Dysphonia in Very Preterm Children: A Review of the Evidence

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Key Words

Voice disorders · Dysphonia · Infant, premature · Infant, extremely premature · Child

Abstract

Introduction: Intubation is a known risk factor for dysphonia yet is essential in the perinatal care of many very preterm infants. Children born preterm, who are frequently resuscitated with endotracheal intubation, may be at risk of dysphonia at school age and beyond. **Objectives:** To identify and describe the evidence pertaining to long-term voice outcomes and risk factors for developing dysphonia in preterm children. **Results:** In addition to case studies and series, three larger-scale studies have reported on dysphonia and voice outcomes in preterm children. Studies reporting treatment outcomes were not available. Factors associated with poor voice outcomes included female gender, birth weight <1,000 g, birth at <27 weeks' gestation, surgical closure of patent ductus arteriosus, emergency versus elective intubations and multiple intubations. Adverse voice outcomes were associated with laryngeal pathology and compensatory supraglottic compression. **Conclusions:** Dysphonia is a

newly reported, long-term complication of preterm birth, yet the number of relevant studies remains limited. Further research is required to confirm the risk factors for developing dysphonia, which will inform future voice treatment studies.

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Introduction

A voice is considered dysphonic when it differs perceptually from norms associated with gender, age, stature and culture, or when it impedes the activities of daily living [1]. Dysphonia may arise as a primary condition, or secondary to disease, illness or structural abnormality [1]. Aetiology of dysphonia may be: (i) organic, resulting from structural anomalies in the respiratory and phonatory systems attributable to a known disease, disorder or injury; (ii) functional, resulting from the way in which the structures are used and cared for by the voice user, or (iii) psychogenic, meaning the absence of any identifiable physiological cause for the voice disorder, with individuals having a normally-appearing larynx [2]. However, such causes are not exclusive and likely to be co-morbid

and complex. For example, early changes in the structures of the larynx can occur with dysfunctional voice production, while hyperfunctional strategies to initiate and sustain phonation occur when individuals attempt to produce a more perceptually acceptable voice to compensate for structural abnormalities [2]. Iatrogenic causes of dysphonia, such as from endotracheal intubation, are also reported. But incidence figures prove difficult to calculate due to the varying nature of the underlying medical conditions and the treatments instituted [3].

The true incidence of dysphonia in childhood continues to be debated. An incidence of observable laryngeal abnormality of 30.3%, using objective endoscopic evaluation, has been reported in children aged 7–16 years, with a greater number of male children affected [4]. Using more subjective perceptual evaluation methods, incidence of up to 38% has been found in children aged 6–10 years, with slightly more girls affected than boys [5].

Children with dysphonia demonstrate insight into their voice disorder from a young age [6]. Affected children report anger, sadness and frustration with their voices, in addition to physical symptoms such as pain and running out of air while speaking [6, 7]. Reports of emotional difficulties increase in adolescence, as do complaints of limitations in activities requiring vocal participation [6]. Listeners, including children, adolescents, teachers and speech-language pathology students, make adverse judgements about children with dysphonia [8, 9]. These judgements extend to non-voice-related personality traits, suggesting that societal prejudices against children with dysphonia are pervasive. Thus childhood dysphonia may significantly impact on social, academic and, consequently, employment outcomes.

Invasive ventilation procedures have been associated with potentially serious and permanent laryngeal sequelae in preterm children [10]. Six studies have identified dysphonia as a symptom of laryngeal pathology following intubation in preterm children [11–16]. Avulsion, scarring, oedema and lesions of the vocal folds have been described [11, 13, 16]. Injury to the cricoarytenoid joint, such as subluxation or fixation, resulted in decreased vocal cord movement [13]. Dysphonia has also been identified as a symptom of acquired airway pathology, including subglottic stenosis and subglottic cysts [11, 12, 14, 15]. Surgical management of such pathology may also result in dysphonia [15]. Surgical ligation of patent ductus arteriosus (PDA) in infancy has been associated with left vocal cord paralysis resulting from accidental resection of the left recurrent laryngeal nerve, which may cause dysphonia [17]. One study reported a case of an adolescent

female using supraglottic phonation as a compensatory voicing strategy secondary to ablation and scarring of the left aryepiglottic fold and vocal cord [11]. Thus, the possibility that adverse voice outcomes may be associated with maladaptive, hyperfunctional voicing behaviours must also be considered. Other causal factors may exist, but the majority of laryngeal injuries reported in the literature to date are the result of intubation.

While there was inconsistency of assessment methodologies between studies, the reports lend further support to the hypothesised link between laryngeal pathology and adverse voice outcomes. Preterm children with a history of intubation should therefore be considered at high risk of dysphonia, as injuries to the airway have been reported in up to 61% of survivors on extubation [16]. Whilst there is evidence regarding laryngeal injury following intubation in preterm children, the translation of this to functional voice outcomes is less clear. This review summarises the literature pertaining to dysphonia in preterm children: incidence and risk factors are discussed, and questions for future research proposed.

Results

Three large-scale observational studies reporting on the incidence of dysphonia in preterm children were identified [18–20]. There were no studies reporting treatment or therapy outcomes. The three studies report on cohorts of extremely preterm children. The literature does not yet extend to voice outcomes in very (28 to <32 weeks' gestation) or moderate-to-late (32 to <37 weeks' gestation) preterm children. A summary of the findings can be seen in table 1.

Discussion

Risk Factors

Dysphonia was found to be associated with extreme prematurity, extremely low birth weight and emergency intubation procedures. There was a strong association with gender and frequency of re-intubation.

While the study of Røksund et al. [19] was limited to a subsection of the extremely preterm population, the studies of Garten et al. [20] and French et al. [18] had access to the entire cohort of NICU discharges in the respective study centres, so selection bias is unlikely. Common factors associated with dysphonia across those studies were birth at <27 weeks' gestation, birth weight <1,000 g and

Table 1. Summary of voice outcomes in extremely preterm children

Study details	Sample size	Inclusion criteria	Exclusion criteria	Dysphonia incidence	Assessment methodology	Risk factors
Garten et al. 2011 [20]	645	All infants with birth weights <1,500 g admitted to NICU between January 1998 and May 2006	Nil	6.6%	Retrospective review of electronic charts and hardcopy documents for diagnoses relating to laryngeal dysfunction Children identified were assessed by a speech pathologist using an in-house categorisation No specific comment as to inter-rater reliability: all children identified by chart review were found to have dysphonia	Birth weight <1,000 g History of endotracheal intubation Gestational age <28 weeks Complicated intubations
Røksund et al. 2010 [19]	13	≤28 weeks' gestational age <i>or</i> ≤1,000 g birth weight 1982–1985 birth dates	Co-morbidities	54%	Self-report of voice difficulties, informal assessment of weakness or hoarseness of voice No reliability assessment	Surgical ligation of patent ductus arteriosus Lower birth weight Longer periods of ventilation and oxygen treatment
French et al. 2013 [18]	67	<25 weeks' gestational age 1996–2004 birth dates	Known disability likely to preclude participation in assessment tasks	58% (moderate to severe)	Prospective clinical assessment: perceptual evaluation (GRBAS) and quality-of-life questionnaire (pVHI) Intra- and inter-rater reliability was moderate	Female gender >5 episodes of re-intubation

GRBAS = Grade, Roughness, Breathiness, Aesthenia, Strain Scale; pVHI = Pediatric Voice Handicap Index.

intubation. The risk factor of number of re-intubations identified by French et al. was not similarly found by Garten et al., yet the median number of intubations was higher in the infants with dysphonia than in the case controls. The variable found in the Garten et al. study, a complicated procedure, was not replicated in the French et al. study due to incomplete documentation, suggesting that the quality of recording may be a potential limiting factor in risk identification. It is clear that intubation is a major contributing factor to voice outcomes in preterm children, but further investigation of intubation variables in this population is required.

One unique finding was the association between female gender and increased risk of dysphonia at school age. This is the first such finding reported in the literature and the study authors were not able to offer an explanation for this. Childhood voice disorders are more common in males than females in term-born populations, with most cases attributable to voice overuse [4]. However, the underlying cause of dysphonia in the extremely preterm cohort appears to differ from that in term-borns. One possible explanation is hormonal differences affecting laryngeal anatomy. In addition, females may more readily adopt compensatory, supraglottic tightening when producing voice, resulting in a strained vocal quality. This finding of susceptibility of females must be further investigated.

Dysphonia was identified in greater than half of extremely preterm individuals undergoing surgical ligation of PDA in the study by Røksund et al. [19]. Dysphonia was also reported in individuals with a clinically significant PDA who did not undergo ligation, suggesting an as yet unexplained potential link between the presence of PDA and voice problems.

Mechanisms of Aetiology of Dysphonia in Preterm Infants

Mechanisms of aetiology of dysphonia in preterm infants are difficult to discern from the research conducted to date (table 1). The strong association with intubation factors may be due to movement of the tracheal tube in situ or unplanned extubation due to infant restlessness and agitation leading to structural damage [21, 22].

Røksund et al. highlight the role of surgical ligation of PDA in the development of dysphonia. Surgical ligation of PDA is often performed when attempts at pharmacological closure are unsuccessful, yet other factors associated with persistence of PDA, such as the development of pulmonary disease, may also influence voice outcomes. A quarter of participants in that study who did not undergo surgical ligation complained of voice symptoms, and the French et al. study found a high incidence of dysphonia, but a low rate of surgical treatment of persistent PDA (4 out of 154 cases). Thus it appears that the procedure itself

is not the only factor relevant to voice abnormalities, and voice outcomes of infants with a clinically significant PDA should be investigated.

None of the studies investigated hyperfunctional voicing behaviour as a possible cause or contributor to the development of dysphonia. Hyperfunctional strategies may be present in such a population to compensate for structural abnormalities, exacerbating the original condition.

Hyperfunctional voicing behaviour consisting of supraglottic constriction can only be reliably detected on fibreoptic endoscopic evaluation of the larynx. This procedure was performed in one study to assess the status of the left vocal cord, and as such no assessment of vocal hyperfunction was reported [19]. This review suggests that further research which includes visualisation of the larynx to better elucidate the mechanisms underlying dysphonia in preterm children is warranted.

Challenges of Voice Assessment

The incidence of dysphonia identified by clinical assessment of voice is higher than that identified by retrospective chart review. The studies utilising clinical voice assessment yielded similar incidence figures, suggesting that this is a more reliable method of diagnosing voice disorders and may be preferable in future studies.

However, there is no consensus regarding an appropriate clinical assessment approach in childhood dysphonia. Expert consensus guidelines recommend assessment in three key areas of voice: perceptual evaluation of voice quality, acoustic analysis of the properties of the voice signal, and a quality-of-life assessment [23]. Acoustic analysis is essential in the evaluation of voice quality, as acoustic assessments are unbiased and more sensitive to change than perceptual instruments, but is rarely reported in the paediatric literature. Each of the three studies used differing methodologies for perceptual assessment of voice quality, ranging from a subjective comment to a standard assessment tool. No study reported any objective acoustic measures. Two studies reported on quality-of-life outcomes, with dysphonia severity being associated with greater impact on affected individuals' quality of life. Controversy regarding a standardised assessment battery for dysphonia may persist, but future studies should include all three types of assessment to completely describe the nature and extent of dysphonia and its effects on preterm children. Further, in children with dysphonia, laryngoscopic assessment of voice production is desirable, to identify the precise mechanisms underlying the vocal dysfunction.

Future Research Directions

The following factors have been found to be associated with dysphonia in preterm children: low birth weight, extreme preterm birth, gender, frequency of re-intubation, complicated episodes of intubation and surgical ligation of PDA. The main foci of the three studies were demographic and iatrogenic variables. None of the studies investigated co-morbid medical conditions associated with prematurity, such as cerebral palsy which is known to affect speech and voice. One study reported the correlation between respiratory variables and left vocal cord paralysis, with positive findings, suggesting a potential link between respiratory health and dysphonia which should be further explored.

All the participants in the reviewed studies were born extremely premature, yet the risk factors identified are not limited to extremely preterm infants. The possibility that other preterm, or term, children with a similar history, develop dysphonia cannot be excluded. Further, all participants were intubated. The incidence of dysphonia in preterm children without a history of intubation should be explored.

Whilst some extremely preterm infants present with dysphonia, the protective effect of hyaluronic acid in infant vocal folds, and its role in tissue regeneration following phonotrauma, may mask laryngeal damage that may not fully declare until the layers of the vocal fold lamina propria begin to differentiate [24]. Dysphonia in infancy is not necessarily predictive of dysphonia at school age as individuals can develop dysphonia with increased language load at the time of emergence of speech or to compensate for underlying laryngeal injury – neither of which will be apparent in infancy. If follow-up is delayed to adulthood, additional costs incurred contacting patients may be incurred and the opportunity for early intervention lost. Children at risk of dysphonia related to birth and/or medical intervention in infancy may benefit from assessment at school age.

No systematic studies reporting on treatment of dysphonia in the preterm population were identified. Investigation of how to ameliorate the effects of dysphonia on the quality of life of affected children is necessary.

Conclusions

Dysphonia is a newly recognised, potential long-term outcome of preterm birth associated with female gender, extreme prematurity, extremely low birth weight, emergency intubation, frequency of re-intubation and surgical

ligation of PDA. Further research into voice outcomes of preterm children is warranted, due to the small number of published studies. Long-term voice follow-up could be offered to those children at risk if efficacious management of dysphonia in this population becomes available.

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