

Using hyaluronic acid for improving vocal function in a prepubescent boy with an atrophied right vocal fold

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Abstract

Objectives: A single case study is reported of a child who underwent several surgical procedures as result of congenital grade III subglottic stenosis. The anterior aspect of the right vocal cord was damaged and underwent atrophy during one of these procedures. Now an active 10 year old, the patient has become increasingly aware of his vocal limitations on functional activities. Injection of hyaluronic acid into the vocal folds has been known to provide improved voice quality in adults though there are no known cases reported of this procedure in children.

Methods: This paper reports voice outcomes following injection of hyaluronic acid into the Reinke's space in a single case study. Voice recordings were made pre, post and one month following injection. The voice recordings were subject to acoustic and perceptual analysis.

Results: Post and follow up voice recordings demonstrate decreased jitter, shimmer and harmonics to noise ratio. Perceptual evaluation indicates improved voice quality.

Conclusion: Injection of hyaluronic acid in children who require voice augmentation is possible and may contribute to increased vocal function and improved voice outcomes.

Introduction

Laryngeal airway narrowing from subglottic stenosis (SGS) may be congenital or acquired, with many cases of SGS acquired following intubation or laryngotracheal injury^[1]. Medical and surgical interventions are used to establish sufficient airway to support respiratory function, including bypassing the obstruction with tracheostomy or reconstructive surgery to repair stenosis^[2]. Two main approaches to reconstructive surgical management exist: laryngotracheal reconstruction (LTR) and partial cricotracheal resection (CTR), and these are well documented in the literature^[3]. Primary surgical outcome indicators continue to be survival or decannulation of the tracheostomy.

Outcomes relating to quality of life (QOL) and voice quality have gained prominence with an increasing awareness of QOL impact following critical care surgery in the paediatric population^[4,5]. In adults, voice quality is often reduced following LTR or CTR^[6], particularly in women^[7]. Similar studies in the paediatric population show a range of findings from poor^[4,8,9], to good voice outcome^[5,10]. Voice outcome may depend on the preoperative condition, such as the grade of stenosis^[9,11,12] or methodological differences in relation to how voice outcome is evaluated. For example, there are various methods used in judging quality of life (e.g. using different health related quality of life questionnaires), various ways of evaluating voice quality (e.g. GRBAS or CAPE-V) and differences in acoustic data reported (e.g. F₀, jitter, shimmer, HNR). Furthermore, published studies have a range of participant numbers, from 12^[8] to 77^[12] reflecting the small caseload. The overarching conclusion that can be drawn from the literature

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is that individual voice outcome data is variable and related to various factors, including aetiology, stenosis grade, surgical procedures, surgical outcomes and how vocal function is evaluated.

Notwithstanding these varied findings, some children and their families seek ongoing advice where voice remains of poor quality several years post LTR/CTR. For these children surgical intervention is limited to procedures that will not affect the normal course of growth, especially given reports that LTR/CTR in childhood does not impact on the normal anatomical development of the larynx^[11,13].

The use of temporary injection laryngoplasty is well documented in the literature with a variety of available products that can be used to bulk out a vocal fold in order to close a phonatory glottis gap and improve vibratory function^[14]. Much of the reported research describes injection laryngoplasty in relation to vocal fold paralysis (VFP) – a condition that has potential for spontaneous recovery. For example, various collagen products (micronized, acellular, cadaveric dermis and bovine) have shown promising voice outcomes up to 6 months following injection laryngoplasty in children with VFP^[15]. This review also describes the varied outcomes using other materials such as calcium hydroxylapatite, autologous fat and hydrated porcine gelatin powder. Many of these materials are subject to restricted use in the paediatric population in the UK, however one material is widely used - hyaluronic acid. Hyaluronic acid has also been used in injection laryngoplasty with improved voice quality in adults with unilateral VFP^[16], and the specific molecular weight of certain hyaluronic acid compounds are considered

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to be effective at augmentation of the vocal folds ^[17]. Its use is also reported for augmentation and medialisation of the vocal folds in children with VFP ^[18].

While these materials may be worthwhile using where the purpose of the procedure is to bulk out an existing but non-functioning vocal fold, little is known about how they might be used where the vocal fold has atrophied following neonatal LTR. These patients present with a greater degree of challenge to the otolaryngological surgeon who is faced with a compromised anatomy.

This paper reports a single case study of a pre-pubertal child who has vocal fold atrophy following neonatal LTR. Voice outcomes following injection of hyaluronic acid into the Reinke's space are reported.

Method

Participant information: The patient in this single case study presented with a congenital type III subglottic stenosis (SGS). During the neonatal period, the patient required tracheostomy for a grade III SGS that was reversed by performing a cricotracheal resection during infancy. During the procedure the anterior aspect of the right vocal fold was damaged and underwent atrophy¹. Further symptomatic SGS recurrence was treated with a laryngotracheal resection and anterior rib graft at 7 years of age. Now aged 10, the patient continues to have a small

¹ The clinical appearance was that of a withered anterior vocal fold, that may or may not be truly atrophied in terms of muscular impulse activity. Laryngeal EMG was not undertaken at that time, but between infancy and 10 years of age, there was no substantial change to the vocal fold clinical appearance.

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subglottic / tracheal stenosis, giving him mild stridor and a phonatory glottis insufficiency resulting in a weak and breathy voice.

The patient is able to participate in a wide range of educational and extra-curricular activities despite his respiratory limitations. As he has matured into pre-adolescence he has become increasingly aware of the limitations his voice quality has on functional activities. This awareness prompted his family to seek further advice and information regarding future surgical management.

Surgical Procedures: The patient was admitted for surgery where 0.4 ml of Rystylene Perlane[®]; (Q-Med, Uppsala, Sweden) hyaluronic acid was injected submucosally /subepithelially into the atrophied area of the right vocal fold in the Reinke's space to bulk out the anterior position of the vocal fold. Both vocal folds were mobile on video endoscopy with a glottal gap evident as a result of the atrophy of the R vocal fold which reduced as the material was injected. There was no significant vertical mismatch of the vocal folds observed during surgery. The patient had a suspension laryngoscopy while under a spontaneously breathing tubeless general anaesthetic. He was discharged home the following day with no complications.

Voice recordings: A range of audio recordings, shown in table 1, were made using the Storz Aida 3 system at pre surgery, post-surgery and one month follow up.

<insert table 1 here>

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Voice analyses: The Multi-Dimensional Voice Program (MDVP) Model 5105 version 3.3.0 software option (KayPENTAX) was used to analyse the fundamental frequency (F_0), jitter percent (JITT), shimmer percent (SHIM) and noise to harmonics ratio (NHR) in our patient's sustained production of /a/ at each time period. These three variables have been measured using MDVP in recently published acoustic studies of paediatric voice ^[19,20,21] and thus provide a normative sample for comparison.

Maximum phonation times were calculated for the sustained vowel [a] and consonants [s] and [z] using the MDVP software where onset and offset of the sustained vowel or consonant could be visualised using the sound waveform. This was particularly necessary given that MPT are short for this patient due to inhalatory stridor. The patient's MPT values were compared to normative values for children ^[22]. Perceptual analysis using the Grade, Roughness and Breathiness aspects of the GRBAS ^[23] scale was performed by a speech and language therapist with extensive clinical experience in working with voice disorders. Judgements about asthenia and strain are known to be less reliable in the perceptual evaluation of children's voice disorders ^[24]. The sound files were randomised by a third party who kept a record of which recording matched each time period. These sound files were played to the expert listener who was 'blinded' to the time of each recording.

Results

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Figure 1 shows the right vocal fold pre and post surgical injection of the hyaluronic acid. Image A, taken pre-injection, shows atrophy of the right vocal fold with associated subglottic stenosis. Image B, shows the right vocal fold bulked up post hyaluronic acid injection and dilation of the subglottic stenosis.

Figure 1: Image of the vocal fold pre and post surgical injection of hyaluronic acid

Table 2 shows the values for F_0 , JITT, SHIM and NHR in our patient's sustained production of /a/ at each time period. While our patient presents with acoustic values for sustained [a] production that are greater than the normative values available in the published literature, JITT decreases across the three time periods.

<insert table 2 here>

Table 3 shows the values for MPT at each time period compared to values for these available in the published literature. Our patient has lower than would be expected MPT for his age, due to the inhalation stridor associated with his SGS.

<insert table 3 here>

Grade, Roughness and Breathiness ratings were assigned to each recording following the GRBAS rating system. In this scale, 0 = normal, 1 = slight, 2 = moderate and 3 = extreme.

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The perceptual rating for the sustained [a] improved between pre and post injection but not by the time of the follow up recording. In the CAPE-V sentences there was improved rating by the time of the follow up recording for five of the sentences. The perceptual rating of the sentence which elicits hard glottal attack did not improve. Comparison of the GRB ratings across all utterances was made by calculating the mean rating in the pre, post and follow up conditions. Figure 2 shows the mean value across the three time points, indicating the general trend for improvement in perceptual rating towards the normal category.

<insert figure 2 here>

The patient and his family reported increased voice quality at home and during school and extra-curricular activities. After a period of 6 months, the patient returned to the clinic reporting decreased vocal function and requested a repeat injection.

Discussion

Injection of hyaluronic acid in the Reinke's space in this single case study was considered to be a successful procedure. There was improvement in vocal function that was observed through acoustic analysis, perceptual evaluation and patient report. The findings for this single case study are similar to those reported in larger studies of adults who have had temporary augmentation using hyaluronic acid ^[15]. Thus it would be interesting to explore the usefulness of this injection material in greater numbers of children. The main advantage to using hyaluronic acid is its viscosity and the manner in which quantity can be controlled during the

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injection procedure ^[16] and these might extend to the management of complex paediatric conditions such as that reported here.

Improved vocal function appears to last for around six months, with the hyaluronic acid dissolving over the course of time leading to a decrease in voice quality. The patient described in this paper has returned for a repeat injection, with the same level of improvement in voice quality noted through patient and parental report. Ongoing repeat injection of hyaluronic acid is currently being considered as a management option for this patient until such time as a more permanent surgical option (e.g. Isshiki type I thyroplasty) is appropriate post puberty.

Conclusion

In this single case study, injection of hyaluronic acid proved to be a positive temporary augmentation that led to improved voice quality and offered the patient a means with which to consider future permanent surgery. There is scope for future research exploring the long term voice outcomes for children who have undergone LTR or CTR and the use of temporary vocal fold augmentation to support children for whom vocal function continues to be compromised, particularly where these children report reduced vocal function that impacts on their lives.

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DRAFT

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Data	Acoustic measure (using MDVP)				Perceptual evaluation		
	Maximum phonation time	F ₀	Jitter	Shimmer	Noise to harmonics ratio	Time judgement	GRB(AS)
Sustained vowel [a]	✓	✓	✓	✓	✓	✓	✓
Sustained consonant [s]	✓					✓	✓
Sustained consonant [z]	✓					✓	✓
Reading passage "The north wind and the sun"						✓	✓
Six sentences from the CAPE-V protocol						✓	✓

Table 1: Audio data recordings and their corresponding analysis method

	Patient			Published normative data		
	Pre	Post	Follow up	Tavares et al ¹⁹	Maturo et al ²⁰	Abu-Rass et al ²¹
F ₀	191.12	280.41	271.96	222.49	226.47	230.93
JITT %	7.42	6.67	4.58	1.71	1.80	1.66
SHIM %	17.40	21.45	19.15	4.01	3.49	2.95
NHR	0.45	0.55	0.40	0.13	0.13	0.12

Table 2: Acoustic analysis comparing patient findings to published normative data

	Pre	Post	Follow up	Tavares et al ²²
Sustained /a/	2.02	1.5	2.8	9.22
Sustained /s/	1.6	1.4	2.3	9.22
Sustained /z/	1.03	0.6	1.5	9.35

Table 3: Maximum phonation times comparing patient findings to published normative data

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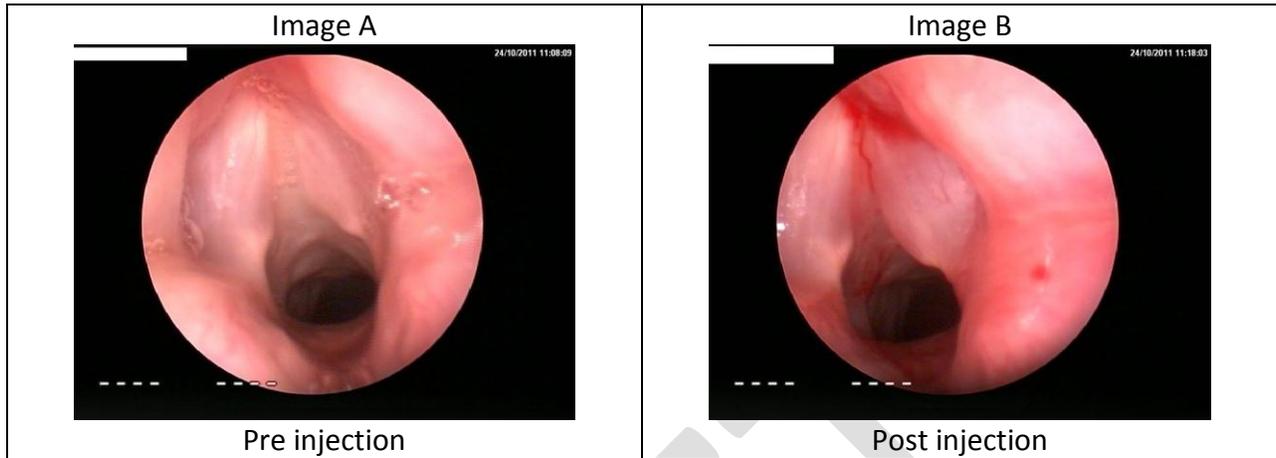


Figure 1: Images taken showing the vocal fold at pre and post surgical injection of hyaluronic acid

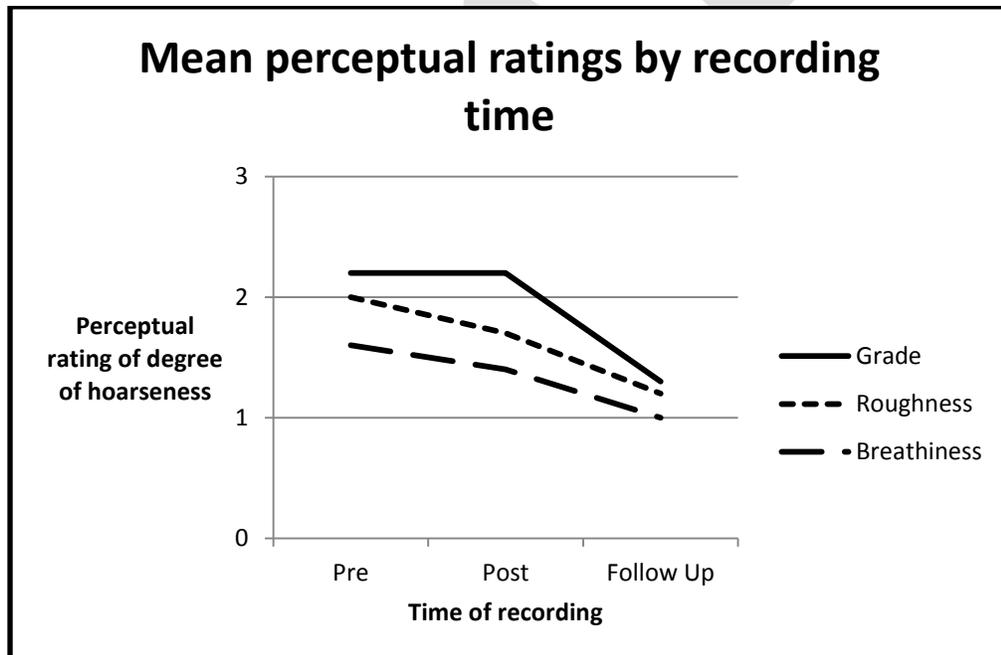


Figure 2: Graph showing the perceptual rating of hoarseness at each time point