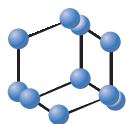


REVIEW ARTICLE

BENTHAM
SCIENCE

Breath-Holding Spells in Pediatrics: A Narrative Review of the Current Evidence

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Abstract: Background: Breath-holding spells are common, frightening, but fortunately benign events. Familiarity with this condition is important so that an accurate diagnosis can be made.

Objective: To familiarize physicians with the clinical manifestations, diagnosis, evaluation, and management of children with breath-holding spells.

Methods: A PubMed search was completed in Clinical Queries using the key term "breath-holding spells". The search strategy included meta-analyses, randomized controlled trials, clinical trials, observational studies, and reviews. Only papers published in the English literature were included in this review. The information retrieved from the above search was used in the compilation of the present article.

Results: Breath-holding spells affect 0.1 to 4.6% of otherwise healthy young children. The onset is usually between 6 and 18 months of age. The etiopathogenesis is likely multifactorial and includes autonomic nervous system dysregulation, vagally-mediated cardiac inhibition, delayed myelination of the brain stem, and iron deficiency anemia. Breath-holding spells may be cyanotic or pallid. The former are usually precipitated by anger or frustration while the latter are more often precipitated by pain or fear. In the cyanotic type, the child usually emits a short, loud cry, which leads to a sudden involuntary holding of the breath in forced expiration. The child becomes cyanosed, rigid or limp, followed by a transient loss of consciousness, and a long-awaited inspiration and resolution of the spell. In the pallid type, crying may be minimal or "silent". The apneic period in the pallid type is briefer than that in the cyanotic type prior to the loss of consciousness and posture. The episode in the pallid type then proceeds in the same manner as a cyanotic spell except that the child in the pallid type develops pallor rather than cyanosis. In both types, the entire episode lasts approximately 10 to 60 seconds. The spells usually disappear spontaneously by 5 years of age.

Conclusion: Although breath-holding spells are benign, they can be quite distressing to the parents. Confident reassurance and frank explanation are the cornerstones of treatment. Underlying cause, if present, should be treated. Interventions beyond iron supplementation may be considered for children with severe and frequent breath-holding spells which have a strong impact on the lifestyle of both the child and family.

Keywords: Cyanosis, pallor, autonomic nervous system dysregulation, cardiac inhibition, iron deficiency anemia, pediatrics.

1. INTRODUCTION

"The onset of a breath-holding spell may be from some mysterious terror or a fright from somebody shouting, or in the midst of crying the child is not able quickly to recover his breath, as often

happens to children; but when any of these things happen to him, at once the body is chilled, he becomes speechless, does not draw his breath, the breathing fails, the brain stiffens, the blood is at a standstill."

Hippocrates

"There is a disease... in children from anger or grief, when the spirits are much stirred and run from the heart to the diaphragms forcibly, and hinder or

ARTICLE HISTORY

Received: September 05, 2018
Revised: November 02, 2018
Accepted: November 08, 2018

DOI:
10.2174/1573396314666181113094047



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stop the breath...but when the passion ceaseth, this symptom ceaseth."

Nicholas Culpeper (1616-1654)

Breath-holding spells, described as paroxysmal nonepileptic events, are common in children and have been recognized since the days of Hippocrates [1]. A breath-holding spell can be a frightening experience for parents because the child may appear lifeless and unresponsive during the event [2, 3].

A PubMed search was completed in Clinical Queries using the key term "breath-holding spells". The search strategy included meta-analyses, randomized controlled trials, clinical trials, observational studies, and reviews. Only papers published in the English literature were included in included in this review. The information retrieved from the above search was used in the compilation of the present article.

2. EPIDEMIOLOGY

Breath-holding spells affect 0.1 to 4.6% of otherwise healthy infants and young children from six months to five years of age [4-6]. The onset is usually between 6 and 18 months of age, and is almost always before two years of age [1, 6-8]. Onset in the neonatal period has rarely been reported [9, 10]. Both sexes are almost equally affected, with a slight male predominance [7, 11]. A history of breath-holding spells in a near relative is present in 20 to 35% of cases [1, 12, 13]. An autosomal mode of inheritance with reduced penetrance may be responsible in a subset of patients with severe breath-holding spells [12, 14, 15]. Several genetic syndromes, such as 16p11.2 microdeletion syndrome and Riley-Day syndrome, have been known to be associated with early-onset, recurrent, severe breath-holding spells [16, 17].

3. ETIOPATHOGENESIS

The exact etiopathogenesis is not known and is most likely multifactorial. It is believed that autonomic nervous system dysregulation plays a pivotal role in the pathogenesis [18-21]. Cyanotic breath-holding spells occur during times of intense cortical activity when the respiratory muscles are being used to express frustration and anger. The ability of some children to breath-hold to the point of cerebral hypoxia may represent a heightened ability to exert cortical control over the respiratory muscles. In one study, 50 children with cyanotic breath-holding spells had significantly higher resting heart rate and diastolic blood pressure [22]. In the same study, significant hypersensitive reactivity of pupils was also observed on instillation of 0.125% pilocarpine into the conjunctival sac of children with known breath-holding spells when compared to the control group of healthy children without breath-holding spells ($p < 0.001$); these findings were compatible with an autonomic nervous system dysfunction [22]. In another case control study, Arslan *et al.* compared the pupil response to instillation of 0.125% of pilocarpine into the conjunctival sac of the right eye using the left eye as control of 30 children with breath-holding spells to 30 age-matched and gender-matched healthy children [23]. The authors found that children with breath-holding spells had

significantly abnormal hypersensitive reactivity of pupils after instillation of 0.125% of pilocarpine into their conjunctival sac. Autonomic dysregulation is also evidenced by the frequent occurrence of respiratory sinus arrhythmia in children with breath-holding spells [2]. In one study of 46 children with breath-holding spells versus 30 healthy children as control, the frequency of respiratory sinus arrhythmia was recorded in 24 hours Holter monitoring [2]. The authors found that children with breath-holding spells had significantly higher runs of respiratory sinus arrhythmia compared with the control group ($p = 0.001$). There was also a significant relationship between the frequency of respiratory sinus arrhythmia and frequency of breath-holding spells. It is conceivable that autonomic dysregulation leads to compromise in cardiac function with a consequent decrease in cerebral blood flow [2].

Vagally-mediated cardiac inhibition plays an important role in the pathogenesis of pallid breath-holding spells [1]. The underlying mechanism is parasympathetic hyperactivity [24]. Ocular compression in this group shows a hypersensitive cardiac inhibitory reflex that is not present in an age-matched control group [8]. The oculo-cardiac reflex is mediated principally by the afferent fibres of the ophthalmic branch of the trigeminal nerve and the efferent fibres of the vagus nerve [1]. Ocular compression has been shown to cause bradycardia and rarely asystole [8]. Pallor and loss of consciousness may occur as a result [8]. In this regard, pallid spells can be prevented by atropine [24]. Rarely, cardiac arrhythmias may also be responsible for some episodes of pallid breath-holding spells.

Delayed myelination of the brain stem has also been postulated as an underlying mechanism as children tend to outgrow the condition before school age [3, 25, 26]. In one study, children with breath-holding spells and a matched control group were subjected to a brainstem auditory evoked potential test [26]. The authors found that the interpeak latencies were significantly prolonged in those children with breath-holding spells ($n = 32$) in comparison to the control group ($n = 21$), suggesting that delayed myelination of the brain might be the cause of breath-holding spells.

It has been hypothesized that an imbalance between oxidant and antioxidant systems might also be involved in the pathophysiology of breath-holding spells [13]. In a case control study, Saad *et al.* compared the serum malondialdehyde, selenium, glutathione peroxidase, and superoxidase dismutase levels of 67 children with breath-holding spells with those of 60 healthy children [13]. The authors found that children with breath-holding spells had significantly higher serum malondialdehyde levels ($p < 0.001$), and lower selenium ($p < 0.001$), glutathione peroxidase ($p < 0.001$), and superoxidase dismutase ($p < 0.001$) levels than those in the control group. The data suggest that the dysregulation of the oxidant and antioxidant systems and selenium deficiency might play a role in the pathophysiology of breath-holding spells.

Iron deficiency anemia or iron deficiency alone is known to be associated with breath-holding spells [2, 19, 20, 27]. Correction of the iron deficiency anemia has resulted in improvement/resolution of breath-holding spells in a significant number of cases [19, 20]. Iron deficiency may have an impact on autonomic nervous system dysregulation as iron is

essential for catecholamine metabolism and functions as a cofactor for various enzymes and neurotransmitters present in the central nervous system [18-20, 25, 28]. Children with iron deficiency anemia are more irritable and more easily provoked, leading to breath-holding [1, 2, 25, 29]. In addition, children with anemia have lower oxygen-carrying capacity and lower cerebral oxygen tension which may precipitate a breath-holding spell [19, 20, 25, 29, 30]. Breath-holding spells in association with other types of anemia, including transient erythroblastopenia of childhood and sideroblastic anemia, have also been described [12, 31]. It has been shown that 7.5 to 69% of children with breath-holding spells have anemia [12, 32]. This is not surprising as the peak age of onset for both breath-holding spells and iron deficiency anemia is between 6 and 24 months old [1, 33].

Some studies showed that children with long QT syndrome were more likely to have breath-holding spells than those without long QT syndrome [11, 15, 34], but this was not confirmed by other studies [18, 35].

Breath-holding spells may be a symptom of a disturbed parent-child relationship [1, 36]. Many of the parents are found to be over-protective and over-solicitous. They experience more overall stress and disruption in their attachment and understanding of their child [36, 37]. Some of the children are found to be generally resistive and remonstrating, especially against a tense and rigid feeding regime and prematurely enforced regulation of toilet habits [1]. Since most attacks are precipitated by emotional factors such as fear or anger, it is possible that some children use these attacks as a manipulative device [1].

Some authors observed that children with breath-holding spells have certain temperamental characteristics which predispose them to get frustrated easily and go in adamant behavior [38]. Subbarayan *et al.* assessed the temperamental traits of 30 children with breath-holding spells and compared them with 30 healthy children matched for age, gender, and socioeconomic status [36]. The authors found that the threshold of responsiveness ($p < 0.001$), intensity of emotions ($p < 0.001$), mood ($p < 0.001$), and distractibility ($p < 0.001$) were higher in children with breath-holding spells compared with the control group. Low frustration tolerance may predispose the child to excessive and vigorous crying which may lead to the breath-holding.

During a breath-holding episode, spasm of the glottis may occur as part of the generalized rigidity and spasm [1]. The abruptness with which a breath-holding spell ends could be interpreted as relaxation of a spasm. The diaphragm and accessory muscles of respiration may be responsible for the maintenance of the expiratory apnea.

The loss of consciousness is the result of an acute reduction of cerebral blood flow and subsequent hypoxia caused by increased intrathoracic pressure and apnea [1, 29]. Children with cyanotic breath-holding spells become blue within seconds, faster than can be accomplished by children who voluntarily holding their breath. It is likely that during a Valsalva maneuver, which may occur with breath-holding spell, there is right-to-left shunting of blood across the foramen ovale [1]. Intrapulmonary shunting involving ventilation perfusion mismatch or flow through bronchopulmonary

or other arteriovenous anastomosis may also be responsible [6].

4. CLINICAL MANIFESTATIONS

Breath-holding spells may be classified as cyanotic or pallid, based on the coloration of the child's face (lips) during the event. Cyanotic breath-holding spells are by far the more common type, accounting for approximately 72% of cases [32]. There is considerable overlap in the clinical features of the two types of breath-holding spells. Also, the two types of breath-holding spells may coexist; however, usually one type predominates [6, 12].

Cyanotic breath-holding spells are often precipitated by anger or frustration, usually in response to a reprimand [1, 8, 26]. A recent study showed that laughter may also be a precipitating factor [17]. The child usually emits a short, loud cry, which leads to a sudden involuntary holding of the breath in forced expiration [1]. The affected child becomes cyanosed rapidly, faster than anticipated with simple breath-holding [8]. The child becomes rigid or limp followed by a transient loss of consciousness [3, 12]. Rarely, the child develops a generalized seizure if the apnea is prolonged [3, 8, 12]. The pattern is quite stereotyped and reproducible [8, 38]. In most cases, the attack terminates with the cyanosis, followed by a long-awaited inspiration and resolution of the cyanosis. The duration of unconsciousness is usually no more than a few seconds. The severity of the cyanosis, unconsciousness, and convulsive movements, vary with the duration of the apnea and the individual child. The total duration of each of the various stages is usually only 5 seconds or less, and rarely lasts more than 10 to 15 seconds [1]. The entire episode lasts approximately 10 to 60 seconds [1]. Episodes that last longer than 1 minute are unusual and suggest the possibility of an alternate etiology [8].

Pallid breath-holding spells are more often precipitated by pain or fear rather than by anger or frustration [1, 6, 26]. Crying may be minimal or "silent" and the apnea is briefer, often consisting of a single deep gasp before the loss of consciousness and posturing. The episode in the pallid type then proceeds in the same manner as that in a cyanotic spell except that the child in the pallid type develops pallor rather than cyanosis [1, 6]. In both types, if the duration of unconsciousness exceeds approximately 45 seconds, there may be tonic posturing, opisthotonus or clonic movements of the extremities [1].

Breath-holding spells are not associated with preceding aura. They usually occur in an upright posture. Bradycardia is common during the pallid breath-holding spells [1, 8]. There is no confusion or fatigue following the attack [1].

The frequency of the spells varies considerably. Some children have one spell every few months while others have as many as five spells a day. In general, breath-holding spells recur infrequently at the onset of the disorder, and gradually increase in frequency until a peak frequency is reached between 12 and 24 months of age [1]. Most affected children experience approximately 10 attacks per month [12]. The spells usually disappear spontaneously by 5 years of age [10].

5. CLINICAL EVALUATION

A detailed history is the mainstay of diagnosis. A characteristic sequence of events is usually enough to distinguish this condition from other disorders. The sequence often begins with the precipitation by anger, frustration, fear, or injury. The initial precipitating factor is subsequently followed by a violent cry, breath-holding in expiration, cyanosis or pallor, limpness or rigidity, unconsciousness, seizure, relaxation, and recovery without a postictal phase. A careful physical examination should be performed to exclude other diagnoses prior to confirming the diagnosis. In pallid breath-holding spells, the events may be reproducible with ocular compression for 10 seconds and bradycardia demonstrated [8]. Ocular compression during electroencephalography with cardiac monitoring should be considered in patients with frequent or atypical pallid breath-holding spells [1]. A positive oculocardiac reflex, defined as an asystole ≥ 2 seconds suggests a breath-holding spell rather than a seizure disorder [39].

6. DIFFERENTIAL DIAGNOSIS

The differential diagnosis of breath-holding spells is listed in Table 1. The differentiation of breath-holding spells from epilepsy is important to avoid the initiation of inappropriate anticonvulsant medications as well as the unwarranted stigmata associated with epilepsy. Features that help to distinguish breath-holding spells from epilepsy include age of onset typically at 6 to 18 months in breath-holding spells whereas epilepsy can occur at any age; family history is often positive for breath-holding spells but may be positive for epilepsy; precipitating factors are almost always present in breath-holding spells and characteristically include frustration, anger, fear, or fear whereas such precipitating factors are usually absent in epilepsy; aura may be present in epilepsy but not with breath-holding spells; breath-holding spells never occurs during sleep whereas epilepsy may occur during sleep; crying is almost always present, cyanosis or pallor always occurs before loss of consciousness (when present), and opisthotonus is common with breath-holding spells whereas crying is usually absent, cyanosis (when present) usually occurs after loss of consciousness, and opisthotonus is less common in epilepsy; tongue-biting and incontinence are not features of breath-holding spells but not uncommon with epilepsy;

Table 1. Differential diagnosis of breath-holding spells.

Epilepsy
Sudden breath-holding during sleep
Sepsis
Hyperkplexia (stiff baby syndrome or startle disease)
Shuddering
Congenital laryngeal stridor
Laryngospasm
Whooping cough

the duration of the attack is usually less than one minute with breath-holding spells but usually more than one minute with epilepsy; bradycardia is common during pallid breath-holding spells whereas tachycardia is common during an epileptic attack; postictal confusion is characteristically absent in breath-holding spells but not uncommon with epilepsy; and interictal electroencephalogram is normal with breath-holding spells but may be abnormal (spike and wave) with epilepsy [1].

Sudden breath-holding during sleep may present as abrupt waking sometimes associated with choking episodes [40]. Such breath-holding during sleep may be a manifestation of obstructive sleep apnea, parasomnia, sleep-related laryngospasm, gastroesophageal reflux, and frontal lobe epilepsy [40].

Apneic episodes may occur in neonates as a sign of sepsis. Premature healthy infants may also have apneic episodes especially during active sleep and usually associated with bradycardia but not associated with cyanosis or pallor [8].

Hyperekplexia (stiff baby syndrome or startle disease) is characterized by neonatal onset of generalized stiffness while awake that may normalize during the first years of life; neonatal apneic episodes; exaggerated startle response to auditory or tactile stimuli; episodic stiffness related to the startle; and exaggerated head retraction response upon tapping the nose-tip or mantle area [41, 42].

Shuddering attacks are paroxysmal involuntary muscle movements with a perception of cold occurring in infants and young children [43, 44]. The attacks typically occur in a sitting or standing position and are precipitated by excitement or frustration [42]. In contrast to breath-holding spells, there is apnea and no color change.

Congenital laryngeal stridor produces a characteristic inspiratory sound that is usually apparent in the first few days of life and rarely persists beyond one year of age.

Laryngospasm causes an inspiratory obstruction with a characteristic high-pitched inspiratory crowing sound and may result in apnea. The characteristic inspiratory crow is absent in breath-holding spells. Laryngospasm often occurs during sleep whereas a breath-holding spell always occur when the child is awake.

Although cyanosis may occur with whooping cough, the characteristic inspiratory whoop, fever, nasal discharge and paroxysmal cough are not seen in breath-holding spells [45].

7. LABORATORY EVALUATION

In the setting of a typical history and a normal physical examination, laboratory evaluation is usually not necessary in patients with cyanotic breath-holding spells. After all, there is no specific test to confirm the diagnosis. A complete blood count and serum ferritin should be performed if anemia is suspected. Electrocardiogram may be considered in children with frequent and severe breath-holding spells, especially those with pallid breath-holding spells whose ocular compression test is positive [11, 21]. The electrocardiogram helps to rule out a prolonged QT syndrome [3, 6, 11].

8. COMPLICATIONS

Breath-holding spells can be very distressful for parents and may have an adverse effect on their quality of life.⁴ Mother of children with frequent and severe breath-holding spells are more likely to suffer from anxiety, depression, and psychosocial problems [34, 44-46].

As far as the child is concerned, breath-holding spells are benign and no sequelae is expected [3, 11]. Brain metabolites such as choline, N-acetyl aspartate, creatine, and myoinositol as well as brain magnetic resonance spectroscopy of children with breath-holding spells have been shown to be normal [47, 48]. No neuronal damage has been demonstrated [47]. Affected children have normal intelligence and neurologic development [1, 2, 8]. The incidence of epilepsy is similar to that of the general population [1]. Rarely, children with breath-holding spells may develop vasovagal syncope at a later date [2, 49-51].

9. TREATMENT

Breath-holding spells are frightening and stressful to parents. Confident reassurance and frank explanation are cornerstones of treatment [1, 6, 52]. Advice regarding the handling of frustration, anger and discipline is appropriate [1]. Parents should be counseled to reduce sources of conflict, such as coercion in eating, premature bowel and bladder training, and excessive parental demands [52]. Parents should be advised to be tolerant and consistent in discipline.

It has been shown that iron supplementation in children with breath-holding spells and concomitant iron deficiency anemia or iron deficiency is effective in decreasing the frequency and severity of the breath-holding spells [12, 18-20]. Furthermore, the autonomic nervous system dysregulation in children with breath-holding spells can be improved by iron supplementation [18, 20]. A Cochrane review of two randomized and quasi-randomized controlled trials comparing iron supplementation with placebo or no therapy in 84 children with recurrent breath-holding spells showed that iron supplementation significantly reduced the frequency of breath-holding spells (odds ratio: 76.48; 95% confidence interval: 15.65 to 372.72; $p < 0.00001$) [53]. In a recent prospective study of 100 children aged 6 to 36 months with breath-holding spells, Jain *et al.* treated these children with elemental iron at a dose of 3 mg/kg/day as a single dose for 12 weeks [25]. Before iron supplementation, 60 patients had moderate anemia (hemoglobin 7 to 9.9 g/dL), 13 patients had mild anemia (hemoglobin 10 to 10.99 g/dL), and 27 children did not have anemia (hemoglobin ≥ 11 g/dL). At 12 weeks, 73% of children showed complete remission and 23% of children showed greater than 50% reduction in frequency of breath-holding spells. Of the 27 children without iron deficiency anemia, their response to iron supplementation was similar to those with iron deficiency anemia. This new finding warrants further investigations in randomized, placebo-controlled trials to further elucidate whether iron supplementation would benefit children with breath-holding spells without iron deficiency anemia. It has been shown that both umbilical cord milking and delayed cord clamping (clamping of the umbilical cord 2 to 3 minutes after birth or on stoppage of um-

bilical cord pulsations) help to decrease neonatal and childhood anemia. Such practice is especially important for the high-risk population where the prevalence of childhood anemia is high [54, 55].

Severe breath-holding spells can be very stressful. Interventions beyond iron supplementation may be considered for some of these children with severe and frequent breath-holding spells which have a strong impact on the life style of both the child and family. In children with pallid breath-holding spells, the use of atropine may be considered to block the vagal reflex if the attacks are frequent and severe and when there is evidence that the attack is secondary to cardiac asystole as indicated by a positive ocular compression test [1]. In a retrospective multicenter study of 84 children with severe pallid breath-holding spells, 45 children received atropine (0.01 mg/kg) in the form of 2% syrup of tincture of belladonna given twice a day and 39 children did not receive belladonna treatment [24]. The two groups of children had similar demographics with the single difference that children in the treatment group presented with more severe spells. Three months after treatment, two (5%) patients in the non-treatment group and 20 (44%) patients in the treatment group had complete remission of the spells ($p < 0.01$) [24]. No major adverse events were encountered. The authors concluded that belladonna is highly effective to alleviate severe pallid breath-holding spells. The recommended dose of atropine sulfate is 0.01 mg/kg/day (maximum 0.4 mg) in two divided doses given orally or subcutaneously [1, 24].

Glycopyrrolate, a synthetic quaternary ammonium compound, has an anticholinergic property that is longer-acting than atropine [56]. The medication has been used with success in the treatment of children with pallid breath-holding spells [56, 57]. The use of glycopyrrolate may be considered in those cases with severe, frequent pallid breath-holding spells associated with bradycardia [56].

Fluoxetine has also been used with success in the treatment of children with pallid breath-holding spells based on case reports [58]. Additional information is necessary before the use of fluoxetine can be considered in the treatment of children with severe and frequent pallid breath-holding spells.

Cardiac pacemaker implantation should be considered for children with pallid breath-holding spells associated with severe bradycardia that is associated with cardioinhibition during breath-holding spells and that is refractory to medical treatment [59-64]. The procedure should also be considered in children with cyanotic breath-holding spells associated with prolonged asystole [65].

Episodes of unconsciousness and convulsions associated with breath-holding spells that are of short duration are usually innocuous and should be treated by proper positioning to insure a patent airway and to prevent aspiration. Anticonvulsants are not indicated in children with this type of breath-holding spells.

Preliminary studies showed that piracetam (2-oxo-1-pyrrolidine) (40 to 50 mg/kg/day in two divided doses), a cyclic derivative of gamma-aminobutyric acid (GABA), is effective in reducing the frequency of breath-holding spells

[4, 66-68]. Piracetam can increase brain tissue oxygenation and increase the inhibitory hyperpolarizing processes like that of gamma-aminobutyric acid which may account for its effectiveness in the treatment of breath-holding spells [68]. In a prospective, double-blind placebo-controlled study, 40 children with breath-holding spells were randomized to receive either piracetam syrup in a dose of 50 mg/kg/day in two divided doses (n = 20) or placebo (n = 20) [68]. These children were followed up monthly for 4 months. Before treatment, the median number of breath-holding attacks/month was 5.5 in the treatment group and 5 in the control group. After treatment, the median number of breath-holding attacks/month was 1 in the treatment group and 5 in the control group. There was a significant decrease in the number of breath-holding attacks after piracetam treatment compared to placebo ($p < 0.001$). No adverse events were encountered. Further studies are necessary to confirm or refute these findings before this medication can be recommended for the treatment of severe cases of breath-holding spells.

Calik *et al.* successfully treated a 12-month-old male infant with a 3-month history of breath-holding spells, on average, 5 attacks per week with oral melatonin at a dose of 0.08 mg/kg once a day [69]. The medication resulted in a significant improvement in the breath-holding spells. Based on their experience, the authors suggested the use of melatonin in the treatment of children with breath-holding spells. Further studies need to be done to confirm or refute their findings before melatonin can be considered in the treatment of children with frequent and severe breath-holding spells.

Successful treatment of severe and frequent breath-holding spells with theophylline has also been described [57, 70]. Further studies are needed to confirm or refute the usefulness of theophylline in the treatment of severe and frequent breath-holding spells.

10. PROGNOSIS

Children with breath-holding spells have an excellent prognosis [1, 8]. As the child grows, the frequency of breath-holding spells decreases [23]. In most children, the spells disappear spontaneously by elementary school age [1, 11]. The prognosis is not altered by the duration or frequency of attacks.

CONCLUSION

Breath-holding spells are frightening events that occur most commonly in otherwise healthy children from 6 to 24 months of age. Although breath-holding spells are benign, they can be quite distressing to the parents. In most children, the spells disappear spontaneously by elementary school age. Confident reassurance and education of the family are cornerstones of treatment. Children with breath-holding spells have an excellent prognosis and have a normal intelligence and neurologic development.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

Professor Alexander Leung, Dr Amy Leung, Dr Wong, and Professor Hon confirm that this article has no conflicts of interest.

ACKNOWLEDGEMENTS

Professor Alexander K.C. Leung is the principal author. Dr. Amy A.M. Leung, Dr. Alex H.C. Wong, and Professor Kam Lun Hon are coauthors. All the authors contributed to drafting and revising the manuscript and approved the final version submitted for publication.

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