Office-based Injection Laryngoplasty: Outcome after Hydroxylapatite Injection

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ABSTRACT

Background: Office-based injection laryngoplasty is a surgical procedure that becomes more popular for vocal fold (VF) augmentation. Hydroxylapatite (Radiesse) is used to narrow the glottal gap in cases with glottal insufficiency.

Objective: To assess voice outcome and patient’s quality of life in selected group of dysphonic patients using office-based hydroxylapatite injection under local anesthesia in cases with glottal insufficiency.

Materials and methods: Forty-one patients with different voice disorders, namely sulcus vocalis, unilateral VF immobility, and VF atrophy were selected. All patients underwent office-based injection of hydroxylapatite under local anesthesia. All patients were evaluated by using auditory perceptual analysis, laryngeal videoendoscope (LVS), acoustic analysis, and voice handicap index (VHI) preoperatively and 3 months postoperatively.

Results: Improvement in glottal gap in all groups of patients was measured by LVS examination. Also, there was significant improvement in acoustic correlates of dysphonia, namely jitter%, shimmer%, noise to harmonic ratio (NHR), and maximum phonation time (MPT) in patients with unilateral VF immobility and VF atrophy. Also improved quality postinjection was reported in all groups measured by VHI.

Conclusion: Office-based injection laryngoplasty with hydroxylapatite is a reliable and effective procedure in management of mild and moderate glottal gap because of unilateral VF immobility and VF atrophy.

Keywords: Hydroxylapatite, Injection laryngoplasty, Sulcus vocalis, Vocal fold atrophy, Vocal fold immobility.

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INTRODUCTION

Injection laryngoplasty is a surgical procedure that has gained popularity in recent years owing to its low procedural cost, technical feasibility, and clinical efficacy. This method involves injection of vocal fold (VF) with one of different natural and synthetic materials. It provides functional voice improvement to patients with glottic insufficiency and can also be used as an adjunct to laryngeal framework surgery.

Radiesse voice gel was developed from a gel carrier substance for calcium hydroxyapatite, a longer-term injection material. It is composed of sodium carboxymethylcellulose, glycerin, and water. It has the benefit of being “off-the-shelf” use, without any need for preparation or harvesting of the injection material. Its inert nature means that it also has the benefit of not requiring any prior allergic testing.

It has also been found that calcium hydroxyapatite gives better mucosal vibratory activity postinjection. It can be injected via a 25–27 gauge needle, which is easily tolerated by patients in addition to its routine use in the transcutaneous approach.

Vocal fold injection with calcium hydroxyapatite may be used to treat permanent causes of mild-to-moderate glottic insufficiency. Specifically, this has been successfully used to treat VF atrophy, paralysis, paresis, and augmentation after previous framework surgery.

Vocal fold augmentation is used in patients with minor degrees of glottic insufficiency due to loss of soft tissue in the VF as sulcus vocalis and scarring of the VF after partial laser cordectomy.

Sulcus vocalis can be regarded as the most difficult-to-diagnose and the most difficult-to-treat clinical entity for laryngologists. Its etiology is poorly understood. Nearly 50% of cases are congenital in origin and the other half is acquired later in life.

Sulcus can be treated with the help of voice therapy, surgery, and both. Surgery for sulcus should enhance glottal closure/efficiency via medialization (with injection or thyroplasty type I) and improve VF vibratory potential by direct manipulation of the lamina propria. The potential future treatments for sulcus are injection of various growth factors, stem cells, and gene therapy.

Vocal fold immobility is a broad term that can be used to describe the abnormal movement of the true VFs. It can be unilateral, where only one true VF is affected, or bilateral, in which both true VFs are affected. The abnormal movement can be described as impaired mobility or fixed VFs (complete cessation of VF movement). If a true VF is immobile, it is described as being fixed in a midline, paramedian, or lateral position.

Unilateral VF immobility can be managed by either one or more of the following procedures: voice therapy, framework surgery, and injection laryngoplasty.

Age-related voice change is characterized by it being weak, harsh, and breathy. These changes are caused by histologic alteration of the lamina propria of the VF mucosa as well as atrophy of the thyroarytenoid muscle. This aging process results in bowing of both VFs and air leakage through the glottis. The patient’s voice
bécomes dysphonic with weak voice and vocal fatigue. Management has been successful with injection laryngoplasty and voice therapy.\textsuperscript{11}

The current research work has been conducted because the newly introduced material of injection (Radiesse) is not yet widely used in our area. In addition, office-based laryngoplasty is an evolving new technique that is not addressed sufficiently in our region.

**Aim of the Study**

The aim of this study is to assess voice outcome and patient’s quality of life in selected group of dysphonic patients, using office-based hydroxylapatite injection under local anesthesia in cases with glottal insufficiency. This might help in selecting the proper material and procedure for VF augmentation.

**Materials and Methods**

This study was conducted on 41 patients presented by dysphonia of different etiological factors from January 2014 to January 2019. The patients were recruited to Phoniatrics Clinic for evaluation of the larynx and management of their voices.

All participants were informed about the nature of the study and informed consent was obtained.

**Inclusion Criteria**

Patients presented to the clinic by dysphonia with glottic insufficiency due to sulcus vocalis (with different degrees of furrows), unilateral VF immobility, and VF atrophy were included in the study.

**Exclusion Criteria**

Patients with previous history of any VF or other laryngeal surgeries.

The selected patients were classified into three groups based on the laryngeal videostroboscope (LVS) findings. The first group included sulcus vocalis, both unilateral or bilateral. The second group included patients with unilateral VF immobility. The third group included patients with VF atrophy.

**Injection Procedure**

All patients were treated by office-based sessions while awake by hydroxyapatite (voice gel) injection. The patient’s nose was anesthetized with lidocaine 2%. The subcutaneous tissue overlaying the cricothyroid membrane is injected with 1 mL, 2% lidocaine. The oral cavity is sprayed with 10% zylocaine by short nozzle and then the supraglottic area of the larynx is sprayed using long nozzle. 2 mL 2% lidocaine is injected in the subglottic area through the cricothyroid membrane, which induces cough and spell of the anesthetic to the undersurface of the VFs.

Radiesse voice gel was injected by a 27-gauge needle through transcutaneous approach in the cricothyroid membrane (Fig. 1). The needle was directed upward and laterally by 45° to the undersurface of the VF lateral to the vocalis muscle. The injection locations were lateral to the vocal process and mid-third of the VF at the depth of vocalis muscle. The required amount of augmentation was based on individual need and usually ranged from 0.5 mL to 1.0 mL. The whole procedure was performed under visualization of the larynx using fiberoptic nasolaryngoscope, used by an assistant. The needle was withdrawn after injection and the procedure was completed. The patient was then kept under observation for 2 hours postinjection and then discharged.

Each patient was subjected to a protocol of voice evaluation that included:

**Elementary Diagnostic Procedures**

A comprehensive history taking and otorhinolaryngological examination. The history included age, gender, precipitating and etiological factors, and a speech sample including counting and a conversation about the daily activities was recorded and assessed by two phoniatrists. The degree of dysphonia was assessed auditory by (modified GRABS scale)\textsuperscript{12} and scored on a 4-point scale (0 = no dysphonia, 1 = mild, 2 = moderate, 3 = severe).

**Clinical Diagnostic Aids**

Each patient was assessed using LVS. This procedure was carried out using a rigid 70° Hopkins rod laryngoscope. A minority of patients could not tolerate this procedure and were therefore evaluated with a flexible fiberoptic nasolaryngoscope inserted via the nose. All patients included in the study were evaluated before and 3 months after VF injection. The vibratory motion of the VFs was assessed for the degree of glottic gap, symmetry, periodicity, and phase closure.

**Additional Instrumental Measures**

Acoustic analysis was carried out in a sound-treated room. A 4-second voice sample of sustained vowel (a) was recorded directly into the computerized Speech Lab (CSL model 4150; Kay Pentax, Lincoln Park, NJ) software using 50-Hz sampling rate and 16-bit quantization. The microphone was placed at a distance of 15 cm from the patients’ mouth. Participants were asked to phonate at their natural pitch and loudness level after several trials of trainings. This phonation sample was subjected to analysis using multidimensional voice program (MDVP) software (Kay Elemetrics Corp., Lincoln Park, NJ, USA). For objective acoustic analysis, the following outcome measures were extracted and analyzed: jitter%, shimmer%, noise to harmonic ratio (NHR), and maximum phonation time (MPT). Acoustic analysis was done preinjection with Radiesse and 3 months postinjection.

**Arabic Voice Handicap Index**

All patients were asked to complete the Arabic version of a voice handicap index (VHI) questionnaire\textsuperscript{13} before injection and 3 months post.

The Arabic VHI is reliably applied to the Arabic-speaking population, as it can help in estimating the degree of voice severity. This self-administered questionnaire consists of 30 questions; the patient responds according to the appropriateness of each item (0 = none to 4 = always). The Arabic VHI is scored from 0 to 120,
with the latter representing the maximum perceived disability due to voice difficulties based on the patient response.

The former protocol of assessment was applied before injection of VFs and 3 months after VF injection.

**Statistical Methods**

Statistical package for Social Sciences version 11 (SPSS, Inc., Chicago, IL) under windows was used for data entry and analysis. Descriptive statistics were carried out for continuous variables by mean, standard deviation (±SD), and range, and for qualitative data by number and percent. Student’s “t” test and ANOVA test were both used to compare continuous variables in various groups. Pearson’s correlation was used to assess the association between the different parametric data. For all tests, a probability (p) value less than 0.05 was considered significant.

**Results**

**Sociodemographic Data and History**

Forty-one patients with different voice disorders, namely bilateral sulcus vocalis, unilateral VF immobility, and VF atrophy, were selected. All patients underwent office-based injection of hydroxylapatite (Radiesse) under local anesthesia. All the patients tolerated the procedure. Patients with sulcus vocalis were 7 males with mean age of 17.3 ± 7 years and 8 females with mean age of 18.4 ± 6 years. Patients with unilateral VF paralysis were 8 males with mean age of 50.2 ± 12 years and 9 females with mean age of 46 ± 11 years. Patients with bilateral VF atrophy were 5 males with mean age of 53.2 ± 10 years and 4 females with mean age of 51.4 ± 9 years.

Table 1 shows the distribution of patients as regards to age, sex, and type of VF pathology. Differences between number of males and females and age groups were insignificant.

**Auditory Perceptual Assessment**

Using modified grade, roughness, breathiness, asthenia, strain (GRBAS) scale before and after injection with hydroxylapatite in patients with sulcus vocalis evidently showed insignificant statistical differences regarding degree of dysphonia, roughness, and breathiness. Patients with unilateral VF immobility showed significant differences regarding degree of dysphonia, roughness, and breathiness. Patients with VF atrophy showed significant differences regarding the former parameters (Table 2).

**LVS Findings**

Comparison of preinjection and postinjection LVS (Table 3) showed significant differences regarding glottal closure (Figs 1 and 2) but insignificant differences as regards to mucosal waves and amplitude in cases with sulcus vocalis. However, there was significant differences in all former parameters in cases with unilateral VF immobility and VF atrophy.

**Acoustic Analysis of Voice**

Comparison of preinjection and postinjection voices for patients with sulcus vocalis showed insignificant differences regarding jitter%, shimmer%, and NHR. Although, there were significant differences regarding the former parameters in cases with unilateral VF immobility and VF atrophy (Table 4).

Additionally, there were significant differences in MPT pre- and postinjection for all groups.

**Voice Handicap Index**

Comparison of preinjection and postinjection VHI values was significant in all groups of patients, namely sulcus vocalis, unilateral VF immobility, and VF atrophy Table 5.

**Table 1:** Distribution of patients as regards age, gender, and vocal fold pathology

| Age groups          | Male (n) | Female (n) | Total (n) | p value |
|---------------------|----------|------------|-----------|---------|
|                     | age = years ± SD | age = years ± SD | % of total |         |
| Sulcus vocalis      | (7) 17.3 ± 7 | (8) 18.4 ± 6 | 15 (37)   | >0.05   |
| Unilateral VF paralysis | (8) 50.2 ± 12 | (9) 46 ± 11 | 17 (41)   | >0.05   |
| Atrophy of VF       | (5) 53.2 ± 10 | (4) 51.4 ± 9 | 9 (22)    | >0.05   |

**Table 2:** Comparison of preoperative and postoperative degree of dysphonia (modified GRBAS parameters)

| Degree of dysphonia | Roughness | Breathiness |
|---------------------|-----------|-------------|
|                     | Preinjection means | Postinjection means | p value | Preinjection means | Postinjection means | p value | Preinjection means | Postinjection means | p value |
| Sulcus vocalis      | 1.3 ± 0.4 | 1.2 ± 0.7 | >0.05 | 1 ± 0.4 | 1 ± 0.5 | >0.05 | 0.8 ± 0.74 | 1.2 ± 3 | >0.05 |
| Unilateral VF paralysis | 1.4 ± 0.6 | 0.9 ± 0.4 | <0.05 | 0.9 ± 0.65 | 0.5 ± 0.4 | <0.05 | 0.9 ± 0.5 | 0.6 ± 5 | <0.05 |
| VF atrophy          | 1.1 ± 0.5 | 0.7 ± 0.4 | <0.05 | 0.8 ± 0.5 | 0.6 ± 0.4 | <0.05 | 1.7 ± 1 | 0.9 ± 0.5 | <0.05 |

**Table 3:** Comparison of preinjection and postinjection laryngeal videostroboscope

| Glottal closure | Mucosal wave | Amplitude |
|----------------|-------------|-----------|
|                 | Preinjection means | Postinjection means | p value | Preinjection means | Postinjection means | p value | Preinjection means | Postinjection means | p value |
| Sulcus vocalis | 1.5 ± 0.4 | 0.7 ± 0.3 | <0.05 | 2.0 ± 0.2 | 1.9 ± 0.4 | >0.05 | 2.1 ± 0.6 | 2.0 ± 0.5 | >0.05 |
| Unilateral VF paralysis | 1.4 ± 0.5 | 0.9 ± 0.4 | <0.05 | 1.6 ± 0.3 | 1.2 ± 0.6 | <0.05 | 0.8 ± 0.2 | 1.2 ± 0.4 | <0.05 |
| VF atrophy       | 1.6 ± 0.4 | 1.1 ± 0.3 | <0.05 | 1.8 ± 0.5 | 1.6 ± 0.4 | <0.05 | 1.6 ± 0.3 | 1.1 ± 0.3 | <0.05 |

Glottal closure: 0 = complete closure, 1 = small gap, 2 = moderate gap, 3 = large gap
Mucosal wave: 0 = normal, 1 = mild restriction, 2 = moderate restriction, 3 = severe restriction
Amplitude: 0 = normal, 1 = mildly diminished, 2 = moderately diminished, 3 = severely diminished
DISCUSSION

In the current study, patients with different VF pathology who are candidates for injection augmentation with calcium hydroxylapatite (Radiesse) were selected. The three groups of patients selected were homogeneous regarding age, sex, and number of patients. Patients with sulcus vocalis were young adults and teenagers as this particular voice disorder is common in younger patients in comparison with VF atrophy. Vocal fold atrophy occurs in aging patients, as a part of the normal aging process.

Authors reported that sulcus vocalis is an epithelial invagination adherent to deep tissues of the VF. Traditionally, dysphonia is believed to result from attenuation or absence of lamina propria and consequent alteration of mucosal dynamics. It is common in teenagers.

Also, Schaeffer et al. claimed that VF atrophy refers to a gradual change in the VFs as people age. The VF muscle may become thinner overtime. These tissue changes affect the vibratory pattern and can cause an abnormal gap between the VFs.

In our study, patients with unilateral VF immobility and VF atrophy showed improvement of glottal closure (Fig. 3) mucosal wave and amplitude after injection with Radiesse. The injected material was successful in decreasing the glottal gap by augmentation of VFs. However, no improvement occurred regarding mucosal wave and amplitude postinjection with Radiesse in comparison to preinjection condition in cases with sulcus vocalis. This might be explained by the presence of fibrous tissue bands in the submucosa of both VFs, causing stiffness that hinders gliding mucosa over hard muscle core.

In the current study, acoustic analysis of voice using MDVP for the three groups of patients showed the following results:

The tested parameters were mean jitter%, shimmer%, NHR, and MPT. The tested parameters are correlates of severity of dysphonia.

In our study, in cases of bilateral sulcus vocalis, there were minor changes in the measured parameters. This might be explained by that injection of the VFs did not improve the elastic properties of the VFs as the fibrous bands causing stiffness were still there. However, the augmentation of the VFs by the injected material improves the glottal gap measured by MPT as correlates of air escape through the glottis during phonation.

Although, Miaśkiewicz et al. mentioned improvement in all parameters (glottal closure, mucosal wave, and amplitude) after sulcus vocalis injection. The author underwent surgical excision of

|                  | Preinjection | Postinjection | p value |
|------------------|--------------|---------------|---------|
| Jitter%          | 6.3          | 5.6           | >0.05   |
| Shimmer%         | 11.3         | 8.1           | >0.05   |
| NHR              | 0.7          | 0.6           | <0.05   |
| MPT              | 13 ± 5       | 10 ± 5        | <0.05   |

Table 4: Comparison of preinjection and postinjection mean jitter%, shimmer%, NHR, and MPT

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Fig. 2: Glottal gap due to unilateral vocal fold immobility
fibrous bands, followed by VF injection augmentation. This might explain the better outcome in comparison to our study.

In the current study, in cases of unilateral VF immobility and unilateral VF atrophy, injection augmentation with Radiesse resulted in improvements of the vibratory properties of the VFs as reflected by the measured acoustic parameters (jitter%, shimmer%, and NHR). Also, improvement of MPT in all groups of patients reflects decreased glottic gap after injection of the VFs.

Dursun et al.13 studied 30 patients with glottic insufficiency after thyroplasty and VF injection. He observed that GRBAS scale of all patients demonstrated significant changes in degree of severity, roughness, and breathiness. Also, they mentioned that, acoustic analysis demonstrated significant change in fundamental frequency, jitter, shimmer, NHR ratio, and MPT.

Comparison of preinjection and postinjection VHI:
The VHI reflects three domains: physical, organic, and emotional. It reflects the quality of life of the patients after laryngoplasty.

In the current study, all patient groups showed significant improvement in all aspects measured by VHI. The improvement was more evident in cases of VF atrophy and unilateral VF immobility than sulcus vocalis. Lower values of VHI after injection reflect the improvement of patient’s symptoms reported by self-assessment.

Injection laryngoplasty of the VFs is a good treatment option for mild-to-moderate glottal gap in cases with unilateral VF immobility and VF atrophy. However, in cases with sulcus vocalis, no improvement occurred as it might need further surgical procedures.16

Miaśkiewicz et al.17 in their study of 14 cases with unilateral VF paralysis, after injection laryngoplasty, either complete glottal closure was achieved or there was a significant improvement in the glottal closure of each subject. They noted great improvement in the postinjection objective and subjective voice outcomes, and patients’ reported improvement in the voice-related quality of life.

![Fig. 3: No glottic gap. Postvocal fold injection laryngoplasty](image_url)

### Table 5: Comparison of preinjection and postinjection voice handicap index

|                  | Preinjection mean ± SD | Postinjection mean ± SD | p value |
|------------------|------------------------|-------------------------|---------|
| VHI sulcus vocalis | 37 ± 7                 | 28 ± 8                  | <0.005  |
| VHI unilateral VF paralysis | 40 ± 9                 | 27 ± 7                  | <0.005  |
| VHI atrophy of VF  | 36 ± 8                 | 25 ± 8                  | <0.005  |

## Conclusion

Office-based injection laryngoplasty with hydroxylapatite is an effective procedure for management of mild and moderate glottal gap due to unilateral VF immobility and VF atrophy. The procedure is not effective for cases of sulcus vocalis. Further research with longer follow-up periods and different cases is recommended.

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