Long-term prognosis for children with breath-holding spells

Anne Lise Olsen[1], Rene Mathiasen[2], Niels Henrik Rasmussen[1] & Finn Ursin Knudsen[2]

ABSTRACT

INTRODUCTION: The aim of this study was to investigate the long-term prognosis for children with severe breath-holding spells (BHS).

MATERIAL AND METHODS: The study was a retrospective cohort study. Data from the medical records of all patients with severe BHS admitted during a ten-year period were recorded and a questionnaire was sent to the families. A matched group of adolescents with febrile convulsions served as controls (n = 289).

RESULTS: A total of 85 out of 115 families (73.9%) responded. The mean age of the included patients was 20.5 years. Among first-degree relatives 21.5% had BHS and 14.6% had epilepsy. The peak age for severe BHS was 16 months. The children had a total of 1-25 attacks. All electrocardiogram (ECG) recordings were normal. One child died of asystolia at the age of 20 years, ECG two weeks previously showed a WPW-block. Twenty-six (30.6%, $p < 0.001$) had fainting spells. Twenty-five (29.4%) had concentration problems. The grades achieved by BHD children at the final school exam did not differ from the mean values achieved by all children in the area.

CONCLUSIONS: In this study on the long-term prognosis of children with BHS, we found a predisposition to fainting spells as expected. We also found that 29.4% of children with BHS had concentration problems. Further follow-up studies are needed to confirm this trend.

Breath-holding spells (BHS) is a clinical entity that is easy to diagnose in its typical form. There are two clinical subtypes of breath-holding spells, which are based on the child's colour – the cyanotic (blue) and the pallid type [1, 2]. Severe BHS causes unconsciousness. About 4% of all children under the age of five years are affected [1].

Breath-holding spells usually resolve spontaneously with no long-term sequelae. In the literature it is generally agreed that the prognosis for breath-holding attacks is excellent, long-term prognosis is considered good and it is expected that the children will develop normally, except for an increased risk of developing syncope later in life. No other lasting sequelae of BHS have been described, but only a few long-term studies were published [1, 3, 4].

The aim of the present study was to examine in more detail the long-term prognosis of children with breath-holding spells.

MATERIAL AND METHODS

This was a retrospective study comprising a hospital cohort. Our local database was searched for all patients admitted with BHS between 1st January 1980 and 31st December 1989 at two neighbouring paediatric departments, at Glostrup and Gentofte University Hospitals both situated in the Copenhagen area. The inclusion criteria were: 1) A minimum of one typical attack of breath-holding spells, including either of the three forms, blue breath-holding spells, pallid breath-holding spells (reflex anoxic seizures or pallid infantile syncope) or the mixed type. 2) Residence in the uptake area, a well-defined part of Copenhagen with a population about 750.000. The exclusion criteria were 1) confirmed epilepsy, and 2) brain damage or severe mental and/or physical disability.

Data from medical records were recorded, including information on pregnancy, birth weight, birth length, gestational age, Apgar score, perinatal problems (i.e. asphyxia, hypoglycaemia, infection, respiratory distress), sex, psychomotor development, physical examination, neurological examination, blood tests, electrocardiography (ECG) and electroencephalography (EEG) and family history among first degree relatives regarding BHS, epilepsy and febrile convulsions. Data on BHS included type of BHS, frequency, associated phenomena, total number of spells and age at first and last BHS.

The parents completed a questionnaire regarding previous and present epilepsy, single afebrile convulsions, fainting, migraine, tension headaches, reading or writing problems, clumsiness, concentration problems, referral for specialized education classes, total number of BHS, and whether the child, according to the parent, had suffered permanent damage from BHS. We also asked about febrile convulsions, epilepsy or BHS among first degree relatives, and whether the child was a product of consanguineous mating. We asked about academic performance and the results at final exams, and whether the child left school after nine or ten years or later. Results at final exams after ten and/or nine years

ORIGINAL ARTICLE

1) Gentofte Hospital, Department of Paediatrics, Denmark, and
2) Glostrup Hospital, Department of Paediatrics, Denmark

Dan Med Bul 2010;57(11):A4217

TABLE 1

Epidemiological data for children with breath-holding spells and a control group (comprising children with febrile convulsions).

	BHS		Controls		
	n/N[a]	(%)	n/N[a]	(%)	p value
Perinatal problems	23/73	(31.5)	73/287	(25.4)	NS
Delayed psychomotor development	1/72	(1.4)	11/274	(4.0)	NS
Abnormal electroencephalography	10/62	(16.1)	33/262	(12.5)	NS
Slightly/moderatly abnormal	7/62	(11.2)	26/262	(9.9)	NS
Severely abnormal	3/62	(4.8)	7/262	(2.7)	NS
BHS in first degree relatives	17/79	(21.5)			–
Epilepsy in first degree relatives	12/82	(14.6)	15/287	(5.2)	0.023
Febrile convulsion in first degree relatives	2/85	(2.4)			–

BHS = breath-holding spells; NS = not significant
a) Number of patients with outcome variable/total number of patients.

TABLE 2

Long-term outcome parameters for children with breath-holding spells and a control group (comprising children with febrile convulsions).

	BHS		Controls		
	n/N[a]	(%)	n/N[a]	(%)	p value
Febrile convulsions	6/85	(7.1)	–	(3.9)[b]	NS
Epilepsy	0/84	(0.0)	6/268	(2.2)	NS
Fainting spells	26/85	(30.0)	17/269	(6.3)	< 0.001
Migraine	9/84	(10.7)	15/253	(5.9)	NS
Tension type headache	25/85	(29.4)	52/268	(19.4)	NS
Minor motor problems	10/85	(11.8)	28/246	(11.4)	NS
Specialized education	26/82	(31.7)	33/269	(12.3)	< 0.001
Concentration problems	25/85	(29.4)	–		

BHS = breath-holding spells; NS = not significant.
a) Number of patients with outcome variable/total number of patients; b) Incidence in the Danish childhood population [6].

were compared with the mean values for the population of the area.

Data collection took place between February 1 2003 and July 1 2003. The mean age of the children at the time of data collection was 20.5 years (range = 14.7-27.9). Children from our previous study on febrile convulsions [5] served as controls, as they had a similar age distribution, were recruited from the same area of Copenhagen, and were admitted to the same paediatric departments. It is well documented that children with febrile convulsion have an excellent prognosis and are comparable with children in general [5]. When available, data for the background population in the area were used for further comparison. Data were analysed using Pearson's χ^2 test.

The local ethical committee approved the study.

RESULTS

A total of 125 patients were admitted with the diagnosis of BHS during the ten-year period covered by the study. Ten patients were excluded due to emigration (n = 2), unknown home address (n = 2), unconfirmed diagnosis (n = 2), death during follow-up (n = 2, see below), psychomotor retardation (n = 2) (neurofibromatosis I (n = 1), shaken baby syndrome with subdural haematoma and retinal bleedings (n = 1).

Two patients died during follow-up, both had pallid spells, none of them had an ECG performed during the time they were admitted to hospital for BHS. One died in a traffic accident unrelated to BHS, and the other due to ECG-verified asystoly at the age of 20 years, following two months of near-fainting attacks. This patient suffered no verified cardiac problems during childhood or adolescence. Resuscitation attempts in the outpatient clinic were unsuccessful. ECG two weeks previously revealed a Wolf-Parkinson-White (WPW)-block with a short PQ-interval, slightly broadened QRS-complexes and delta waves in the standard recordings.

Among the 115 questionnaires sent, 85 families (73.9%) to 34 girls and 51 boys responded. The mean birth weight was 3,212 g, (range: 1,500-4,400 g), (n = 78), the mean birth length was 50 cm (range: 44-56 cm), (n = 70), mean gestational age was 39 weeks (range: 30-43 weeks), (n = 50). The proportion with perinatal problems was 31.1% versus 25.9% in the controls, and did not differ from the values observed in the normal population. In the BHS group 17 first-degree relatives (21.5%) had BHS and 12 (14.6%) had epilepsy, i.e. much higher incidences than in the background population (**Table 1**).

A total of 38 (44.7%) had blue BHS only, 13 (15.3%) had pallid BHS only, nine (10.6%) had the mixed form and 25 (29.4%) could not be classified. Age of onset ranged from one to 55 months, and the spells resolved spontaneously at the age of 18-96 months. A total of 5.5% had BHS before the age of one month, 11.0% before the age of three months and 18.8% before the age of six months, 44% within 12 months, 84% within 24 months, and only 2% (two children) at the age of 48 months or more. The peak age was 16 months. The children had a total of 1-25 attacks. A total of 29% had only a single attack, 11% two attacks, 7% three attacks, 39% had 4-7 attacks and only 14% suffered eight or more attacks.

Neurological examination performed during the hospital stay was normal in all children.

Haemoglobin was measured in 25 children and was normal in 23 and slightly below normal in two.

All ECG recordings were normal (14/14), and there were similar incidences of abnormal EEG findings in the two groups, 16.1% versus 12.5% (Table 1). No children in the BHS group developed epilepsy.

Twenty-five (29.4%) had previously had or currently suffered regular headaches (not including migraine) and nine (10.7%) suffered or had suffered from migraine (**Table 2**).

In the BHS group, the mean grade achieved at the official final exam after attending school for nine years (using a scale ranging from 0 to 13) was 8.11 (range: 6.70-10.90) (n = 44), this did not differ significantly from the mean value for the normal population 8.18, range not available, (n = 14,713).

After ten years of schooling, the official final exam grades of the children with BHS (mean 8.05, range 6.50-10.40) were not different from the mean values observed in the whole area (mean 7.99, range not available, n = 2,461).

In nine (10.6%), academic performance was reduced and 26 (31.7%) needed to attend specialized education classes (Table 2).

The parents of 25 children (29.4%), 13 girls (38% of all girls) and 12 boys (23% of all boys), confirmed that their child had experienced concentration problems.

The distribution of BHS types did not differ in this gruop compared to the group without concentration problems. A total of 48% had blue BHS only versus 43% in the group without concentration problems; 16% versus 15% had pallid BHS only; 16% versus 5% had the mixed form; and 20% versus 33% could not be classified.

Comparing the number of attacks in the two groups, we found that 28% of the children in the group with reported concentration problems had one attack versus 30% in the group without concentration problems; 12% versus 10% had two attacks; eight versus seven percent had three attacks; 28% versus 43% had 4-7 attacks and 24% versus 10% had more than eight attacks.

Breath-holding spells usually resolve without long-lasting sequale. Photographer: *Anne Lise Olsen.*

DISCUSSION

We found a similar distribution between pallid, blue, mixed and not classified spells to that reported in previous studies [1, 3, 4]. There were no significant differences in perinatal data when comparing the BHS group to a normal birth-cohort or to the control group. No significant perinatal problems were reported.

It has been suggested, that iron deficiency may play a role in the pathogenesis of BHS [7, 8] but in this study 25 children were examined, 23 of whom had a normal haemoglobin level. The patient who died aged 20 from undiagnosed WPW, draws attention to the importance of performing an ECG, at least in all children with pallid BSH, in order to identify prolonged QT-syndrome or other cardiac arrhythmia [2].

Our results confirm the previously established familial tendency to BHS [1, 4]. We also found a familial tendency to epilepsy (Table 2), which has not been described in previous follow-up studies.

The long-term outcome in this study confirms the predisposition to fainting spells [1, 3, 4]; there were 26 children (30.6% in the BHS group versus 6.3% of the controls, $p < 0.001$) who later developed fainting spells.

In a prospective study performed in 2001, DiMario found that four of 95 children with BHS were in special education classes [4]. Haverkamp & Noeker evaluated cognitive performance in 28 patients, and found no significant difference in cognitive performance between patients and siblings [9].

32% of the children in our study needed specialized education. Nevertheless, they achieved a normal exam result, which may be the result of the special education received, or a result of cohort selection. Although in our experience most of the children with severe BHS are admitted to hospital. We have not been able to compare the need for specialized education in our population, with the need in an unselected population, but a contemporary Danish study has shown similar frequencies among children in the same area who were referred to a school-psychologist; 29,7% of these children received specialized education during nine years of school attendance [10].

Lombroso & Lerman and Laxdal et al stated that ‘‘breath-holders” are frequently stubborn, disobedient, aggressive, hyperactive and irritable [1, 3].

We found that 29.4% of the children had concentration problems. We did not reveal considerable differences when comparing the types of BHS found in this group to those found in the group without concentration problems. The proportion of children who had more than eight attacks in the group with concentration prob-

lems was slightly higher than in the other group, but when we compared children who had more than four attacks, proportions were similar 52% versus 53%.

We did not ask specifically about attention deficit hyperactive disorder, and we did not use a specific rating-scale, and this may be considered limitations of this study.

CONCLUSION

In this study on the long-term prognosis of children with BHS we found a predisposition to fainting spells as expected. We also found a familial tendency to epilepsy, which was not described in previous follow-up studies.

Furthermore, almost a third (29.4%) of the children with BHS reported that they had concentration problems. We were unable to find any differences between the types and frequencies of attacks in the children with concentration problems compared with the children who did not report concentration problems. Further follow-up studies are needed to evaluate our findings.

CORRESPONDENCE: *Anne Lise Olsen*, Peblinge Dossering 16, st. tv., 2200 Copenhagen N, Denmark. E-mail: fugl@dadlnet.dk.

ACCEPTED: 3 August 2010

CONFLICTS OF INTEREST: None

LITERATURE

1. Lombroso CT, Lerman P. Breath holding spells (cyanotic and pallid infantile syncope). Pediatrics 1967;39:563-81.
2. Galen N, Breningstall MD. Breath-holding spells. Pediatr Neurol 1996; 14:91-7.
3. Laxdal T, Gomez MR, Reiher J. Cyanotic and pallid attacks in children (breathholding spells). Dev Med Child Neurol 1969;11:755-63.
4. DiMario FJ Jr. Prospective study of children with cyanotic and pallid breath-holding spells. Pediatrics 2001;107:265-9.
5. Knudsen FU, Paerregaard A, Andersen R et al. Long term outcome of prophylaxis for febrile convulsiones. Arch Dis Child 1996;74:13-8.
6. Vestergaard M, Christensen J. Register-based studies on febrile seizures in Denmark. Brain Dev 2009;31:372-7.
7. Boon R. Does iron have a place in the management of breath holding spells? Arch Dis Child 2002;86:77-81.
8. Kolkiran A, Tutar E, Atlay S et al. Autonomic nervous system function in children with breath-holding spells and effects of iron deficiency. Acta Pediatrica 2005;94:1227-31.
9. Haverkamp F, Noeker M. Traditional view empirically revisited: normal intellectual functioning in breath-holding spells. Eur J Pediatr 1998;157: 354.
10. Egelund N. Various measures during 9 years of schooling. Tidsskrift for pædagogisk psykologi og rådgivning 1981;18.1:21-44.