IRON DEFICIENCY ANEMIA AS A CAUSE OF BREATH HOLDING SPELLS

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ABSTRACT

Objective: *To assess the efficiency of iron therapy in reducing the frequency of breath holding spells.*

Material and Methods: *This was a prospective, interventional study conducted in the department of Pediatrics, Hayatabad Medical Complex, Peshawar. A total of 50 patients between the ages of 6 months and 5 years with breath holding spells and mild to moderate iron deficiency anemia were studied. After giving them iron therapy for 8 weeks, they were assessed for the improvement in their anemia and its impact on the frequency of breath holding spells.*

Results: *Fifty children with iron deficiency anemia and breath holding spells were studied prospectively. Thirty-one (62%) cases were males and 19 (38%) females. The mean age was 27 months (SD ±12.6). The mean baseline hemoglobin was 9.79gm/dl. After 4 weeks of iron therapy it was 10.54gm/dl and after 8 weeks it was 11.23gm/dl. There was a statistically significant rise in the hemoglobin level with 8 weeks of iron therapy ($p<0.001$). This rise in the hemoglobin level was associated with a statistically significant fall in the frequency of breath holding spells with 8 weeks of iron therapy ($p<0.001$).*

Conclusion: *It appears that treating iron deficiency anemia is effective in reducing the frequency of breath holding spells.*

Key words: *Breath Holding Spells, Hemoglobin, Iron Deficiency Anemia.*

INTRODUCTION

Breath holding spells are a well recognized, common problem affecting children between the ages of 6 months and 5 years[1]. Breath holding spells are an involuntary, reflex, non-epileptic paroxysmal disorder. They are characterized by the following sequence of symptoms:

1. A precipitating factor such as slight injury or emotional upset;
2. Crying of short duration;
3. A respiratory gasp and breath holding in respiration;
4. Cyanosis and/or pallor;
5. Opisthotonic rigidity and loss of consciousness; and
6. Flaccidity or convulsing movements.

Three types of breath holding spells are described: cyanotic, pallid and mixed. Pallid breath holding spell is precipitated by trauma rather than anger, and is more often associated with cardiac asystole and EEG slowing than in cyanotic breath holding spells. Generalized epileptic seizures may be triggered by breath holding spells [2, 3]. Parenting a child who exhibits breath holding spells is more stressful than parenting a healthy child [4]. The presence of an underlying dysfunctional autonomic nervous system in children with breath holding spells has been proposed [5,6]. Breath holding spells have also been associated with iron deficiency anemia [7-,11]. 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 tissues[12,13]. Several studies have reported abatement of breath holding spells with iron treatment, which may suggest a relation between iron deficiency anemia and breath holding spells[8,14,15].

The purpose of this study was to find out the effect of iron therapy on the frequency of breath holding spells in iron deficient children.

MATERIAL AND METHODS

We studied 50 children with breath holding spells and concomitant iron deficiency anemia between March 2003 and March 2004.Age range was 6

months to 60 months (5 years).Proper history was taken from parents. Spells were defined as the child's breathing stopped in expiration after a deep inspiration during crying. Hemoglobin concentration and mean corpuscular volume was determined. Those falling in the range of mild (hemoglobin 8-12 gm/dl and mean corpuscular volume 60-75fl) to moderate iron deficiency anemia (hemoglobin 5-8gm/dl and mean corpuscular volume 50-59fl) were enrolled after taking consent from parents. Other parameters of iron deficiency anemia like serum iron, total iron binding capacity and transferrine saturation could not be done due to financial restraints. Patients with a hemoglobin level of less than 5gm/dl, a history of febrile convulsions or epilepsy, current treatment with anticonvulsants and medications, other causes of microcytic hypochromic anemia like thalassemia, a clinically identified mental disability or severe malnutrition were excluded from our study.

Parents were advised to note the frequency of the breath holding spells per week (up to 4, 5-10, more than 10).Children were started on elemental iron 6mg/kg/day orally for a period of 8 weeks. Parents ware advised to bring their children for follow up to the outpatient department at 4 and 8 weeks after the start of iron therapy. Frequency of breath holding spells, hemoglobin level and mean corpuscular volume was recorded at both follow ups.

Student-t test was used for the statistical evaluation.

RESULTS

Out of 50 children, 31 (62%) were males and 19 (38%) females. Mean age was 27 months (SD±12.6) (Table-1).

AGE WISE DISTRIBUTION

Age of patients in months	Frequency	Percentage
6-11 months	4	8%
12-24 months	26	52%
25-60 months	20	40%

Table 1

The mean baseline hemoglobin was 9.79gm/dl. At 4 weeks follow up it was 10.54gm/dl and at 8 weeks it was 11.23gm/dl. The difference in the baseline hemoglobin level and at 8 weeks follow up is significant (Table-2). In other words, the improvement in the hemoglobin level with 8 weeks of iron therapy is statistically significant with a p value of <0.001.

There was a significant fall in the frequency of breath holding spells from the start to the end of the study Table-3.

DISCUSSION

Breath holding spells can be dramatic and recurrent. Most pediatricians have offered parents the reassurance that these alarming episodes are not life threatening and are likely to resolve spontaneously with time. An association between iron deficiency anemia and breath holding spells has been recognized in the past. In 1963 Holwach and Thurston demonstrated a low hemoglobin values in 102 breath holding patients at the St. Louis Children's Hospital [16]. Bhatia *et al* analyzed 50 cases of breath holding spells [14]. Mean hemoglobin, serum iron and percentage transferrin saturation was significantly lower and total iron binding capacity was higher in the study group as compared to the controls (p value < 0.001). There was a significant decrease in severity and frequency of spells with oral iron therapy. Colina

HEMOGLOBIN

	5-7.9gm/dl	8-10gm/dl	>10gm/dl
Baseline	2 (4%)	27 (54%)	21 (42%)
At 4 weeks	0	11 (22%)	39 (78%)
At 8 weeks	0	2 (4%)	48 (96%)

p value < 0.001

Table 2

FREQUENCY OF BREATH HOLDING SPELLS NUMBER OF SPELLS/WEEK

	<5	5-10	>10
Baseline	3 (6%)	38 (76%)	9 (18%)
At 4 weeks	17 (34%)	26 (52%)	7 (14%)
At 8 weeks	42 (84%)	8 (16%)	0

p value < 0.001

Table 3

and Abelson reported the abatement of breath holding spells in two children after treatment of their anemia [8]. Daud *et al* showed that children treated with iron had significant reduction in the frequency of breath holding spells (88%) compared with the frequency (6%) in the placebo group [15]. The treated group showed a significant improvement of a number of blood indices compared with the placebo group. Baseline mean levels of hemoglobin and total iron binding capacity were predictive of a favorable response to iron treatment.

Hilal Mocan *et al* evaluated the prognosis of breath holding spells after iron treatment [7]. After three months of iron therapy, there was a significant difference in the frequency of cyanotic spells between children who had received iron and those who had not (84% v 21.4%). They suggested that iron may be crucial in the treatment of breath holding spells because iron deficiency may be the main underlying defect.

Infancy and childhood is the critical period for brain growth, and nutrient deficiencies during this time may affect psychomotor development and neurocognition [17]. Iron deficient infants are often apathetic, listless, irritable and anorexic. These symptoms resolve rapidly with iron supplementation but less well known is the fact that long-term neurocognitive impairment may persist. Young children with iron deficiency anemia have been found to score 12 to 15 points lower on the Bayley infant development scale than their iron sufficient peers[18, 19].

It is not known exactly how iron deficiency causes breath holding spells but it has been proposed that iron plays a role in catecholamine metabolism and neurotransmitters in the central nervous system[19]. It is possible that a functional deficiency of those neurotransmitters may predispose a child to these breath holding spells and the correction of spells may be related to the restoration of neurotransmitters. However, iron deficiency is not the only factor responsible for breath holding spells because not all children with breath holding spells were iron deficient at baseline[7].

It has been hypothesized that the clinical and hematological picture of breath holding spells relates to the interaction of cerebral erythropoietin, nitric oxide and interleukin 1[20, 21].

It has been suggested that increased brain erythropoietin production has a protective effect during breath holding spells, but where this does not compensate for the severity of anoxic spells, and then seizures develop.

Serum ferritin level may be the earliest laboratory finding of iron deficiency anemia [15]. We have not been able to evaluate the serum ferritin level due to financial restraints.

CONCLUSION

There is a high incidence of iron deficiency anemia associated with breath holding spells. A full blood count and where possible serum ferritin level would therefore be warranted in the work up of these children. Treatment is more likely to be successful when there is concomitant iron deficiency anemia. Length of iron therapy can vary between 4 and 16 weeks. A course of 8 weeks would seem reasonable, long enough to improve anemia.

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