

Iron supplementation reduces the frequency and severity of breath-holding attacks in non-anaemic children

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Abstract

Iron supplementation reduces the frequency and severity of breath-holding attacks (BHAs), particularly in children with iron deficiency. The issue of iron supplementation is less clear for Westernized children with BHAs who present to an outpatient community clinic and are not iron-deficient. The first case series of iron-replete children with frequent and disabling breath-holding attacks who have responded to a course of oral iron supplementation is reported. This intervention is safe, improves quality of life for both child and carer, and is significantly cost-effective in terms of health resource utilization.

Introduction

For several years, the medical literature has associated the incidence of breath-holding attacks (BHAs) in children with iron deficiency.¹⁻³ A recent Cochrane Systematic Review suggests that iron supplementation reduces the frequency and severity of breath-holding attacks, particularly in children with iron deficiency (OR 76.48; 95% CI 15.65 to 373.72; $P < 0.00001$).⁴ Due to study design, trial limitations and the populations studied (high rate of consanguinity and an up to 10% prevalence of haemoglobinopathy), the issue of iron supplementation is less clear for Westernized children with breath-holding attacks (BHAs) who present to an outpatient community clinic and are not iron-deficient.

I wish to report a small case series of iron-replete children with frequent and disabling breath-holding attacks who have responded to a course of oral iron supplementation in my practice.

Case Reports

Case #1

A 2-year-9-month-old girl presented with

mostly pallid BHAs every three days since the age of 8 months and associated loss of consciousness with attacks. Electrocardiogram (ECG) and electroencephalogram (EEG) were both normal. Paternal aunt had childhood BHAs. Haemoglobin at end of trial was 145 g/L. Subsequent BHAs was not associated with loss of consciousness.

Case #2

A 15-month-old boy presented with mixed cyanotic and pallid BHAs since the age of 3 months. He had 2-8 episodes per day, with transient loss of consciousness, triggered at the onset of tantrums or if his father leaves the room. He had no thalassaemia, his ECG and EEG were both normal, and no family history of BHAs was found. Reduction in BHAs to one every 2-3 days was noted at 8 weeks, to one every 3 weeks at 12 weeks of treatment. No loss of consciousness with further BHAs was noted. The father is now able to leave child's side and child placed into day care.

Case #3

A 2-year-2-month-old boy presented with predominantly cyanotic BHAs for the past three months. Highly anxious mother calls an ambulance with each BHA, usually once every fortnight. BHAs were provoked by minor trauma or reprimand, he had no thalassaemia, and his ECG and EEG were normal. He had no family history of BHAs. We noted a reduction in BHAs to one in every six weeks, with no loss of consciousness now. Ambulances were no longer called.

All children were administered elemental iron at 5mg/kg/day for a period of three months (12-16 weeks) in divided doses, as per the Cochrane protocol.⁴ Compliance was monitored from medication usage (prescription refills and the presence of black stools) and patients reviewed at 4-6 weekly visits. A BHA diary was kept from baseline until the end of the treatment period. All children tolerated the oral iron supplementation for the three months and no adverse events were reported (such as possible gastro-intestinal intolerance).

From Table 1, there was a 67-99% (mean 86%) reduction in the frequency of BHAs from baseline. In all cases, the severity (progression to loss of consciousness) was reduced. From follow-up parental reports, this effect has been maintained after the iron supplementation was ceased at 12-16 weeks. Parents and child care workers also reported improvements in the child's behaviour.

While children with BHAs are expected to outgrow this condition by the age of seven to eight years,⁵ some will also do this from the age of three-to-four years. However none of the children in this series fall into this age bracket, and the dramatic reduction in episodes over three months appears swift, so the effect is

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considered attributable to the iron intervention rather than ageing.

While the number of cases is small and the intervention is not blinded or controlled for with a placebo, the magnitude of the results and clinical outcomes warrant further study. This finding is significant as it is the first documented case in the medical literature of *non-iron deficient* children with BHAs responding to a trial of iron supplementation. It is also the first published case reports of BHAs in an Australian population. To study this effect further, an application for an NHMRC-funded multicentre double-blinded placebo-controlled randomized control trial in an Australian setting has been submitted.

The cost-effectiveness (and tolerability) of the intervention cannot be ignored. From 1 July 2011 in NSW, the cost of an ambulance call-out is A\$320 + \$2.89 per kilometer to the nearest hospital (up to a total cost of A\$5248).⁶ For case C, whose parents called an ambulance out on three occasions within one month, this cost is considerable (at least \$1000) in comparison with the price of a bottle of Ferro-liquid at A\$15. Freeing up health resources ever under high demands has benefits to our society beyond monetary costs. Similarly, the quality of life gained for the caregiver and child is considerable as the BHAs resolve.

Although investigations, such as an EEG, ECG and haemoglobin electrophoresis, were carried out in these cases, the diagnosis of breath-holding attacks is a clinical one made on a typical history, which all of these children met. Frequently these other investigations are performed for differential diagnostic purposes and prior to presentation at the initial clinic visit.

Iron deficiency is implicated in conditions other than anaemia (a late manifestation) and BHAs. It is increasingly recognized to be a

Table 1. Patient demographics and effect of iron supplementation on breath-holding attacks.

Case	Gender	Age at clinic presentation (months)	Ethnicity	Family history of BHAs	Baseline Hb (g/L)	Av BHA frequency (No. per week)		% reduction
						Before	After	
A	F	31	Anglo-Saxon	Y	106	2.3	0.17	93%
B	M	15	Asian	N	112	35	0.33	99%
C	M	14	Arabic	N	120	0.5	0.17	67%

BHAs, breath-holding attacks

cause of restless legs, febrile seizures, thrombosis, impaired immunity and poor behaviour.⁷ It is known that children who have experienced BHAs may become adolescents with syncope episodes. A recent retrospective cohort study also showed a 29.4% incidence of concentration problems.⁸

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