

# The Role of Phenobarbital in Treatment of Sever Breath Holding Attack

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## Abstract

**Background:** Breath-holding spell (BHS) is a paroxysmal-nonpileptic widespread-incident which mostly happens in infants and toddlers of 6-18 months of old with very low incidence following the age of 5 years of old.

**Objective:** To study the effect of phenobarbital in treating an infant with severe breath holding attack.

**Methods:** This prospective study conducted over three years from 1<sup>st</sup> of June 2014 until 1<sup>st</sup> of June 2017 and involve 86 patients with severe breath holding attack that consult the outpatient clinic in Al-Diwaniyah Maternity and Children Teaching Hospital, Al-Qadisiyah, Iraq, patients were divided into two groups each involve 43 patients the 1<sup>st</sup> group given phenobarbital tablet 5mg/kg once at night for one month and the other group not give any medication and just support of the parent their age are between 4 and 48 months, the diagnosis is made on clinical base and video recording of more than one attacks for each patient done by the parent and the following parameters were documented: age, sex, residence, type of feeding, number of attacks per month, family history of the same disease, additionally 21 patient have chest x-ray and echocardiography to exclude any possibility of congenital heart disease all were normal EEG done in 7 patient to rule out the possibility of epilepsy also they were normal.

**Results:** There is no difference in the residence and type of feeding in both groups, after one month there is significant decrease in number of attacks among treated group (p-value <0.05) in all age groups while there is little change in no. of attacks in group without treatment (p-value >0.05) (Table 1). The follow up was continued for another 3 months and there is no change in number and the severity of attacks in the phenobarbital-treated group. Also, there is no side effect of the drug was detected (Table 2).

**Conclusion:** Phenobarbital is very effective and safe treatment, particularly in short course, additionally there is no side effect has been recorded during and after therapy and there is no relapse after stopping treatment.

**Keywords:** Phenobarbital; Breath-holding spell (BHS); Breath Holding Attack.

## INTRODUCTION

Breath-holding spell (BHS) is a paroxysmal-nonpileptic widespread-incident which mostly happens in infants and toddlers of 6-18 months of old with very low incidence following the age of 5 years of old. When such incident happens, pain and/or frustration induces extreme crying in the affected child. The sequence rationale of BHS symptoms consists of provocation, crying until it becomes a noiseless weeping, the parallel occurrence of cyanosis or paleness, tonic/clonic episodes of spasms or movements, and eventual syncope and coma [1-3]. In addition, signs of extreme anger and annoyance could add up to the general symptoms that intensify the worriedness of parents [3].

The frequency of the BHS occurrence is estimated to be as 0.1-4.6% [1,2]. Almost 85% of the patients have the facial-cyanotic type of this condition. Pallid-BHS condition occurs when a child gets annoyed [3]. Only one type of BHS could happen in a child; however, more than one type might be present in a patient. The incorrect nomenclature of this condition doesn't explain the reality of exhale-based occurrence of the problem.

Based on the available information, syncope and coma might occur via involvement of autonomic dysregulation [4-10], and this is could be found when a child has both cyanotic and pallid types of BHS [11]. Genetic-based with an autosomal dominant genotype has been correlated [10,12-15]. Incomplete myelination in brain stem has been linked to the occurrence of BHS [16].

Patient history, clinical symptoms, lack of incontinence, and no postictal phase provide valued information to diagnose the BHS. Video-based surveillance of a case is recommended to acquire accurate diagnosis. Arrhythmia could be removed from the list of reasons using an electrocardiogram (ECG). Iron-based anemic-children are predisposed to BHS [17,18]. Clinically-approved treatment of the BHS is not present; however, literature-provided methods are mentioned such as providing the patients with iron [19,29] with no response to this supplement in some literature [3,21,22]. Iron provision has been found to treat BHS even if the patients had no signs of anemia, and that anemia strengthens BHS [17,18]. According to some studies, BHS was significantly

treated in good safety using Piracetam more than glycopyrrolate, theophylline, or fluoxetine [23-29]. Cardiac-pacemaker implantation was used in some patients to treat BHS [27]. Recommendation to test patients using ECG to eliminate the presence of prolonged QT-syndrome, a serious type of cardiac arrhythmia, is suggested [28,29].

According to the literature [26-30], treatments using pharmacological substances are not needed at all times but to minimize the effects of the symptoms. For best of our knowledge, there is no similar study was done before. So, the current study was purposely aimed to study the hypothesized effect of phenobarbital in treating an infant with severe breath holding attack.

## MATERIALS AND METHODS

This prospective study conducted over three years from 1st of June 2014 until 1st of June 2017 and involve 94 patients with severe breath holding attack that consult the outpatient clinic in Al-Diwaniyah Maternity and Children Teaching Hospital, Al-Qadisiyah, Iraq, 86 patient was involved in this study, they divided into two groups each involve 43 patients, the 1st group given phenobarbital tablet 5mg/kg once at night for one month and the other group do not give any medication and just support of the parent, their age is between 4 and 48 months, the diagnosis is made on clinical base and video recording of more than one attacks for each patient done by the parent and the following parameters were documented: age, sex, residence, type of feeding, number of attacks per month, family history of the same disease, also detail history to classify the type of attack, and detail examination were done to exclude any organic disease and 21 patient have chest x-ray and echocardiography to exclude any possibility of congenital heart disease all were normal EEG done in 7 patient to rule out the possibility of epilepsy also they were normal. Eight patient were excluded because they miss follow up.

## Statistical analysis

The resulted data were analyzed using Chi-square and are significant when  $p < 0.05$ .

**RESULTS**

After one-month detail, the review was done to both group and the result was recorded. In this study, most of the patients are under the age of two years in both groups and there are no differences in sex between both groups with male and female are equally affected. There is no difference in the residence and type of feeding in both groups, after one month there are significant decrease in number of attacks among treated group (p-value <0.05) in all age groups while there is little change in no. of attacks in group without treatment (p-value >0.05) (Table 1). The follow up was continued for another 3 months and there is no change in number and the severity of attacks in the phenobarbital-treated group. Also, there is no side effect of the drug was detected (Table 2).

**Table 1: General parameters of the patients in both groups**

Patient	With treatment	Without treatment
age		
4-12 mo.	21	27
13-24 mo.	16	11
25-48 mo.	6	5
Sex		
Male	31	26
female	12	17
Residence		
Rural	22	23
urban	21	20
Type of feeding		
Breast	15	11
Bottle	10	12
mixed	18	20

**Table 2: Attack-based counting of one-month treatment, before and after.**

Patient age, month	No. of attacks	Treatment group	Without treatment group	P-value
4-12	Before treatment	12	11	<0.05
13-24		7	7	
25-48		4	5	
4-12mo.	After treatment	4	9	
13-24 mo.		4	8	
45-48 mo.		2	5	

**DISCUSSION**

Breath holding spell could be a worrying-inducing condition to parents due to loss of response from the child via cerebral hypoxia [1-3]. In this study, most of the patients are under the age of two years in both groups and there are no differences in sex between both groups with male and female are equally affected. Additionally, there is no difference in the residence and type of feeding in both groups. After one month there are significant decrease in number of attacks among treated group (p-value <0.05) in all age groups while there is little change in number of attacks in group without treatment (p-value >0.05) and this may be explained by that breath holding attack may be caused by some abnormal electrical activity inside the brain which cause this frightening attack and the use of phenobarbital may cause some suppression of these electrical activities and lead to decrease the number and the severity of the attack [3,7-9], additionally, we didn't found any previous similar study, so further studies are required to determine the exact cause of breath holding attack and the exact action of phenobarbital to treat this disease.

**CONCLUSION**

Breath holding attack is a very frightening experience for the child and the parent. Phenobarbital is very effective and safe treatment, particularly in short course, additionally, there is no side effect has been recorded during and after therapy and there is no relapse after stopping treatment.

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