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Retinal haemorrhage in infants with pertussis

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ABSTRACT

Aims It has been hypothesised that paroxysmal coughing in infantile pertussis (whooping cough) could produce retinal haemorrhages identical to those seen in abusive head trauma. We aimed to test this hypothesis.

Methods This is a prospective study of infants hospitalised with pertussis in Auckland, New Zealand, from 2009 to 2014. The clinical severity of pertussis was categorised. All infants recruited had retinal examination through dilated pupils by the paediatric ophthalmology service using an indirect ophthalmoscope.

Results Forty-eight infants with pertussis, aged 3 weeks to 7 months, were examined after a mean of 18 days of coughing. Thirty-nine had severe pertussis and nine had mild pertussis. All had paroxysmal cough, and all were still coughing at the time of examination. No retinal haemorrhages were seen.

Conclusions We found no evidence to support the hypothesis that pertussis may cause the pattern of retinal haemorrhages seen in abusive head trauma in infants.

What is already known on this topic?

- Retinal haemorrhages are common in paediatric abusive head trauma.
- It has been hypothesised that pertussis may produce retinal haemorrhages, but no retinal haemorrhages were seen in one study of 35 infants with pertussis.

What this study adds?

- This study investigated 48 infants, most of whom had severe pertussis. No retinal haemorrhages were seen.
- These findings add further clinical evidence against the hypothesis that paroxysmal coughing causes severe retinal haemorrhages.

INTRODUCTION

Retinal haemorrhages are frequently described in paediatric abusive head trauma. The orthodox view of their pathophysiology is that they are a direct consequence of head trauma, with vitreoretinal traction playing a major role.[1]

In 2006, Geddes and Talbert suggested that paroxysmal coughing from any cause (in effect, high pressure Valsalva manoeuvres) could cause a sustained rise in intracranial pressure. They hypothesised that this might be sufficient to cause retinal and subdural bleeding identical in appearance to abusive head trauma.[2] Their hypothesis was based on considerations of vascular anatomy, early case reports of subdural haemorrhage in pertussis and computer modelling. Importantly, they noted that there are no reports, either clinical or postmortem, of retinal haemorrhages in children with pertussis.

Pertussis, caused by infection with the Gram-negative bacterium *Bordetella pertussis*, is characterised by bouts of paroxysmal coughing. In many countries, low rates of pertussis would make it difficult to test the hypothesis that pertussis causes retinal haemorrhage. In New Zealand, the infant pertussis hospitalisation rate (2000–2009 average annual rate: 196/100 000) is more than three times higher than that reported from the USA.[3] As a result, New Zealand was a suitable location to study whether retinal haemorrhages occur in infants with pertussis.

Our aim was to test the Geddes and Talbert hypothesis by determining the frequency of retinal haemorrhage in infants with paroxysmal coughing due to pertussis.

METHODS

This prospective study was conducted in Auckland, New Zealand. Between October 2009 and December 2014, infants of 12 months or less admitted to two children's hospitals in Auckland (Starship and Kidz First) were eligible for recruitment if pertussis was diagnosed. Written informed consent was obtained from the parents. Enrolled infants were examined by the paediatric ophthalmology service using the gold standard technique: indirect ophthalmoscopy through pharmacologically dilated pupils. If retinal haemorrhages were found, the study included a protocol for RetCam photography and further investigation (including assessment for non-accidental injury) as indicated. Pertussis was confirmed if the infant received a clinical diagnosis of pertussis by the admitting paediatrician resulting in an International Statistical Classification of Diseases and Related Health Problems 10th Revision discharge code for pertussis. Laboratory confirmation of *B. pertussis* infection was by culture and/or PCR.

Clinical notes were reviewed, and demographic factors (age, gender, ethnicity), birth history, immunisations and medical history were recorded. Pertussis severity was categorised using the scale of Préziosi and Halloran.[4] This scale applies a numerical score for the presence of clinical signs: severity of cough (typical paroxysms with whoops 4, typical paroxysms without whoops 3, atypical paroxysms only 1); apnoea 6; pulmonary signs 3 (bronchitis or bronchopneumonia as diagnosed by a physician on auscultation); mechanical complication 3 (subconjunctival haemorrhage, or umbilical or inguinal hernia); facial swelling 3; conjunctival injection 3;

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Table 1 Pre-existing conditions among the 48 infants hospitalised with pertussis

Medical condition	n	Percentage of cohort
Delivery prior to 37 weeks' gestation	9	19
Cardiac condition	4	8
Respiratory condition	2	4
Neurological condition	2	4
Intrauterine growth retardation	1	2
Inguinal hernia	1	2

and post-tussive vomiting 2. A score of more than 6 represents severe disease.

Ninety-five per cent CIs for the proportion of patients with retinal haemorrhage were calculated by Wilson's method.

RESULTS

Forty-eight infants were recruited, of whom 24 were male. The mean age was 2.2 months (range 0.75–7.0). The sample was ethnically diverse: Māori (New Zealand indigenous population) (n=18, 38%), Pacific (n=17, 35%), European (n=10, 21%) and Asian (n=3, 6%). Most (n=34, 71%) were unimmunised. Thirty-eight (79%) had no pre-existing conditions and 10 (21%) had pre-existing conditions, as shown in table 1.

In all cases, pertussis was confirmed by PCR (n=44, 92%) and/or culture (n=19, 40%). Thirty-nine infants (81%) had severe pertussis and nine (19%) had mild pertussis. The mean severity score for the entire cohort was 10. All cases had severe cough: 15 (31%) had typical paroxysms with whoops, 32 (67%) had typical paroxysms without whoops and 1 had atypical paroxysms. Complications of pertussis were present in 41/48 (85%) (table 2).

Ophthalmoscopy was performed by seven consultant ophthalmologists (42 cases), two fellows in ophthalmology (4 cases) and one senior registrar in ophthalmology (2 cases). No infant had retinal haemorrhages (0/48, 95% CI 0.0% to 7.4%). The mean duration of cough by the time of ophthalmoscopy was 18 days (range 4–57 days). Infants were examined a mean of 11 days from admission (range 2–58). All were still coughing at the time of ophthalmoscopy. For the infant examined on day 58, it was day 14 of their cough. This was an ex-preterm infant who contracted pertussis while already a long-standing inpatient for chronic lung disease.

DISCUSSION

We identified no retinal haemorrhages in 48 infants hospitalised with pertussis. This absence of retinal haemorrhages is consistent with the one previous study that also examined the frequency of retinal haemorrhages in pertussis and found none in a cohort of 35 infants in Spain.[5] That study did not describe disease severity.

Table 2 Complications of pertussis among the 48 infants hospitalised with pertussis

Complication	Infants (n)	Percentage of cohort
Apnoea	38	79
Pneumonia	18	38
Hernia	2	4
Seizures	2	4
Failure to thrive	1	2
No complications	7	15

Most infants in our cohort (39/48, 81%) had severe pertussis. All had paroxysmal cough. According to the hypothesis of Geddes and Talbert, this should cause sustained increase in intracranial pressure. Despite this, no retinal haemorrhages of any description were present.

On average, infants were examined on the 18th day of their cough. Although we cannot exclude the possibility that haemorrhages present earlier had resolved by the time of examination, these infants remained in hospital because of the severity of their persistent cough. If there is substance to the hypothesis, one would expect the risk of haemorrhage to continue as long as repetitive paroxysmal cough persists. Abusive head trauma typically causes severe, bilateral, multilayered retinal haemorrhages. In abusive head trauma, intraretinal haemorrhages usually resolve within 1–2 weeks, but preretinal haemorrhages persist for up to 111 days.[6] If paroxysmal coughing causes retinal haemorrhages identical to abusive head trauma, one would expect them to remain visible in infants for similar periods of time after coughing has ceased.

Our paper replicates and expands the findings of the Spanish study.[5] In two studies of pertussis now involving a combined total of 83 infants, one in Europe and one in the Western Pacific, no retinal haemorrhages have been found (0/83, 95% CI 0.0% to 4.4%). We conclude that there is no clinical evidence to support the hypothesis that paroxysmal coughing may cause the pattern of retinal haemorrhages seen in paediatric abusive head trauma.

Our study cannot entirely exclude the possibility that some form of retinal haemorrhage might be caused by pertussis. First, it is possible that minor retinal haemorrhages might have been missed on examination. Second, even when combined with the Spanish study, these are not large numbers. However, it may be difficult to obtain ethics approval to subject sick infants to further such studies when there is no clinical evidence for the validity of the Geddes and Talbert hypothesis.

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Contributors NR analysed the data, wrote the first draft of the manuscript and approved the final manuscript. SP was the primary investigator during the study, collected most of the data, double-checked the data analysis and approved the final manuscript. SD helped design the study, performed or supervised the ophthalmoscopy and approved the final manuscript. JN contributed to data collection and approved the final manuscript. CCG helped design the study, edited the draft manuscript and approved the final manuscript. PK designed the study, contributed to data collection, supervised and reviewed the data analysis, revised the draft manuscript, and approved the final manuscript.

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