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Original Article* / *Çalışma - Araştırma

Injection laryngoplasty outcomes in vocal fold paralysis using calcium hydroxylapatite

Vokal fold paralizilerinde kalsiyum hidroksilapatit ile enjeksiyon larengoplasti sonuçları

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Objectives: This study aims to evaluate our injection laryngoplasty experience in patients with unilateral vocal fold paralysis.

Patients and Methods: Sixty-eight patients (32 males, 36 females; mean age 59.5 years; range 27 to 86 years) who were diagnosed with unilateral vocal fold paralysis at our clinic and who underwent injection laryngoplasty using calcium hydroxylapatite between January 2005 and June 2012 were included in this study.

Results: Mean follow-up period was 36 weeks (range 0-340.4 weeks). Data of 29 patients with post-injection Voice Handicap Index (VHI) scores were retrospectively analyzed. Of these patients, 16 (55%) were female, and the mean patient age was 60 (range 27 to 86 years). Seventeen patients underwent suspension laryngoscopy in the operating room, 12 patients underwent in-office percutaneous injection. Post-injection mean VHI score was 36.7 (range 4 to 87). Percutaneous injection laryngoplasty was performed to half of the 20 patients with pre- and post-injection VHI data. Mean VHI scores of these 20 patients improved by 27.9 points. Mean VHI score improved by 35.1 points in the percutaneous group, and by 20.7 points in the suspension group (p=0.29). Post-injection VHI score of one patient with lung cancer decreased, as his general health deteriorated.

Conclusion: This study supports injection laryngoplasty in vocal fold paralysis. Calcium hydroxylapatite is a safe and effective treatment method in both percutaneous and operating room procedures.

Keywords: Calcium hydroxylapatite; in-office procedure; injection laryngoplasty; voice handicap index.

Amaç: Bu yazıda, tek taraflı vokal fold paralizili hastalarda enjeksiyon larengoplasti deneyimlerimiz değerlendirildi.

Hastalar ve Yöntemler: Ocak 2005 - Haziran 2012 tarihleri arasında kliniğimizde tek taraflı vokal fold paralizi tanısı konulan ve bu nedenle kalsiyum hidroksilapatit kullanılarak enjeksiyon larengoplasti uygulanan 68 hasta (32 erkek, 36 kadın; ort. yaş 59.5 yıl; dağılım 27-86 yıl) çalışmaya dahil edildi.

Bulgular: Ortalama takip süresi 36 hafta (dağılım 0-340.4 hafta) idi. Enjeksiyon sonrası Ses Handikap İndeksi (SHİ) skoru olan 29 hastanın verileri retrospektif olarak incelendi. Hastaların 16'sı (%55) kadın ve ortalama hasta yaşı 60 idi (dağılım 27-86 yıl). On yedi hastaya ameliyathanede süspansiyon larengoskopi, 12 hastaya klinik şartlarında perkütan enjeksiyon uygulandı. Enjeksiyon sonrası ortalama SHİ skoru 36.7 (dağılım 4-87) idi. Enjeksiyon öncesi ve enjeksiyon sonrası SHİ verileri olan 20 hastanın yarısına perkütan enjeksiyon larengoplasti uygulandı. Bu 20 hastanın ortalama SHİ skoru 27.9 puan artış gösterdi. Ortalama SHİ skoru perkütan grubunda 35.1 puan, süspansiyon grubunda 20.7 puan düzeldi (p=0.29). Akciğer kanseri olan bir hastanın genel sağlığı kötüleşirken enjeksiyon sonrası SHİ skoru düştü.

Sonuç: Bu çalışma vokal fold paralizilerinde enjeksiyon larengoplastiyi desteklemektedir. Kalsiyum hidroksilapatit gerek perkütan gerek ameliyathane süspansiyon işlemlerinde güvenilir ve etkili bir tedavi yöntemidir.

Anahtar Sözcükler: Kalsiyum hidroksilapatit; klinik şartlarında işlem; enjeksiyon larengoplasti; ses handikap indeksi.

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Patients with unilateral vocal fold paralysis (UVFP) often suffer reduced quality of life because of voice and swallowing difficulties. Unless there is severe swallowing impairment, treatment focuses on improving voice quality, thereby improving quality of life.[1] Management options include observation, voice therapy, and surgery. Various techniques have been proposed for managing vocal fold paralysis. These techniques include laryngeal framework surgery, reinnervation surgery, and injection laryngoplasty (IL). Injection laryngoplasty has several potential advantages when compared with other procedures. These advantages include avoidance of an open surgical procedure, lower procedural cost and morbidity, as well as the potential application of these techniques to the outpatient clinical setting with minimal anesthetic requirements.[2] Injection laryngoplasty has traditionally been performed under general anesthesia in the operating room. Recently there has been a resurgence of interest in awake IL, a technique first reported in 1985 by Ward et al.[3] Awake IL has been demonstrated to be a safe and clinically comparable alternative to IL under general anesthesia. The ideal vocal fold injection material should be biologically inert, "available off the shelf" (no preparation required for use), present no risk of infectious disease transmission, be a good rheologic match with injection site biologic tissue, and have the ability to be used with a fine-gauge injection needle.[4] In its natural state in the body, calcium hydroxyapatite (CaHA) is a major component of the mineral constituent of both bone and teeth. Calcium hydroxyapatite has been used as a biomedical implant in a variety of applications in the body, including dental, orthopedic, and head and neck bony reconstructions. In these locations, CaHA has proven to be a stable implant material with minimal inflammatory response and no evidence of toxicity. Recently, CaHA has been formulated for vocal fold augmentation.[4]

The purpose of this study is to evaluate the safety and efficacy of CaHA for vocal fold augmentation in UVFP and to compare awake IL to more traditional IL under general anesthesia by using the Voice Handicap Index (VHI) scoring system and to review our experience with it.

PATIENTS AND METHODS

This study was approved by the institutional review board of the University of Arkansas for Medical Sciences. A retrospective chart review of patients diagnosed with unilateral vocal fold paralysis at our institution who underwent IL with calcium hydroxylapatite between January 2005 and June 2012 was performed. During this period 91 ILs were performed. Sixty-eight patients (36 females, 32 males; mean age 59.5 years; range 27 to 86 years) who underwent injections due to UFVP were included in this study. Standard demographic information, comorbidities, pre- and post-procedure VHI scores, procedure technique as under local (awake) or general anesthesia (asleep) was recorded. All clinic and operative notes, along with videostrobolaryngoscopic examinations, were reviewed for any complications that occurred secondary to IL. In order to evaluate patient satisfaction, self-administered VHI scores were used. Speech therapy notes were reviewed. At our institution, patients who receive voice therapy undergo pre and post-therapy acoustic measurements with the KayPENTAX Computerized Speech Lab 4500 (KayPENTAX, Montvale, NJ).

RESULTS

The leading etiologic factor was thyroidectomy. Thirteen patients (19.1%) had thyroidectomy, 10 (14.7%) idiopathic UFVP; eight patients (11.7%) had lung, two patients (2.9%) esophageal, and two patients (2.9%) thyroid carcinoma; seven patients (10.2%) had intubation history; three patients (4.4%) had intracranial surgery; three patients (4.4%) had trauma history; four patients (5.8%) had thoracic interventions, eight patients (11.7%) had glomus tumor/resection, two patients (2.9%) had undergone a carotid endarterectomy, one patient (1.4%) a cervical fusion, and five patients (7.3%) had other reasons.

Twenty-four patients (35.2%) underwent awake IL (Figure 1), 41 patients (60.2%) underwent asleep IL (Figure 2) and three patients underwent multiple injections both awake and asleep. There were five complications and all were related with awake IL. The perioperative complications were minimal bleeding in one patient and difficulty tolerating the procedure because of gagging reflex in two patients. The postoperative complication was vocal fold stiffness in two patients. Eleven patients (16.1%) underwent speech therapy before IL and nine patients (13.2%) had speech therapy following IL. Six patients (8.8%) underwent thyroplasty after IL. The main reason

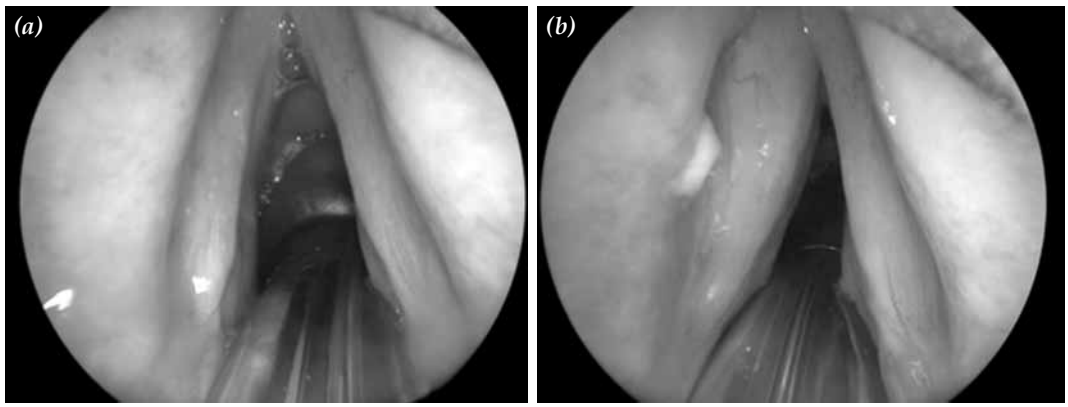

Figure 1. ***(a)*** *Preoperative direct laryngoscopy* ***(b)*** *post-injection outcome.*

for thyroplasty was short-lived benefit from the injection laryngoplasty. At this point reinjection and thyroplasty was discussed with patients and these patients chose to undergo thyroplasty with implant. Average follow-up period was 36 weeks (range 0-340.4 weeks).

The subgroup of 29 patients who at least had a post-injection VHI score was analyzed further. Sixteen patients (55%) were female; the mean patient age was 60 years old (range 27-86 years old). Seventeen patients underwent direct microlaryngoscopy with suspension, 12 patients underwent in-office percutaneous injections (through the cricothyroid membrane). Post-injection VHI scores were between 4 to 87 (mean, 36.7). Majority of the patients whose VHI scores were more than 40 were cancer patients undergoing active treatment. Pre- and post-injection VHI data was available for 20 patients and half of them were percutaneously injected. Average VHI in the 20 patients improved 27.9 points. While the average VHI in the patients percutaneously injected improved 35.1 points, average VHI in the direct laryngoscopy group improved 20.7 points. (T-test, p=0.29). There was worsening of one patient's post-injection VHI score; this patient had lung carcinoma and deterioration of his general health.

DISCUSSION

Enhancing quality of life by creating a more effective and understandable voice is the primary purpose of phonosurgical vocal fold injection.[5] Injection laryngoplasty for the treatment of UVFP has been subject to dramatic changes in recent years. Advancement of both injection techniques

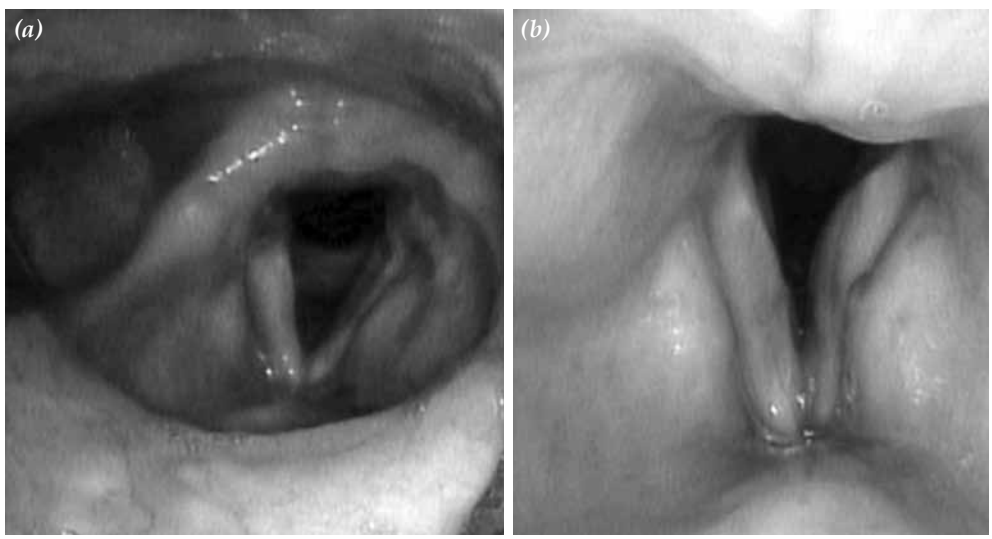

Figure 2. *In-office injection:* ***(a)*** *pre-procedure and* ***(b)*** *post-injection.*

and biocompatible materials have propelled the field of laryngology to a new level.[6] Injection materials can be categorized by the origin of material as xenograft, homograft, autograft, and synthetic materials. Calcium hydroxyapatite is one of the synthetic materials.[2] Only a moderate amount of information is available about CaHA as a vocal fold augmentation material.[4] It is a calcium phosphorus compound that is a basic component of bone and teeth. It is provided in the form of microspheres with gel carrier so that it can be injected through a fine needle. In an animal study, the histologic analysis showed no resorption of microspheres up to a 12-month observation period, but some reduction in medialization was noted because of the resorption of the gel carrier. Therefore, slight over-injection and/or repeated injection may be necessary.[2] Chhetri et al.[7] looked at the histology, host tolerance, and mucosal wave vibration in canine larynges up to 12 months after CaHA vocal fold injection. The histologic results throughout the study showed no significant immunologic response, and no CaHA was found in the lymph nodes of the neck or other parts of the body. No evidence of stiffness in the *in vivo* canine stroboscopy model was found during the mucosal wave vibrational assessment. On the other hand, Tanna et al.[8] reported on a case of intense inflammatory response in a patient after CaHA vocal fold augmentation. The CaHA material was partially removed four weeks after injection, and histologic examination revealed a "chronic inflammatory infiltrate and numerous foreign body giant cells". Rosen et al.[4] prospectively evaluated the effectiveness of CaHA up to 12-month time point in 63 patients. At 12 months, 81% of patients subjectively reported at least moderate improvement in their voice. Belafsky and Postma[9] reported a 100% improvement on a self-administered disease-specific outcome measure in a total of 39 vocal fold injections in 23 individuals who were injected with CaHA. Carroll and Rosen[10] later reported the average length of benefit as 27.2 months with a range of 8 to 60 months in 20 patients with 22 separate injections. There were three complications out of 108 injections: one superficial injection and two infraglottic submucosal collections of CaHA. Although not life threatening, these complications did require surgical removal. A more recent paper by Gillespie et al.[11] describes a 21% complication rate with CaHA, and the majority of the complications were due to superficial injection of CaHA. Our complication rate was 7.3% and all were minor complications, this is in concurrence with the literature indicating CaHA as a safe and effective alternative for vocal fold augmentation. We should note that despite having no major complications noted in UFVP patients, we encountered two older patients who underwent bilateral vocal fold injections due to presbylarynx, who had shifting of the material to the vocal fold free edge. Both patients had significant vocal fold atrophy and both injections were performed under general anesthesia. In both cases the material had to be removed with microlaryngoscopy and incision. One of these patients received speech therapy following this. Special attention needs to be paid in this patient population where the structures are significantly altered due to atrophy.

Recently available flexible laryngoscopic imaging technologies (distal chip camera) and new injection materials, which are able to flow through a fine-gauge needle, have made performing IL in the office a viable alternative to traditional, operating room-based IL.[12] Sulica et al.[13] reported that the number of in-office injections increased from 11 to 43% between 2003 and 2008. Two factors have been fundamental in permitting this return to the clinic setting. The first is the availability of a variety of injectable materials, most of them recently adapted or introduced for laryngeal use. The second advance is the improved quality of visualization of the larynx in the awake patient. In their study, decisions regarding method of injection (awake vs. asleep) were usually based on physician and/or patient preference and several medical comorbidities led surgeons to avoid a general anesthetic in seven cases.[13] In our series the average number of comorbidities was 2 in the awake group and 1.7 in the asleep group. While patient preference does play a role in the selection of the technique, the most important factor determining the mode of injection in this series has been the general health of the patient. Patients undergoing therapy for malignancies such as esophageal or lung carcinoma have been injected in the office in order not to introduce risks of general anesthesia. Also, the awake injection group was slightly older (62.5 years old vs. 57.5 in the asleep group, p=0.07). On the other hand, professional voice users were generally injected in the operating room, to achieve a more precise injection.

Mathison et al.[3] have demonstrated equivalent outcomes in Voice Related Quality of Life (VRQOL) measures in patients who undergo awake versus asleep IL in a retrospective case-control review of 141 patients with 166 injections. In this study, 105 IL were performed under general anesthesia. Average VRQOL in the awake patient improved by 25.05 points whereas average VRQOL in the asleep patient improved 20.81 points. Bove et al.[12] analyzed reimbursement in awake and asleep injection laryngoplasties in a group of 197 patients with a total of 211 injections. Awake IL was found to be less expensive than traditional injection under direct vision and general anesthesia ($11,890 compared to $1,408 for in-office injections).[12] Mathison, however has noted increased complications with awake injection, including rapid absorption of the injected material, vasovagal reactions, inadvertent injection into the superficial lamina propria, and vocal fold hematoma. They used five different products-- micronized dermis, hyaluronic acid, collagen, CaHA, and sodium carboxymethyl cellulose.[3] In this series of 68 patients, all complications were noted in office injections and they were all minor complications. Our experience does show that there is a steeper learning curve for in-office injections, but that is a reproducible procedure once mastered.

We measured voice outcomes by self-assessed VHI scores. The voice handicap index is a widely used self-administered questionnaire that assesses the patients' perceived degree of handicap related to their voice.[14] Average VHI in the 20 patients (awake and asleep totally) improved 27.9 points in a period of 1.8 to 81.8 weeks. Average VHI in the patients percutaneously injected improved 35.1 points, and average VHI in the asleep patients improved 20.7 points. There was no statistically significant relationship ($p=0.29$). Selecting appropriate patients for IL is critical to the success of such a technique. The ideal IL patient would present with a symptomatic complaint that they are motivated to improve upon.[2]

Conclusions

This study supports injection laryngoplasty, both percutaneous and under direct laryngoscopy, with calcium hydroxyapatite as a safe and effective intervention for patients with VF paralysis.

Declaration of conflicting interests

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REFERENCES

1. Rosen CA, Thekdi AA. Vocal fold augmentation with injectable calcium hydroxylapatite: short-term results. Journal of Voice 2004;18:387-91.
2. Kwon TK, Buckmire R. Injection laryngoplasty for management of unilateral vocal fold paralysis. Curr Opin Otolaryngol Head Neck Surg 2004;12:538-42.
3. Ward PH, Hanson DG, Abemayor E. Transcutaneous teflon injection of the paralyzed vocal cord: a new technique. Laryngoscope 1985;95:644-9.
4. Rosen CA, Gartner-Schmidt J, Casiano R, Anderson TD, Johnson F, Remacle M, et al. Vocal fold augmentation with calcium hydroxylapatite: twelve-month report. Laryngoscope 2009;119:1033-41.
5. Nakayama M, Ford CN, Bless DM. Teflon vocal fold augmentation: failures and management in 28 cases. Otolaryngol Head Neck Surg 1993;109:493-8.
6. Woo SH, Son Y, Lee SH, Park JL, Kim JP. Comparative analysis on the efficiency of the injection laryngoplasty technique using calcium hydroxyapatite (CaHA): the thyrohyoid approach versus the cricothyroid approach. Journal of Voice 2013;27:236-41.
7. Chhetri DK, Jahan-Parwar B, Hart SD, Bhuta SM, Berke GS. Injection laryngoplasty with calcium hydroxylapatite gel implant in an in vivo canine model. Ann Otol Rhinol Laryngol 2004;113:259-64.
8. Tanna N, Zalkind D, Glade RS, Bielamowicz SA. Foreign body reaction to calcium hydroxylapatite vocal fold augmentation. Arch Otolaryngol Head Neck Surg 2006;132:1379-82.
9. Belafsky PC, Postma GN. Vocal fold augmentation with calcium hydroxylapatite. Otolaryngol Head Neck Surg 2004;131:351-4.
10. Carroll TL, Rosen CA. Long-term results of calcium hydroxylapatite for vocal fold augmentation. Laryngoscope 2011;121:313-9.
11. Gillespie MB, Dozier TS, Day TA, Martin-Harris B, Nguyen SA. Effectiveness of calcium hydroxylapatite paste in vocal rehabilitation. Ann Otol Rhinol Laryngol 2009;118:546-51.
12. Bové MJ, Jabbour N, Krishna P, Flaherty K, Saul M, Wunar R, et al. Operating room versus office-based injection laryngoplasty: a comparative analysis of reimbursement. Laryngoscope 2007;117:226-30.
13. Sulica L, Rosen CA, Postma GN, Simpson B, Amin M, Courey M, et al. Current practice in injection augmentation of the vocal folds: indications, treatment principles, techniques, and complications. Laryngoscope 2010;120:319-25.
14. Lau DP, Zhang EZ, Wong SM, Lee G, Chan YH. Correlating voice handicap index and quantitative videostroboscopy following injection laryngoplasty for unilateral vocal paralysis. Otolaryngol Head Neck Surg 2010;143:190-7.