Vocal Cord Medialization by Transcutaneous Injection of Calcium Hydroxylapatite

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Summary: Transcutaneous vocal cord augmentation has increasingly become the method of choice when treating causes of vocal cord insufficiency. Many substances have accompanied this technique, but they all have problems. One newer substance is calcium hydroxylapatite (CaHA). CaHA may produce fewer problems and offer a longer-lasting treatment. Twenty-one patients were treated in the Pacific Voice Clinic with trancutaneous injection of CaHA for vocal cord paralysis (n = 19) and vocal scarring (n = 2). Maximum phonation time (MPT) was the measure of vocal performance. An improvement was seen in 20 patients with the MPT, who improved from 4.6 seconds before treatment to 10.8 seconds at posttreatment of 3 months (n = 15). This improvement was maintained at 6 months (MPT = 12 seconds, n = 12). Follow-up was incomplete because of the terminal nature of some diagnoses and the large geographical area covered by the clinic. Three subjects had submucosal injection of CaHA (two resolving spontaneously). Two other patients had extrusion of the material.

With short-term and medial-term follow-up on a small group of patients, encouraging results were seen with transcutaneous injection of CaHA for vocal cord augmentation.

Key Words: Trancutaneous—Calcium hydroxylapatite—Vocal cord augmentation.

INTRODUCTION

Various techniques of vocal cord medialization have been described. The two most common procedures are medialization thyroplasty[1] and injection augmentation of the vocal cord.[2]

Transcutaneous laryngeal injection of bulking agents to cause a more medial vocal cord position has increasingly become the procedure of choice for vocal cord paralysis because it can be offered to the patient at his or her initial presentation in the clinic and does not require access to an operating room.[3]

Various agents have been used by physicians over the last 100 years since paraffin was first injected in 1911. Paraffin caused an intense inflammatory reaction, and all other injectable substances have had problems. For example, a paste made of gelatin powder (Gelfoam, Upjohn, Kalamazoo, MI) reabsorbs within a few weeks,[4] and injected fat often produces unpredictable results because of variability in spontaneous reabsorption.[5]

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Teflon[6] causes a permanent bulking effect but has been associated with long-term granulation formation. It has been suggested that this effect may have been caused by overinjection or misplacement of the Teflon material (Mentor, Indianapolis, IN).[7]

Collagen, both bovine and human, has been extensively used by physicians, but the risk of prion transfer now makes bovine material unacceptable. Autologous human collagen requires harvesting and, therefore, an additional incision, and the results are generally not permanent, typically lasting 3 to 6 months.

More recently, hyaluronic acid (HA) has been used by physicians as an implant material; it is a naturally occurring substance that is thought to cause fewer problems with inflammatory reactions.[8]

However, clinical experience has shown that, although the immediate and medium-term effects of HA injection are good, substantial reabsorption occurs in the long term. Therefore, patients might need to undergo numerous procedures.

New biomaterials are now available, and we used one such material in this study. Radiesse is a patented, proprietary mixture of an aqueous-based gel carrier blended with spherical particles of synthetic CaHA (BioForm Company, San Mateo, CA). The gel carrier suspends the CaHA particles (diameter range 25μm to 45μm) and allows them to be readily delivered through injection needles. The key compound of the implant, synthetic CaHA, is identical in composition to the mineral portion of human bone, which makes it exceptionally compatible with the human body. The CaHA particles are suspended in a patented pharmaceutical-grade aqueous gel carrier that provides for easy injection. The high viscosity of the gel carrier, together with its elasticity, minimizes the extravasation of the implant from the injection site. Once injected, the gel carrier provides the matrix in which cellular infiltration can occur. As the gel is absorbed, the natural tissue structure replaces the gel, which forms a long-lasting implant of CaHA particles and the surrounding tissue.

The purpose of this study was to investigate the short- and medium-term effects of injected CaHA in patients with glottic insufficiency caused by vocal cord paralysis.

Although this treatment is primarily aimed at patients with vocal cord paralysis, the nature of the referral pattern to the Pacific Voice Clinic meant that other conditions were treated. These patients will be commented on in the following sections.

METHODS

The Pacific Voice Clinic is a tertiary referral clinic that specializes in voice disorders and receives patient referrals from a large geographical area, which often necessitates that the consultation is a once-only diagnosis/treatment session. Thus, further follow-up is often impossible. Some patients in this treatment population were terminally ill, and follow-up was not possible for that reason.

All patients who were clinically suitable for vocal cord augmentation were considered eligible for the study, which included 19 patients with the primary diagnosis of vocal cord palsy. A further 2 patients with laryngeal scarring were treated (see Table 1). These patients were included to demonstrate the entire experience of CaHA at the Pacific Voice Clinic.

The study period was July 2002 to May 2003; during this time, 650 new patients were seen in the Voice Clinic.

The average age of the group was 71 years with a standard deviation of 15.7 years. Maximum phonation time (MPT) was the measure chosen to quantify the change in voice function before and after vocal cord augmentation because it is simple to collect and was available on videotaped recordings of most subjects reviewed in this retrospective study. The time was measured with the counter on the videotapes.

We used a standard method of transcutaneous injection of the CaHA. The Radiesse implant product is sterile in a prefilled syringe, which contains

TABLE 1. *21 Patients (Aged 48–84 Years, Mean 71)*

♦ 2 with vocal cord scar (both men)	
■ Postradiation	1
■ Postintubation	1
♦ 19 unilateral paralysis (12 women, 7 men)	
■ Metastatic CA in chest	6
■ Thoracic surgery	5
■ Idiopathic	4
■ Miscellaneous	4

1.0 mL of the material. A standard 25-gauge one-quarter inch needle is attached to the syringe. With the patient in a semirecumbent position, the nasal cavity and pharynx are topically anesthetized with lidocaine spray, and a transnasal flexible videolaryngoscopy is performed. If gagging is a significant problem, 2 mL of 2% lidocaine (without epinephrine) is injected into the laryngotracheal lumen via the cricothyroid membrane. While an assistant maintains a satisfactory view of the larynx on the video monitor, the operator inserts the needle into the vocal cord through the cricothyroid membrane, which enters the larynx about 3 or 4 mm lateral to the midline, on the side being augmented. The needle slips under the inferior edge of the thyroid cartilage and passes into the vocal fold substance in an upward and lateral direction. The detailed position will depend on the patient's laryngeal anatomy, but movement seen on the video will suggest tip location. Then a small amount of the product is injected, and some expansion of the fold can be seen. The needle can then be moved around a little during the injection to evenly distribute the product into the areas most suitable for optimal vocal function.

RESULTS

A summary of patient demographics and etiologies is shown in Table 1.

A summary of the MPT results is shown in Table 2. Twenty-one patients received transcutaneous vocal cord injections. Vocal cord paralysis was the most common indication (19 of 21), and the other indication was vocal cord scarring (2 of 21). Follow-up data at 3 months are available for 15 patients, and 6-month data are available in 12 patients. Clear improvement in MPT at 3 and 6 months is noted.

Three complications were noted to be caused by the injection.

TABLE 2. *Mean Phonation Times*

Pretreatment MPT (21 cases)	Range: 1 to 14 s	Mean: 4.6 s
3-month MPT (15 cases)	Range: 4 to 22 s	Mean: 10.8 s
6-month MPT (12 cases)	Range: 4 to 22 s	Mean: 12 s

In the first case, a 74-year-old woman, the injected material flowed into about half of the length of the Reinke space before the needle was repositioned more laterally. The voice was initially hoarse, enough to be cause for concern. However, when she returned for reexamination 2 weeks later, the subepithelial material had resolved, perhaps by extrusion, and quality of the voice was very good. Good voice quality was maintained at 3 months.

In the second case, a 72-year-old woman, the subepithelial material was retained, and the voice stayed unsatisfactory. Much material was removed at microlaryngoscopy via a microflap technique; however, the voice remained raspy because of scarring.

The third case of subepithelial injection, in a 79-year-old man, provided a reasonably good result until he died a few months later without requiring further treatment for the vocal paralysis.

In one patient, the material seemed to extrude spontaneously. After the injection, the voice was good, and all seemed to be well, but, on a return visit 3 months later, the voice and laryngeal examination showed that the condition had returned to its original state.

A summary of complications is shown in Table 3.

Case-by-case details are shown in Table 4.

The data are incomplete for several reasons. Many patient deaths unrelated to the injection material have occurred. Also, some patients visited the voice clinic from great distances and have not been reviewed again. After discussion with clinical statisticians, statistical analysis was not felt to be appropriate for this study because of the small number of patients and the incomplete follow-up. However, the results are important and worthy of publication. The clinical impression is that the improvement

TABLE 3. *Complications*

♦ No complications	16
♦ Submucosal injection	3
■ 1 removed at laryngoscopy (SK)	
■ 1 resolved spontaneously (good result—CD)	
■ 1 died at 3 months (KR)	
♦ Extruded	2
■ 1 no further treatment	
■ 1 medialisation thyroplasty	

TABLE 4. *Patient Details*

Patient	Age	Sex	Diag	Cause	Date	Vol	MPT (pretreatment)	MPT (3 months)	MPT (6 months)	Complications
1	80	f	L paral	Thoracic surgery	8-Jul-02	0.5	4	11	11	Nil
2	68	m	Scar	Post DxT	8-Jul-02	0.5	2 overseas	na		Nil noted
3	67	f	L paral	Lung carcinoma	11-Jul-02	0.5	2	8 na		Nil noted
4	48	f	R paral	Brainstem mets	25-Jul-02	0.4	4 died 1mo	na		Nil noted
5	64	m	Scar	Intubation	25-Jul-02	0.6	3	7	9	Nil
6	79	m	L paral	Idiopathic	1-Aug-02	0.8	3	12 na		SMI
7	71	f	L paral	Lung carcinoma	6-Aug-02	1	1 died 3 day	na		Nil noted
8	60	f	L paral	Breast metasteses	11-Sep-02	0.5	6 died	na		Nil noted
9	71	m	L paral	Thoracic surgery	12-Sep-02	1	4	9	11	Nil
10	74	f	L paral	Idiopathic	18-Sep-02	0.5	7	15	15	Nil
11	72	f	L paral	Thoracic surgery	5-Oct-02	0.2	5	10 na		SMI (MLrem-6 months
12	84	f	L paral	Thoracic aneurysm	8-Nov-02	1	5	7	7	Nil
13	55	f	L paral	Breast carcinoma	13-Nov-02	0.8	5	7	7	Nil
14	74	m	L paral	Thoracic surgery	19-Nov-02	1	3	7	7	Nil
15	58	m	R paral	Idiopathic	14-Jan-03	0.5	14	20	20	Nil
16	84	m	L paral	Thoracic surgery	29-Jan-03	1	4	22	22	Nil
17	76	f	L paral	Breast metastases	13-Feb-03	0.6	4	4	4	Extr-1mo
18	74	f	L paral	Postviral	27-Feb-03	0.6	8	8	13	SMI (OK-3 months)
19	76	m	L paral	Carotid surgery	11-Mar-03	1	3	21	18	Nil
20	81	m	L paral	Lung carcinoma	12-May-03	0.7	5	10 na		Nil
21	82	f	L paral	Idiopathic	21-May-03	0.4	4	6 na		Extr (MedThy)
Average	71					0.7	4.6	10.8	12	

Abbreviations: SMI, submucosal injection; Extr, extruded; MLrem, Microlaryn—removal; L paral, L Vocal cord paralysis; R paral, R Vocal cord paralysis.

in patients with dysphonia from scarring is not as good as that seen in other groups.

DISCUSSION

Vocal cord augmentation via transcutaneous injection of calcium hydroxylapatite has been performed on a small group of patients with encouraging results.

The complication rate appears to be satisfactory, and the short- and medium-term results are satisfactory. One other group has also had satisfactory experiences with CaHA in 20 persons[9] in whom general anesthetic was used by physicians to allow placement. This study appears to support the hypothesis that good results can be gained by local anesthetic transcutaneous injection, although direct comparison of the studies and study populations is not possible. They also demonstrated minimal inflammatory reaction in a donated larynx.

Vocal cord augmentation is also performed for airway protection, but this retrospective study was specifically aimed at voice improvement. Further data such as barium swallows and other objective studies are not available to allow any meaningful further discussion.

Overall, this article demonstrates that good short- to medium-term results can be achieved with transcutaneous injection of CaHA in a "real-world" group of patients. The long-term results are awaited.

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