Annexure). A complete physical examination was done and cardiac, neurological and respiratory diseases excluded clinically. EEG was taken to rule out true seizures. If the EEG was abnormal, the child was excluded from the study. The children were then randomly allotted into one of the three groups- A, B or C using computer-generated random numbers. A baseline haemoglobin estimation was done to look for the presence of anemia in all children. Parental counselling was done regarding BHS, its treatment and prognosis. They were also given a patient information form containing information about breath holding spells. They were also advised to maintain a spell diary everyday for information regarding number of spells per day.

Statistical Methods For Analysis Of Results- All statistics were analysed using SPSS 10 and EPI INFO software.

RESULTS

Total number of children with breath holding spells initially screened was 98. Out of this, 8 children (8.16%) were found to have abnormal

EEG and hence were excluded from the study. 90 children were enrolled in the study after obtaining written parental consent. An information brochure regarding BHS was also handed over to the parents. Out of the 90 children studied, 50% had onset of breath holding spells before one year of age, with 7 out of 90 children (7.7%) having onset before 6 months of age. The overall male: female ratio was found to be 1.6:1, indicating a slight male preponderance. Cyanotic breath holding spells were seen in 68.9% of children and is the most common type of BHS. Pallid spells were seen in 21.1% of children, while both types of spells were seen in 10.0% of children. Maximum number of children (47.8%) had less than one episode per week. 34.4% of the children had between 1 to 3 episodes per week. About 6.7% of children had more than 10 episodes per week. 83.3% of children had simple breath holding spells without seizure activity. 16.7% of children developed hypoxic seizures at the end of the episode. None of the children in the study had life-threatening events such as status epilepticus or cardiac arrest requiring emergency medical intervention. Anger (57.8%) was the most common factor precipitating the occurrence of breath holding spells, followed by pain (56.7%). Fear was the cause in 30% of children. More than one factor was implicated in 40% of children. Behaviour disturbances were noted in 73 out of 90 children (81%). The most common behaviour disturbance in these children was temper tantrums (37.8%), followed by head banging (34.4%). Thumb sucking was noted in 31.1%, pica in 25.6%, incessant cry in 15.6% and nail biting in 3.3% of the children. More than one behaviour disturbance was noted in 43.3% of the children. Prior to treatment, the mean frequency of spells per week in Group A was 3.29. The mean frequency of spells in Group B was 3.17. The mean frequency of spells in Group C was 3.83. The three groups were comparable with respect to baseline characteristics. On completion of treatment, the mean frequency was 1.80 spells per week in Group A, 1.86 in Group B and 2.27 in Group C. The mean frequency of spells was lower in Groups A and B, but this difference was not statistically significant. Following treatment for three months, the mean frequency of spells decreased by 45% in Group A, 41% in Group B and 41% in Group C. Though the reduction was more in the Diazepam group, it was not found to be statistically significant ($p=0.88$). At the end of one year of follow up, the mean frequency of spells per week was 0.13 in Group A, 0.07 in Group B and 0.13 in Group C. The difference between the groups was not statistically significant. The number of children who could be considered cured as evidenced by reduction in spell frequency by at least 50% at the end of treatment was 76.7% in Group A, 93.3% in Group B and 90% in Group C. The difference was not statistically significant ($P=0.55$). The mean maximum spell-free interval was found to be 8.70 months in Group A, 10.31 months in Group B and 10.33 months in Group C. This was analysed by one-way ANOVA and it was found that there was no statistically significant difference between the three groups. During treatment period no adverse drug reactions or problems were complained of. During follow up, one child in Group C was admitted for bronchopneumonia and was discharged after 7 days following clinical improvement.

DISCUSSION

Out of 90 children with breath holding spells studied, the median age of onset was 12.46 months (range 4 months to 4 years). In the studies by Bhatia M. S. et al., Mocan H et al., and Anil B. G et al. the mean age of onset was 9.6 months, 17 months and 14.2 months respectively. In our study, 45 children (50%) had onset of BHS before one year of age, with 7 children (7.7%) experiencing their first spell before six months of age. Bridge et al. and Lombroso and Lerman² had reported the age of onset from the neonatal period to about four years. In our study, out of 90 children, there was a male preponderance with a male: female ratio of 1.6:1. This is similar to earlier studies by Bhatia M. S. et al. (M:F=3:1), Mocan H et al. (M:F=1.6:1) and Anil B. G. et al. (3:2). But DiMario has reported equal incidence of BHS in both sexes in his study. 68.9% of children in our study had cyanotic type of BHS, 21.1% had pallid type while 10.0% had mixed type of spells. In the study by Bhatia M. S. et al., 96% had cyanotic type while 4% had pallid type of BHS. Lombroso and Lerman, Livingston, Bhatia M. S. et al. and Anil B. G. et al have reported tonic-clonic convulsions in 46%, 49%, 84% and 82% respectively. In our study, convulsions were observed in 16.7% of the children. None of them had life-threatening events like status epilepticus or cardiac arrest. 47.8% of the children in our study had less than 1 spell per week, followed by 34.4% of children with 1-3 spells per week. 6.7% of children had more than 10 spells per week.

CONCLUSION

Half the children had onset of spells before one year of age. There was a

male preponderance in the occurrence of spells noted in our study. 68% of spells were cyanotic type. Tonic-clonic movements were present in 16% of children with BHS in our study. 47% of children had frequency of spells less than one per week and 6.7% of children had more than 10 spells per week. Anger and pain were the most common triggering factors in 57.8% and 56.7% of children, respectively. Behaviour abnormalities were reported in 81% of the children, with temper tantrums being the most common (37.8%). A positive family history of BHS was present in 6.7% of the children only. There was a significant reduction in the frequency of spells in each group following treatment, but there was no statistically significant difference between the groups. The cure rate following treatment was also comparable among the three groups. Neither diazepam nor piracetam was found to produce a statistically significant maximum spell-free interval more than the control group. The mean haemoglobin levels, pre- and post-treatment were comparable in all three groups. From this study, we conclude that the role of diazepam and piracetam was not found to be significant as compared to the control group, though there are reports to the contrary. The role of diazepam or piracetam in the sub group of children with severe breath holding spells has to be studied.

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