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Long-Term Efficacy of Percutaneous Steroid Injection for Treating Benign Vocal Fold Lesions: A Prospective Study

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Objectives/Hypothesis: This study assessed the long-term efficacy and recurrence rates of percutaneous steroid injections (PSIs) for benign vocal fold lesions.

Study Design: Prospective clinical study.

Methods: A prospective human clinical trial was performed from October 2008 to September 2014 at Soonchunhyang University Hospital, Bucheon, Korea. Percutaneous steroid injection was performed in 84 consecutive patients with small benign vocal fold lesions, such as vocal fold nodules, polyps, and Reinke's edema, who could not be treated with voice therapy or surgery. Patients had acoustic aerodynamic, perceptual, stroboscopic, and voice handicap index evaluations before PSI and also 3, 6, 12, and 24 months after PSI.

Results: Of the 84 patients, 37 (44.0%) showed complete remission; 22 (26.2%) showed partial remission; five (6%) had no response; and 20 (23.8%) developed recurrences after PSI. Most of the objective and subjective parameters that improved statistically ($P < 0.05$) 3 months after PSI remained stable until 24 months. For the recurrences, the average recurrence time interval after PSI was 8.5 $\pm$ 8.2 (range 3–36) months. Recurrence was associated with voice abuse after PSI and professional voice users ($P < 0.05$). Complications during follow-up included minimal vocal fold hematomas in 2.4% (2 of 84) and mild vocal fold atrophy in 1.2% (1 of 84).

Conclusion: Percutaneous steroid injection is a useful alternative modality for treating benign vocal fold lesions without morbidity. However, recurrence rates were higher with voice abuse after PSI and professional voice users.

Key Words: Steroid, vocal fold, recurrences.

Level of Evidence: 4.

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INTRODUCTION

With the advancement of percutaneous injections techniques and endoscopy, recent articles have proposed that vocal fold steroid injection might provide an alternative treatment option for benign lesions of the vocal folds.[1]

Although there are some differences, vocal nodules, vocal polyps, and Reinke's edema have common histologic characteristics, including edema, a thick basement membrane, inflammation, and vessel wall thickness.[2] Additionally, all of these benign vocal fold lesions and pathologic lesions are confined to Reinke's space.[3]

Percutaneous steroid injections (PSI) could maintain a high concentration of steroid in Reinke's space without puncturing the mucosa and could induce a maximum potent antiinflammatory effect with minimal side effects.[4–6]

Currently, standard treatments for benign vocal fold disease include voice therapy and laryngomicroscopic surgery. Voice therapy is the standard treatment options for vocal nodules, and laryngomicroscopic surgery is the preferred option for vocal polyps. However, if a patient's occupational and economic status and facilities cannot support voice therapy and laryngomicroscopic surgery, PSI could be a useful alternative.[7]

To date, no prospective studies have shown the long-term utility of PSI in the management of benign vocal fold lesions. Therefore, this is a first prospective study to demonstrate the long-term efficacy of PSI.

MATERIALS AND METHODS

Patients

A prospective human clinical trial was performed from October 2008 to September 2014 at Soonchunhyang University Hospital, Bucheon, Korea. Percutaneous steroid injection was performed in patients with small benign vocal fold lesions, such as vocal fold nodules, polyps, and Reinke's edema, who could not be treated with voice therapy or surgery.

Most of the patients who underwent PSI could not receive four to six sessions of voice therapy due to economic or social reasons and did not want general anesthesia. Professional voice users were defined as those who use their voices professionally,

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TABLE I.
Patient Demographics and Treatment Information (n = 84).

Variable	Value
Mean age in years ± SD (range)	46.8 ± 10.6 (18–84)
Mean injected volume at each side (mL)	0.17 ± 0.6
Interval from PSI to whitish steroid particle disappearance (days)	20.6 ± 8.9
Interval from PSI to recurrence in months (range)	8.5 ± 8.3 (3–36)
Disease distribution of PSI	
Vocal nodule, number (%)	30/84 (35.7%)
Reinke's edema	30/84 (35.7%)
Vocal polyp	24/84 (28.6%)
Mean size reduction of lesions (%)	76.3 ± 33.2

PSI = percutaneous steroid injection; SD = standard deviation.

such as teachers, pastors, telemarketers, counselors, instructors, actors, and salespeople.

The patients had acoustic aerodynamic, perceptual, stroboscopic, and voice handicap index (VHI) evaluations before and at 3, 6, 12, and 24 months after PSI. Eighty-four patients completed acoustic aerodynamic, perceptual, stroboscopic, and VHI evaluations 12 months after PSI; and 46 patients completed 24 months of follow-up. Patients who showed no change in lesion size (n = 5) or recurrence (n = 20) after PSI were excluded from statistical analyses. Table I lists demographic information and patient characteristics. Informed consent was obtained from all patients prior to their enrollment in the study. The study design was approved by the institutional review board (SCHBC IRB 09 10).

Objective and Subjective Voice Evaluation

Vocal function data were collected prior to PSI at 3, 6, 12, and 24 months after PSI. Mean percentage of jitter, mean percentage of shimmer, and harmonics-to-noise ratio (HNR) data were extracted from the steady-state portion of a sustained [a] vowel using the Multi-Dimensional Voice Program (model 4500; Kaypentax, Lincoln Park, NJ). The maximum phonation time produced on a sustained [a] vowel was recorded using the Computerized Speech Lab (model 4500; Kaypentax) and averaged across three trials. Psychosocial data were collected using the Korean language version of the VHI. Endoscopic and videostroboscopic data were collected using the Rhino-Laryngeal Stroboscope (RLS model 9100; Kaypentax). The glottal gap was rated using a previously reported 4-point equal-appearing interval scale with 0 = severe, 1 = moderate, 2 = mild, and 3 = absent.[8] Mucosal wave was rated using a previously reported 4-point equal-appearing interval scale with 0 = absent, 1 = severely reduced, 2 = mildly reduced, and 3 = intact.[8]

Percutaneous Steroid Injection Procedure

All of the PSI procedures were performed percutaneously under local anesthesia by a single surgeon (S.W.L.) under transnasal flexible fiberscopic monitoring (Olympus laryngobronchoscope ENF T3, V2; Olympus Medical, Center Valley, PA). Next, 0.1 to 0.2 cc of triamcinolone acetonide (40 mg/mL; Shin Poong Pharm Co., Ltd, Seoul, South Korea) was injected into Reinke's space to avoid deeper injection into the vocalis muscle to prevent vocal fold atrophy.[4]

With regard to the choice of approach of PSI, a surgeon chooses from the cricothyroid approach, transcartilaginous approach, and thyrohyoid approach depending on the vocal fold and neck conditions of the patients (Fig. 1).[8]

Image Analysis

Endoscopic images taken serially after PSI were used to determine treatment outcome and calculate the reduction of the square for benign vocal fold lesions. To minimize measurement bias, the author used identical pixel capture images (500 × 400 pixels) and adjusted the length of the endoscopic image from the anterior commissure to the vocal process of the arytenoid cartilage of the contralateral vocal fold.[9] The lesion area was circumscribed using Image J software (Image J 1.43u; National Institutes of Health, Bethesda, MD) and Adobe Photoshop imaging analysis software (Adobe Systems Inc., San Jose, CA). We defined the degree of size reduction based on endoscopic images at 12 months after PSI.[10]

Treatment Outcome Measurement

Endoscopic images were taken and interpreted by participating laryngologists after PSI at each expected follow-up examination to determine the treatment outcome. Treatment responses were categorized as complete remission, partial remission, no change, and recurrences during the 2-year follow-up period (Fig. 2).

Complete remission was defined as an 80% to 100% decrease in lesion size compared with the original size, partial remission a 20% to 79% decrease in size, and no change as a

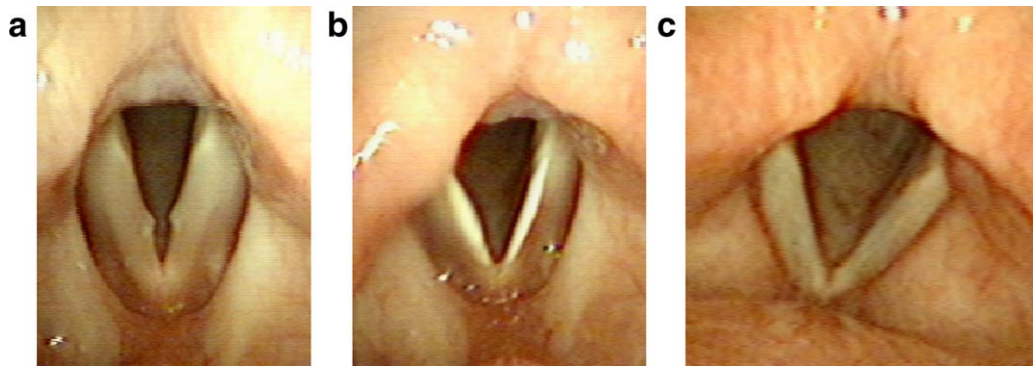

Fig. 1. Representative serial fiberscopic images after PSI for vocal nodule patient. (A) Vocal nodule before PSI, (B) at the end of the second weeks after PSI, and (C) at the end of 3 months after PSI. PSI = percutaneous steroid injection.[Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

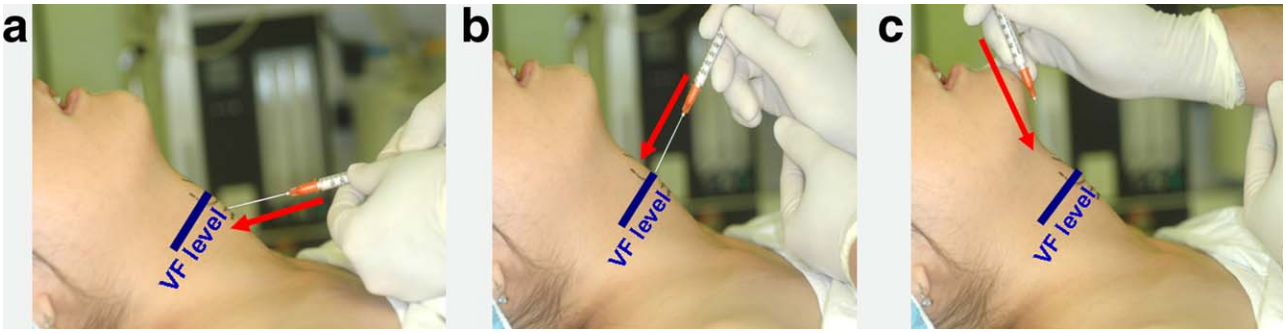

Fig. 2. Representative photographs of PSI using the cricothyroid approach (A), transcartilaginous approach (B), and thyrohyoid approach (C). PSI = percutaneous steroid injection.[Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

0% to 19% decrease in size. Recurrence was defined as a positive response after initial PSI treatment, with regrowth of the lesion during the 2-year follow-up period. The mean follow-up period at the time of analysis was 31.3 ± 9.4 months.

Statistical Analysis

Statistical analyses were performed using paired *t* test and *chi*-squared test (Korean Version of SPSS 14.0 for Windows, SPSS Inc., Chicago, IL). *P*-values less than 0.05 were considered to indicate statistical significance. Vocal function data analysis was performed for 59 patients among 84 1-year follow-up patients after PSI, after the exclusion of 20 patients with recurrence and five patients with no lesion change.

RESULTS

Treatment Outcomes

Table I summarizes the patient demographics and treatment information. Etiologic diseases consisted of vocal nodules (35.7%; 30 of 84), Reinke's edema (35.7%; 30 of 84), and vocal polyps (28.6%; 24 of 84). The mean size reduction of the benign vocal fold lesions after a single PSI was 76.3% ± 33.2% of the original lesion size. Tables II and III present the treatment outcome data after PSI. The overall treatment response after a single PSI was complete response in 44.0% (37 of 84), partial remission in 26.2% (22 of 84), and no lesion change in 6.0% (5 of 84) of the patients; the recurrence rate during follow-up was 23.8% (20 of 84). No statistically significant differences were observed in treatment outcomes according to the type of lesion ($P = 0.453$). Considering "complete remission" and "partial remission" as responsive results, the overall long-term response rate was 70.2%.

Objective and Subjective Voice Evaluation

Table IV presents voice analysis data after PSI. The average percentage of jitter and shimmer was decreased significantly at 3 months after PSI and remained stable until 12 months ($P < 0.05$). Harmonics-to-noise ratio was also increased significantly at 3 months after PSI and remained stable until 12 months ($P < 0.05$). Voice handicap index-30 scores improved significantly at 3 months postoperatively and remained stable at 12 months. Stroboscopic analyses revealed that the average mucosal wave and posterior glottic gap grades were significantly improved at 3, 6, and 12 months after PSI ($P < 0.05$).

Voice Analyses for Long-term Follow-up Patients

Table V presents the voice analysis data for the 46 patients followed up for 2 years after PSI. In these long-term follow-up patients, the percentage of jitter, shimmer, VHI, grade of mucosal wave, and posterior glottic gap was improved significantly 12 months after PSI and remained stable at 24 months ($P < 0.05$). In contrast, HNR was improved significantly at 12 months after PSI ($P < 0.05$) but not at 24 months ($P > 0.05$) after PSI.

Recurrences

Of the 84 patients, 20 (23.8%) showed recurrence, and the average recurrence time interval after PSI was 8.5 ± 8.2 months (range: 3–36 months). Ninety percent (18 of 20) of these patients demonstrated recurrence within 12 months after PSI.

Univariate analysis revealed that smoking and lesion type were not associated with recurrence. However, voice abuse after PSI and professional voice use were associated with high recurrence ($P < 0.05$). Non-voice abusers after PSI showed 5.7% recurrence, but voice abusers had a recurrence rate of 54.8%. Nonprofessional voice users had a 15.1% recurrence rate, whereas professional voice users had a 38.7% recurrence rate ($P < 0.05$).

TABLE II.
Overall Treatment Response Rates After Percutaneous Steroid Injection for Benign Laryngeal Lesions.

Results	Number (%)
Complete remission	37/84 (44.0%)
Partial remission	22/84 (26.2%)
No response	5/84 (6.0%)
Recurrence	20/84 (23.8%)
Total	84/84 (100.0%)

CR = complete response; PR = partial response.

TABLE III.
Treatment Response Rate After Percutaneous Steroid Injection for Each Benign Laryngeal Lesion.

	CR Number (%)	PR Number (%)	No Response Number (%)	Recurrence Number (%)	Total Number (%)
Vocal nodule	16 (53.3%)	6 (20.0%)	0 (0 %)	8 (26.7%)	30 (35.7%)
Reinke's edema	13 (43.3%)	9 (30.0%)	2 (6.7%)	6 (20.0%)	30 (35.7%)
Vocal polyp	8 (33.3%)	7 (29.2%)	3 (12.5%)	6 (25.0%)	24 (28.6%)

CR = complete response; PR = partial response.

Postoperative Complications

No serious adverse events related to PSI were observed during the follow-up period, including airway obstruction or material migration. However, two patients exhibited minor vocal-fold hematoma that resolved spontaneously without any intervention. One patient demonstrated persistent, whitish steroid particles at Reinke's space over 1 month. Additionally, one patient exhibited mild vocal fold atrophy after PSI and difficulty with a high-pitched voice, both of which were improved at 3 months without any intervention.

DISCUSSION

Currently, the standard treatments for benign vocal fold lesions such as vocal nodules, vocal polyps, and Reinke's edema are voice therapy and laryngomicroscopic surgery. Voice therapy is the treatment of choice for vocal nodules, and laryngomicroscopic surgery is for vocal polyps.[7] Voice therapy is a modified kind of cognitive behavioral therapy that corrects the patient's bad voice habits and improves vocal hygiene education. However, voice therapy requires multiple sessions and takes a long time to have an effect, which may reduce compliance due to economic or occupational reasons.

In Asian countries, voice therapy has been introduced relatively recently, and the public's understanding of the mechanism of voice therapy is poor. Thus, PSI for benign vocal fold lesions might fulfill the therapeutic gap between voice therapy and laryngomicroscopic surgery; PSI could be a useful alternative modality for small benign vocal fold lesions.[11]

Using PSI to treat benign vocal fold lesions is based on the rationale that these lesions result from phonotrauma, chronic inflammation, and subsequent remodeling of Reinke's space,[7] which share common histologic characteristics including edema, thick basement membrane, inflammation, and vessel wall thickness at Reinke's space.[2,12]

Steroids are very powerful antiinflammatory drugs; PSI can maintain a high concentration at Reinke's space, and reduce the inflammatory reaction of vocal fold lesions while preventing the potential systemic adverse effects of the steroid.[13]

Percutaneous steroid injection has other advantages: the technique requires only simple equipment such as a flexible endoscope and disposable needle, and the procedure is a modified version of injection laryngoplasty, which is a familiar procedure to ear, nose, and throat surgeons.[5]

Despite these advantages, the role of PSI has not been established for the treatment of benign vocal fold lesions. There is a lack of large prospective series with long-term follow-up, and no studies have conducted recurrence and complication analysis.

The author (S.W.L., along with J.H.W) previously reported the efficacy of PSI for benign vocal fold lesions in a prospective multicenter study in 2011 based on 6 months of follow-up data. In that series, 34.8% showed complete remission; 49.6% showed partial remission;

TABLE IV.
Voice Analysis Data After Percutaneous Steroid Injection (n = 59).

	Baseline	3 Months After PSI	6 Months After PSI	12 Months After PSI
MPT (sec)	11.9 ± 4.2	12.4 ± 2.6	12.9 ± 2.1	12.3 ± 1.9
Jitter (%)	1.65 ± 1.92	1.06 ± 0.72*	0.95 ± 0.44*	0.91 ± 0.41*
Shimmer (%)	4.58 ± 2.58	2.82 ± 0.97*	2.82 ± 1.06*	2.62 ± 0.68*
HNR (dB)	23.9 ± 5.8	26.5 ± 4.9*	26.6 ± 5.3*	26.9 ± 4.1*
VHI	47.3 ± 23.9	37.5 ± 26.6*	29.9 ± 19.6*	24.5 ± 22.5*
Mucosal wave	1.77 ± 0.55	2.56 ± 0.50*	2.68 ± 0.51*	2.65 ± 0.65*
Glottic gap	1.80 ± 0.61	2.78 ± 0.42*	2.77 ± 0.48*	2.65 ± 0.64*

The recurrence cases and no change of lesion cases were excluded from this analysis.
*Significantly improved from the baseline and after PSI.
Baseline = baseline voice data.
Jitter (%) = percentage of jitter.
Shimmer (%) = percentage of shimmer.
Mucosal wave = grade of the mucosal wave.
Glottic gap = grade of the glottic gap.
HNR = harmonics-to-noise ratio; MPT = maximum phonation time; PSI = percutaneous steroid injection; VHI = voice handicap index.

TABLE V.
Voice Analysis Data of Long-term Follow-up Patients (n = 46).

	Baseline	12 Months After PSI	24 Months After PSI
MPT (sec)	12.3 ± 4.3	12.4 ± 1.9	12.6 ± 2.9
Jitter (%)	1.41 ± 0.89	0.91 ± 0.41*	1.00 ± 0.50*
Shimmer (%)	3.64 ± 1.46	2.61 ± 0.68*	2.77 ± 0.68*
HNR (dB)	24.6 ± 5.5	26.9 ± 4.1*	25.8 ± 3.7
VHI	46.6 ± 24.3	24.3 ± 22.8*	26.0 ± 22.4*
Mucosal wave	1.70 ± 0.58	2.64 ± 0.65*	2.61 ± 0.71*
Glottic gap	1.73 ± 0.62	2.73 ± 0.62*	2.83 ± 0.38*

Cases of recurrence and no change of lesion cases were excluded from this analysis.
*Significantly improved from baseline after PSI.
Baseline = baseline voice data.
Jitter (%) = percentage of jitter.
Shimmer (%) = percentage of shimmer.
Mucosal wave = grade of the mucosal wave.
Glottic gap = grade of the glottic gap.
HNR = harmonics-to-noise ratio; MPT = maximum phonation time; VHI = voice handicap index.

11.3% showed no response; and 4.3% showed recurrence.[11]

Wang et al. conducted a meta-analysis using data from published articles about vocal fold steroid injection for benign vocal fold lesions and found that the recurrence rates after vocal fold steroid injection were between 4% and 31%.[14] However, these recurrence rates were very variable.[9,14] Additionally, the follow-up period was too short, from 4 weeks to 6 months, to prove the efficacy of PSI.

The present study is the first clinical study to show long-term efficacy and recurrence rates of PSI over 2 years prospectively by a single surgeon (S.W.L.). To our knowledge, this dataset represents the largest and longest prospective clinical series of PSI for benign vocal fold lesions.

The combination of complete remission and partial remission was considered as the responsive group after PSI. The overall response rate after single PSI was 73.3% for vocal nodules, 73.3% for Reinke's edema, and 62.5% for vocal polyps. The mean size reduction after PSI was 76.3%.

The recurrence analysis revealed that smoking and type of lesion were not associated with recurrence, but voice abuse after PSI and professional voice use were associated with recurrence ($P < 0.05$). We believed that PSI treatment could improve the benign vocal fold lesion with a potent antiinflammatory action within a short-term period. However, without correction of the fundamental cause, such as voice abuse and bad voice habits, regrowth of the lesion could occur in the long term.

CONCLUSION

Percutaneous steroid injection is a useful alternative modality for treating benign vocal fold lesions without morbidity. However, the recurrence rates are higher with voice abuse after PSI and professional voice users.

BIBLIOGRAPHY

1. Tateya I. Laryngeal steroid injection. *Curr Opin Otolaryngol Head Neck Surg* 2009;17:424–426.
2. Dikkers FG, Nikkels PG. Benign lesions of the vocal folds: histopathology and phonotrauma. *Ann Otol Rhinol Laryngol* 1995;104:698–703.
3. Martins RH, Fabro AT, Domingues MA, Chi AP, Gregorio EA. Is Reinke's edema a precancerous lesion? Histological and electron microscopic aspects. *J Voice* 2009;23:721–725.
4. Mortensen M, Woo P. Office steroid injections of the larynx. *Laryngoscope* 2006;116:1735–1739.
5. Mallur PS, Rosen CA. Vocal fold injection: review of indications, techniques, and materials for augmentation. *Clin Exp Otorhinolaryngol* 2010; 3:177–182.
6. Wang CT, Lai MS, Liao LJ, Lo WC, Cheng PW. Transnasal endoscopic steroid injection: a practical and effective alternative treatment for benign vocal fold disorders. *Laryngoscope* 2013;123:1464–1468.
7. Johns MM. Update on the etiology, diagnosis, and treatment of vocal fold nodules, polyps, and cysts. *Curr Opin Otolaryngol Head Neck Surg* 2003;11:456–461.
8. Lee SW, Kim JW, Koh YW, Shim SS, Son YI. Comparative analysis of efficiency of injection laryngoplasty technique for with or without neck treatment patients: a transcartilaginous approach versus the cricothyroid approach. *Clin Exp Otorhinolaryngol* 2010;3:37–41.
9. Wang CT, Liao LJ, Lai MS, Cheng PW. Comparison of benign lesion regression following vocal fold steroid injection and vocal hygiene education. *Laryngoscope* 2014;124:510–515.
10. Moon IH, Park KN, Kim HK, Lee S. Utility and safety of commercially available injection laryngoplasty materials in a rabbit model. *J Voice* 2015;29:125–128.
11. Woo JH, Kim DY, Kim JW, Oh EA, Lee SW. Efficacy of percutaneous vocal fold injections for benign laryngeal lesions: prospective multicenter study. *Acta Otolaryngol* 2011;131:1326–1332.
12. Wallis L, Jackson-Menaldi C, Holland W, Giraldo A. Vocal fold nodule vs. vocal fold polyp: answer from surgical pathologist and voice pathologist point of view. *J Voice* 2004;18:125–129.
13. Jin HJ, Lee SH, Lee SU, et al. Morphological and histological changes of rabbit vocal fold after steroid injection. *Otolaryngol Head Neck Surg* 2013;149:277–283.
14. Wang CT, Liao LJ, Cheng PW, Lo WC, Lai MS. Intralesional steroid injection for benign vocal fold disorders: a systematic review and meta-analysis. *Laryngoscope* 2013;123:197–203.