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ORIGINAL RESEARCH
Pediatric Cardiology

Is iron supplementation the only treatment choice for breath holding spells?

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ABSTRACT

Objective: Breath holding spells (BHS) are common non-epileptic paroxysmal disorder in childhood. The aim of this study is to evaluate the clinical, laboratory, and treatment responses of patients followed up with BHS.

Material and Methods: The files of 73 cases diagnosed with BHS in the Paediatric Neurology Outpatient Clinic of Afyonkarahisar Health Sciences University Hospital between December 2017 and January 2020 were evaluated retrospectively. Medical history, physical examination (PE), spell type (pallid, cyanotic, and mixed), spell degree (complicated and uncomplicated), family history, laboratory findings, electrocardiography, echocardiography, and electroencephalography findings were used.

Results: Forty-one (56%) of the BHS cases were male and 32 (44%) were female. The mean age of the patients was 21.7±14.5 (min–max: 2–72) months. Forty-five cases (62%) under the age of 2 years were detected. There was a family history of BHS in 11 (15%) cases. PE was normal in 72 (99%) cases. Sixty-five (89%) of the cases were cyanotic, 5 (7%) were pallid type and 3 (4%) were mixed type. The complicated type was detected in 26 (36%) cases and the uncomplicated type in 47 (64%) cases. There were detected only iron deficiency (ID) in 42 (58%) cases, B_{12} deficiency in 3 cases (4%), ID+B_{12} deficiency in 14 cases (19%). Iron supplementation was given to 56 (75%) in cases, iron+B_{12} treatment to 14 (19%) in cases, B_{12} treatment to 3 (4%). The three cases who did not benefit with other treatments were given piracetam. There were 42 cases with ID. Thirty-one (73%) ID cases had a complete response to iron therapy, three ID cases (7%) had 50% or more response, and 2 cases (5%) had <50% response. Iron therapy had complete response in 14 (19%) cases without ID or B_{12} deficiency. Complete response was obtained in 12 (86%) cases, 50% or more were obtained in 1 (7%), and <50% were obtained in 1 (7%) of the patients who received iron+B_{12} treatment. Complete response was obtained in all patients treated with B_{12} or piracetam. In the cyanotic cases, complete response was obtained in 43 (66%), 50% and above in 4 (6%), and <50% in 2 (3%). Complete response was obtained in all pallid type cases. Of the mixed type cases, complete response was obtained in 2 cases (66%) and 50% and above response in 1 case (34%).

Conclusion: Patients with BHS was benefited from iron therapy, although there was no ID. In patients with B12 deficiency, B12 treatment had also been observed to reduce BHS. Although this finding is new information for the literature, B12 replacement treatment has also been observed to reduce BHS. This finding is new information for the literature. B12 replacement should be considered among the treatment options besides iron replacement.

Keywords: B_{12}; breath-holding; iron.

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Katılma nöbeti tedavisinde sadece demir desteği yeterli midir?

ÖZET

Amaç: Katılma nöbetleri, çocukluk çağında sık görülen epileptik olmayan bir paroksismal bozukluktur. Bu çalışmanın amacı, katılma nöbetleri tanısı ile takip edilen hastaların klinik, laboratuvar ve tedavi yanıtlarını değerlendirmektir.

Gereç ve Yöntemler: Afyon Karahisar Sağlık Bilimleri Üniversite Hastanesi Çocuk Nöroloji Polikliniği'nde Aralık 2017-Ocak 2020 tarihleri arasında katılma nöbeti tanısı konulan 73 olgunun dosyaları geriye dönük olarak değerlendirildi. Tıbbi öykü, fizik muayene, tipi (solgun, siyanotik, karışık), derecesi (komplike, komplikasyonsuz), aile öyküsü, laboratuvar bulguları, elektrokardiyografi, ekokardiyografi ve elektroensefalografi bulguları kullanıldı.

Bulgular: Katılma nöbeti olgularının 41'i (%56) erkek, 32'si (%44) kadındı. Hastaların yaş ortalaması 21,7±14,5 (min-maks: 2-72) aydı. İki yaş altı 45 (%62) olgu tespit edildi. On bir (%15) olguda ailede katılma nöbeti öyküsü vardı. Yetmiş iki (%99) olguda fizik muayene normaldi. Olguların 65'i (%89) siyanotik, 5'i (%7) soluk tip ve 3'ü (%4) mikst tipteydi. Yirmi altı (%36) olguda komplike tip, 47 (%64) olguda komplike olmayan tip saptandı. Kırk iki (%58) olguda sadece demir eksikliği, 3 (%4) olguda B_{12} eksikliği ve 14 (%19) olguda demir eksikliği + B_{12} eksikliği tespit edildi. Katılma nöbeti olan olguların 56'sına (%75) demir, 14'üne (%19) demir+B±, 3'üne (%4) sadece B_{12} ve diğer tedavilerden fayda görmeyen 3 (%4) olguya pirasetam tedavisi verildi. Kırk iki demir eksikliği olgusunun 31'i (%73) demir tedavisine tam yanıt, 3'ü (%7) %50 veya daha fazla yanıt ve 2'si (%5) %50'den az yanıt verdi. Demir eksikliği veya B_{12} eksikliği olmayan 14 (%19) olguda demir tedavisine tam yanıt elde edildi. Demir+B_{12} tedavisi alan hastaların 12'sinde (%86) tam, 1'inde (%7) %50 ve üzeri, 1'inde (%7) %50'den az yanıt alındı. B_{12} veya pirasetam tedavisi verilen tüm hastalarda tam yanıt alındı.

Tartışma: Demir eksikliği olmamasına rağmen, katılma nöbetleri olan hastalarda demir tedavisinin fayda sağladığı bulundu. B_{12} eksikliği olan hastalarda B_{12} tedavisinin katılma nöbetlerini de azalttığı gözlemlendi. Bu bulgu literatür için yeni bir bilgi olmakla birlikte demir replasmanı yanında B_{12} replasmanı da tedavi seçenekleri arasında düşünülmelidir.

Anahtar Kelimeler: B_{12}; katılma nöbeti; demir.

INTRODUCTION

Breath holding spells (BHS) are non-epileptic events that result in apnea, loss of consciousness, and changes in skin color and postural tone as a result of a crying attack and holding the breath after pain and irritation. BHS starts at the earliest in the 6th month of life and usually end by the age of 6 years (1). They usually do not leave any cardiac or neurological sequelae. BHS are divided into three subgroups, known as cyanotic, pallid, and mixed types according to the change in skin color that occurs during the event (2). The most common type, the cyanotic type, usually occurs after the child experiences anger, pain, or fear. Sometimes, cyanosis deepens and can lead to secondary hypoxia, resulting in loss of tone and myoclonic jerks. In severe cases, generalized hypertonia can often be confused with epileptic seizures. Furthermore, the postictal period can be seen after BHS (3). The pallid type usually occurs after a painful condition. The child stops breathing, develops bradycardia, becomes pallid, and loses consciousness. During the event, contractions may develop in the body, which may be confused with convulsions, and bladder control may be lost. This usually takes less than a minute, and consciousness is restored without any intervention (4). The type that has the characteristics of both types is the mixed type (5). The degree of BHS is classified as non-complicated and complicated. The non-complicated type lasts for a few minutes and there is no loss of consciousness or loss of tone during the event. The complicated type lasts longer and is often accompanied by loss of consciousness and postural tone (6).

BHS can be confused with epilepsy, since convulsion-like contractions can be seen in cases with severe BHS, and postictal sleepiness can be seen after the event. Therefore, epilepsy should be excluded by electroencephalography (EEG) in differential diagnosis (7). Electrocardiogram (ECG) examination should be performed to exclude long QT syndrome in differential diagnosis (8, 9). In this study, we aimed to examine the demographic characteristics of cases with BHS, the factors that may cause them, the accompanying cardiac or neurological findings, the identified deficiencies, and the treatment responses after the treatments given for these deficiencies.

MATERIAL AND METHODS

The files of 73 patients who applied to the Paediatric Neurology Outpatient Clinic of Afyonkarahisar Health Sciences University Hospital with the complaint of spells while crying between December 2017 and January 2020 and were diagnosed with BHS were evaluated retrospectively. By examining the outpatient follow-up files of the patients, medical history, physical examination (PE), age, gender, first presentation complaints, age at onset of complaints, spell type (pallid, cyanotic, and mixed), spell degree (complicated and non-complicated), family history, prenatal/natal/postnatal features, laboratory findings, EEG, ECG, and echocardiography (ECHO) findings were determined. Anemia is defined as a decrease in the number of erythrocytes in children or hemoglobin (Hb) amount below the fifth percentile of the normal Hb amount determined by that age and gender. Iron deficiency (ID) anemia was diagnosed when Hb and mean erythrocyte volume (MCV) levels were below the reference values for age and gender, and ferritin level was <12 ng/mL. Cases with Hb and MCV levels below the reference values for age and gender and with high ferritin levels

Table 1. General characteristics of BHS patients

Variable	n	%	Variable	n	%
Gender			ECHO		
Girl	32	44	Normal	54	74
Boy	41	56	PFO	8	11
Age at onset			Secundum ASD	8	11
6 months>	10	14	MR (minimal)	2	3
6–12 months	6	8	PFO+PS	1	1
12–24 months	24	33	Accompanying deficiencies		
24 months<	33	45	ID+	42	58
Age at application			B_{12} deficiency+	17	24
24 months>	45	62	ID+B_{12} deficiency+	14	16
24 months<	28	38	Treatments		
Family history			Iron	56	75
Yes	11	15	Iron+B_{12}	14	19
No	62	85	B_{12}	3	4
Spell types			Piracetam	3	4
Cyanotic	65	89	Complete response to treatment		
Pallid	5	7	1. According to the spell types		
Mix	3	4	Cyanotic	43	66
Spell degree			Pallid	4	100
Complicated	26	36	Mix	2	66
Non-complicated	47	64	2. According to the degree of spell		
EEG+ECG			Complicated	19	73
Normal	73	100	Noncomplicated	31	66

BHS: Breath holding spells; EEG: Electroencephalography; ECG: Electrocardiogram; ECHO: Echocardiography; PFO: Patent foramen ovale; PS: Pulmoner stenosis; ID: Iron deficiency; ASD: Atrial septum secundum; MR: Mitral regurgitation.

were accepted into the ID group. Vitamin B_{12} level <200 pg/dL was considered as deficiency. There is no control group in this study. The clinical findings and laboratory findings of the patients at the first admission and the clinical findings and laboratory findings determined at the interview 6 months later were compared. Patients with ID and B_{12} deficiency were called 6 months after the treatment. Six months later, patients who did not apply to the clinic were interviewed by telephone and their complaints were questioned. During this period, whether the spells had ceased and their current mental and neurological conditions were questioned. A correlation was made between the age at which the seizure ended and the laboratory findings at the time of admission, onset age, BHS type, and duration. Among the patients who were evaluated after at least 6 months of treatment, those who did not have any spells in the last month were grouped as complete response, those with less than half the number of spells seen in 1 month as 50% or more response, and those with more than half of the spells in a month were grouped as <50% response.

Quantitative variables were expressed as mean±standard deviation (SD), median±interquartile range and median range (maximum–minimum), and categorical variables as n(%). Percentage and number values were recorded in categorical measurements. Pearson's correlation coefficients were calculated for arithmetic mean, SD, and unrelated measurements using the SPSS Statistics, version 23.0 (IBM, Armonk, NY) program. Pearson's Chi-square test was preferred for intergroup comparisons. Pearson Chi-square test and Fisher's exact test were used to analyze categorical data. In the study, $p<0.05$ was considered significant.

RESULTS

Forty (56%) of the BHS cases were male and 32 (44%) were female. The mean age of the cases was 21.7 months±14.5 (min–max: 2–72 months). There were 10 cases (14%) with complaints before 6 months of age, 6 (8%) between 6 and 12 months of age, 24 (33%) between 12 and 24 months of age, and 33 (45%) cases after 24 months of age. The number of children under 24 months

of age at presentation was 45 (62%). Family history was present in 11 (15%) cases. While FM was normal in 72 (99%) cases, hypotonia was detected in one case. When the spell types of the cases were examined; 65 (89%) were of the cyanotic type, 5 (7%) were of the pallid type, and 3 (4%) were of the mixed type. Complicated type cases were found in 26 (36%), and non-complicated type cases were found in 47 (64%) patients. Thyroid function values, EEG, and ECG examinations were found to be normal in all cases. ECHO was normal in 54 (74%) cases, PFO (patent foramen ovale) in 8 cases (11%), secundum atrial septum secundum in 8 (11%) cases, trace mitral regurgitation in 2 (3%) cases), and PFO+PS (Patent foramen ovale+Pulmonary stenosis) was detected in 1 case (1%). There was only ID in 42 (58%) of the cases, only B_{12} deficiency in 3 (4%) cases and ID+B_{12} deficiency in 14 (16%) cases. No iron or B_{12} deficiency was found in 14 (19%) of the BHS cases. B_{12} deficiency was found in three of the cases with a family history. B_{12} deficiency was detected in 9 (35%) of the complicated type cases and 8 (17%) of the uncomplicated cases (p=0.079). Iron replacement, B_{12} replacement, iron+B_{12} replacement, and piracetam options were used in the treatment. Iron supplementation was given to 56 (75%) of the cases, iron+B_{12} to 14 (19%), and piracetam treatment to 3 (4%) of the cases B_{12} and 3 (4%). When the response to treatment was examined according to spell type, complete response was obtained in 43 (66%) of cyanotic cases, complete in all pallid type cases, complete in 2 cases (66%) of the mixed type and more than 50% response was obtained in one case of the mixed type (34%). Complete response was obtained in 19 (73%) of complicated type cases and 31 (66%) of non-complicated cases (Table 1).

The patients were grouped according to gender and age and compared and analyzed separately. The findings of the examination of BHS cases according to gender are shown in Table 2. When the distribution of girls and boys over 0–24 months and over 24 months was examined, a significant difference was found (p=0.001). Only ID was found in 18 (24%) girls and 24 (32%) boys (p=0.845). When the complete blood count values were examined, mean hemoglobin (Hb) was 11.5 g/dL in girls and 11.3 g/dL in boys (p=0.445), mean hematocrit (Htc) 35% in girls and 34% in boys (p=0.393), and MCV 77 fL in girls and 75 fL in boys (p=0.208). There was a total of three patients with only B_{12} deficiency. Other B_{12} deficiencies were found with ID. Four girls (6%) and 10 boys (14%) (p=0.20) were found to have B_{12} deficiency+ID. When the spell types were compared according to gender, the cyanotic type was found in 28 (38%) girls and 36 (36%) boys (p=0.651); the pallid type was found in 3 (4%) girls and 2 (3%) boys (0.651). Since the mix type was seen in a total of three patients, no statistical evaluation was performed. The degree of spells was examined. The complicated type was found in 13 (18%) girls and 13 (18%) boys (p=0.430). The uncomplicated type was found in 19 (26%) girls and 28 (38%) boys (p=0430). The cases were divided into two groups, 50% or more and <50% response, according to the treatment response. Response to treatment was found to be 50% and above in 24 (32%) girls and 30 (41%) in boys (p=1.0). <50% response was found in 8 (11%) girls and 10 (14%) boys (p=1.0) (Table 2).

Table 2. Comparison findings of BHS patients by gender

Variable	Girl		Boy		p
	n	%	n	%	
Age groups					0.001
0–24 months	13	18	32	44	
Over 24 months	19	26	9	12	
ID+	18	24	24	32	0.845
Hb mean (g/dL)	11.5		11.3		0.445
Htc mean (%)	35		34		0.393
MCV mean (fL)	77		75		0.208
B_{12}+ID deficiency	4	6	10	14	0.20
Spell types					
Cyanotic	28	38	36	49	0.651
Pallid	3	4	2	3	0.651
Spell degrees					
Complicated	13	18	13	18	0.430
Non-complicated	19	26	28	38	0.430
Response to treatment					
≤50%	24	32	30	41	1.0
>50%	8	11	10	14	1.0

P-value <0.05 indicating significant; MCV: Mean corpuscular volume; ID: Iron deficiency.

Examination findings of BHS cases according to age are shown in Table 3. When the ages of the patients were examined, 45 (62%) were found between 0 and 24 months and 28 (38%) over 24 months. ID was 30 (66%) in cases 0–24 months of age and 12 (42%) in cases over 24 months (p=0.045). B_{12} deficiency was present in 15 (33%) of the 0–24-month-old cases and 2 (7%) of the cases over 24 months (p>0.05). B_{12}+ID was detected in 12 (26%) cases 0–24 months of age and 2 (7%) over 24 months (p>0.05). The mean value of Hb was 10.8 g/dL in cases 0–24 months of age and 12 g/dL over 24 months (p=0.00); the mean Htc value was 33.8% at 0–24 months and 36.8% over 24 months (p=0.003); The mean MCV value was 75.8 at 0–24 months and 76.8 over 24 months (p>0.05). Family history was detected in 6 (13%) cases in 0–24 months and in 4 (14%) cases over 24 months (p>0.05). The response to treatment was 50% and above in 28 (62%) cases aged 0–24 months and 26 (92%) of those over 24 months; a response of <50% was found in 16 (35%) cases at 0–24 months of age and 2 (7%) cases over 24 months (p=0.005) (Table 3).

When the response to treatment was evaluated as all therapies given; 60 (82%) had complete response, 4 (5%) had 50% or greater response and 3 (4%) had a <50% response. When the response to iron treatment in ID cases was examined; 31 (73%) complete, 3 (8%) 50% and above responses, and 2 (5%) responses <50% were obtained. Since 6 (14%) of 42 patients with ID were not followed up, their response to treatment was

Table 3. Comparison findings of BHS patients by age group

Variable	0–24 months (n=45)	Over 24 months (n=28)	p
ID+	30	12	0.045
B_{12} deficiency+	14	3	0.08
B_{12} +ID+	12	2	0.064
Hb mean (g/dL)	10.9	12	0.000
Htc mean (%)	33.8	36.2	0.003
MCV mean (fL)	75.8	76.8	0.530
Spell types			
Cyanotic	40	24	1.0
Pallid	3	2	
Spell degree			
Complicated	16	10	0.592
Non-complicated	29	18	
Family history	6	4	0.89
RT			
≤50%	28	26	0.005
>50%>	16	2	

P-value <0.05 indicating significant; RT: Response to treatment; ID+: Iron deficiency.

not evaluated. Complete response was obtained in 14 (19%) patients who did not have ID but were given iron treatment. When the response to iron+B_{12} treatment was examined for patients who have both iron and B_{12} deficiencies; 12 (86%) complete response, 1 (7%) 50% or more response, and 1 (7%) <50% response were received. Complete response was obtained from all patients who were given B_{12} and piracetam treatment.

DISCUSSION

BHS is a transient paroxysmal disorder seen in healthy children, mostly between the ages of 6 and 36 months and of the male gender (10–13). In this study, in accordance with the literature, the mean age of onset was found to be 21.7 months±14.5 (min–max: 2–72 months), and the frequency of males was found to be higher (9, 12, 14–16). In addition, in this study, when girls and boys in the age group under 24 months were compared, it was found that the frequency of males was significantly higher. The age of onset of BHS is frequently reported as 24 months and before in the literature. In the previous studies, onset before 6 months was found to be about 12%. Few cases of neonatal onset have been reported (10, 13, 17). In this study, in accordance with the literature, the number of cases with an age of onset before 24 months was found to be significantly higher. The cases with the age of onset before 6 months were found to be 14%. In many studies, it has been reported that 15–50% of the patients have a family history of BHS (13–15, 18, 19). In addition, there is a limited number of studies in the literature reporting that BHS is inherited in an autosomal dominant manner (1, 20). In this study, the frequency of family history was 15%, in accordance with the literature. Many studies found that most BHS cases had normal PE; EEG, ECG, and ECO evaluations have been reported to be normal (14, 19). However, before the diagnosis of BHS, it is important to rule out diagnoses such as epilepsy and long QT syndrome, which can often be confused with this diagnosis. EEG findings of the patients in the study were normal. While long QT was not detected in the ECG evaluations of the patients, ECHO evaluation revealed congenital heart disease in 26% (n=19) patients. Some studies also identified patients with congenital heart disease (14, 21, 22). Three types of seizures — cyanotic, pallid and mixed — were seen in BHS. The pathophysiology of all three types is thought to be autonomic nervous system dysregulation. At the same time, loss of consciousness during seizures was thought to be due to cerebral anoxia (11). In the literature, it has been observed that cyanotic type BHS was more common. The pallid and mixed type were seen in the following order (16, 19, 20, 23). In this study, in accordance with the literature, the cyanotic type was found to be the most common type. In addition, non-complicated BHS was found to be more common, in accordance with the literature (14). In the literature, it has been reported in many studies that Hb, Htc, and MCV levels are lower in BHS cases than in healthy children (14, 16, 19, 21, 24, 25).

In most of the studies, ID was found at a high rate in the 0–24-month age group (14, 16, 24). In this study, Hb, Htc, and MCV values were found to be low in cases with BHS, in accordance with the literature. In addition, while Hb, Htc, and MCV values did not differ according to gender in this study, it was found that Hb and Htc levels were significantly lower in favor of 0–24 months in the groups over 0–24 months and over 24 months. Iron and B_{12} deficiency are important causes of nutritional anemia in childhood. In this study, in accordance with the literature, ID was detected in 42 (58%) of the cases (14, 16, 19, 24, 25). The combination of BHS and ID was found to be higher in the 0–24-month group compared to the >24-month group. However, anemia was not detected in 31 (42%) of the BHS cases. There are various opinions regarding the role of iron in the BHS. One of them is that iron contributes to BHS due to its role in enzymatic mechanisms known to be involved in the central nervous system. The other is that the decrease in the hemoglobin level due to ID and the increase in iron consumption secondary to the increase in erythropoiesis due to hypoxia also deepens anemia or leads to the development of immediate anaemia (26–28).

In this study, the high rate of response to treatment in the group without ID supports the view that instant anemia develops. It has also been reported that children with ID are more irritable. Consequently, they cry more and have a higher frequency of spells. In addition, cerebral anoxia occurs more rapidly during spells, as the oxygen carrying capacity is low due to low hemoglobin (28). One of the most common causes of anemia after ID is B_{12} deficiency. In two studies conducted in our country, B_{12} levels were examined in cases with BHS, and no relationship with BHS was reported (23, 29).

In another study, in a comparison between healthy children and children with BHS, B_{12} deficiency was found to be significantly higher in those with BHS (30). In this study, B_{12} deficiency cases in BHS cases were examined in two groups. The first group consisted of only three cases with B_{12} deficiency, and the second group consisted of 14 cases with B_{12}+ID. B_{12} is involved in DNA and RNA synthesis, methylation reactions, methionine, and the homocysteine cycle as well as the synthesis of dopaminergic and serotonergic neurotransmitters (31). Therefore, serious neurological findings are a common addition to anemia in B_{12} deficiency, especially in childhood, when brain development is occurring the most rapidly (32–34). Especially if there is B_{12} deficiency in breast milk in the first 2 years, anemia and neurological findings can be seen in this age group (15). B_{12} hypotonia, hypertonia, convulsions, and coma in early infancy; developmental delay, mental retardation, encephalopathy, convulsions and subacute combined degeneration in early childhood and mild developmental delays, mental retardation, myelopathy, and behavioral disorders in late childhood can be seen (32). However, the mechanism of action of B_{12} in terms of BHS is unknown. In B_{12} deficiency anemia, it is thought that hypoxia is deepened, and BHS is triggered as in ID. Iron treatment should be given in cases with ID (6). Studies have reported that 50–92% of BHS cases benefit from iron treatment (19, 21). In this study, a complete response was obtained in all BHS cases receiving iron therapy. Patients with B_{12} deficiency were divided into two groups as only those with B_{12} deficiency and those with B_{12} deficiency+ID and were treated. Three patients with B_{12} deficiency alone were given only B_{12} treatment and a complete response was obtained in terms of BHS. In the second group, 14 patients were given iron+B_{12} treatment, and a complete response was obtained. For the second group of patients, it is difficult to interpret B_{12} in terms of treatment efficacy since B_{12} was given together with iron therapy. Another option in resistant spell treatments is piracetam. Its mechanism of action increases the inhibitory hyperpolarization effect through gamma aminobutyric acid and increases the oxygen utilization of the central nervous system. It is preferred in cases with frequent and severe spells despite other treatments (21). In a study in the literature, complete response was observed in all three patients who received piracetam treatment (16). In another study, a double-blind study was conducted and a significant response was obtained (35). In another double-blind study, no difference was reported (36). In this study, a complete response was obtained in three patients who had piracetam treatment. It is important to inform the family after excluding possible cardiac and neurological pathologies in the age range where BHS is common.

Study Limitation

A limitation of this study is the small number of cases. Studies involving more patients are needed to understand the pathophysiology of B_{12} deficiency in BHS and the role of B_{12} deficiency in BHS treatment.

CONCLUSION

In this study, in accordance with the literature, a good response to iron treatment was obtained in both cases with and without ID. The good response to B_{12} treatment in B_{12} deficiency cases detected in the study is a new finding for the literature.

Ethics Committee Approval: The Afyonkarahisar Health Sciences University Hospital Non-Interventional Clinical Research Ethics Committee granted approval for this study (date: 02.08.2019, number: 2019/9).

Informed Consent: Verbal informed consent was obtained before the interview.

Conflict of Interest: No conflict of interest was declared by the authors.

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Authorship Contributions: Concept – DÇ; Design – ABİ; Supervision – DÇ; Fundings – ABİ; Materials – DÇ, ABİ; Data collection and/or processing – DÇ, ABİ; Analysis and/or interpretation – ABİ; Literature review – DÇ; Writing – ABİ, DÇ; Critical review – ABİ, DÇ.

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Hasta Onamı: Görüşmeden önce sözlü bilgilendirilmiş onam alındı.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

Yazarlık Katkıları: Fikir – DÇ; Tasarım – ABİ; Denetmele – DÇ; Kaynaklar – ABİ; Malzemeler – DÇ, ABİ; Veri Toplanması ve/veya İşlemesi – DÇ, ABİ; Analiz ve/veya Yorum – ABİ; Literatür Taraması – DÇ; Yazıyı Yazan – ABİ, DÇ; Eleştirel İnceleme – ABİ, DÇ.

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