

Efficacy of Intralesional Steroid Injection in Small Benign Vocal Fold Lesions

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Summary: Objectives. The present study was conducted to study the efficacy of intralesional steroid (ILS) injection in small benign vocal fold lesions and compare the outcomes with microlaryngeal surgery in terms of improvement in symptoms and reduction in lesion size.

Methods. The current randomized control trial was conducted in the Department of Otolaryngology at the Postgraduate Institute of Medical Education and Research in Chandigarh between 2014 and 2015. The clinical diagnosis was based on appearance of the lesion during endoscopy and the mucosal vibration pattern. Subjects with lesions of size less than or equal to 5 mm were included.

Results. A total of 29 subjects were included in the study and 15 (nine men and six women) of them were randomized to receive ILS injection. Fourteen (13 men and one woman) were randomized to the second group to receive initial microlaryngeal surgery. We noted significant reduction in the size of the lesion among subjects undergoing ILS injection at 12 weeks (1.11 + 1.45 mm) as compared to baseline (2.63 + 1.28 mm) with no recurrence.

Conclusions. ILSs are effective in reducing size of lesion and also improve acoustic parameters, perceptual analysis, and grade of dysphonia in patients presenting with small benign vocal cord lesions.

Key Words: Benign vocal cord lesions—Intralesional steroids—Methylprednisolone—Microlaryngeal surgery—Small vocal polyp—Small vocal cord lesions.

INTRODUCTION

Disturbances in voice are often a cause of distress not only in those who use their voice professionally but also for individuals for daily communication. Benign lesions have the potential to cause changes in voice, reduction of loudness, and pitch breaks. It has been shown that almost one in three individuals have at least one lifetime voice disorders and 7.2% miss one or more working days.¹ Lesions are even more common among professional voice users due to recurrent phonotrauma.²

Vocal nodules, polyps, and cysts are common benign lesions affecting the vocal cords. Reinke edema mostly occurs in middle-aged women with history of vocal abuse and smoking. The treatment modalities for these benign vocal fold diseases often include a multidisciplinary approach with a spectrum from vocal hygiene education through phonosurgery. Behavioral alterations including avoidance of phonotraumatic behavior and vocal exercises have long been used for treatment but are not easy as they require incorporation of new motor learning and cognitive processes.³ Availability of lasers and microsurgical equipment has revolutionized treatment options in recent times. Endoscopic surgery offers binocular vision, good lighting, precision, and visualization of lesions and has been the mainstay of treatment over the last few decades. Apart from cold instrumentation, lasers have played an important role in management in recent times.⁴ However, instrumentation has

been criticized to cause increased scarring and dysphonia.⁵ Focus of treatment has now shifted to conservative approaches and intralesional steroid (ILS) injections have been offered as simple office procedures for vocal nodules, polyps, cysts, granulomas, scars, and Reinke edema.⁶ Triamcinolone, methylprednisolone and dexamethasone have all been used for these lesions with mixed success.^{7–10} In-office steroid injections have been trumpeted as relatively simple procedures that can be performed in local anesthesia and are associated with early voice recovery with minimal postoperative fibrosis and scarring despite some initial technical difficulties. Researchers using different injection techniques have often reported mixed results.^{7,8,10–15} Vocal fold hematoma, atrophy, and recurrence have been reported as side effects and complications of the technique in previous studies.^{7,11,14,16}

The present study was conducted to study the efficacy of ILS injection in small benign vocal fold lesions and compare the outcomes with microlaryngeal surgery (MLS) in terms of improvement in symptoms and reduction in lesion size.

METHODS

The current randomized control trial was conducted in the Department of Otolaryngology and Head and Neck Surgery at the Postgraduate Institute of Medical Education and Research in Chandigarh between 2014 and 2015 after approval by the institutional ethics committee. All subjects presenting to the outpatient department clinics with complaints of change in voice were assessed by videolaryngostroboscopy using 90° transoral rigid endoscope. The clinical diagnosis was based on appearance of the lesion during endoscopy and the mucosal vibration pattern. Subjects with lesions of size less than or equal to 5 mm were included after they provided written and informed consent. Those found unfit for general anesthesia, suspected to

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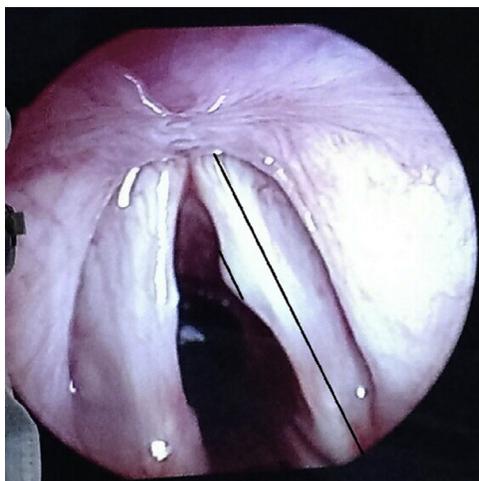


FIGURE 1. Calculation of lesion size. The average length of vocal folds in women and men is 12 mm and 14 mm, respectively. The size of vocal fold lesion was calculated with respect to the vocal fold length using *Corel* version X7.

have a malignancy, and had history of postsurgical failure were excluded from the study. Subjects younger than 18 years of age or those older than 70 years were excluded.

Demographic and clinical data were collected for all participants with particular focus on vocal behavior and adjunctive factors such as laryngopharyngeal reflux, allergies, and addictions. The size of lesions was assessed using imaging software (*Corel*, version X7, Ottawa, Canada) ([Figure 1](#)). All subjects underwent voice assessment using *Doctors* speech software (2.6



FIGURE 4. Intralesional steroid being injected at the base of lesion.

version, Seattle, US) (Vocal assessment, version 4.0). Voice handicap index (VHI) and grade, roughness, breathiness, asthenia, and strain (GRBAS) scale were used to analyze voice. All participants received at least two sessions of voice therapy before receiving intervention, which was determined using randomization into two groups using computer-generated tables. The first group received 1 mL intralesional methylprednisolone acetate (40 mg/mL) using rigid laryngoscopy under microscopic guidance infiltrated submucosally above lamina propria. Blanching of the base of lesion was considered as the end point of the injection and the amount of drug received was noted for



FIGURE 2. Instruments and steroid used for the intralesional steroid injection.

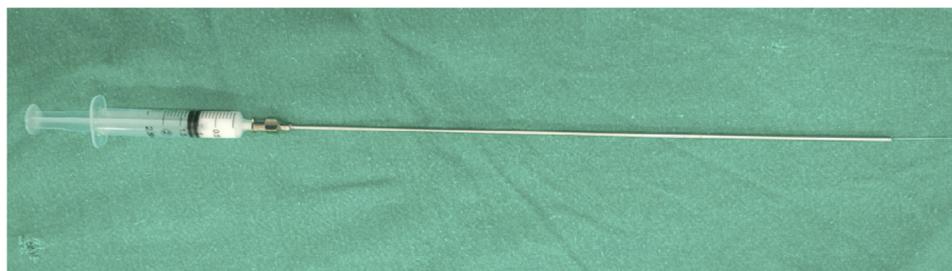


FIGURE 3. Syringe with needle (Bruning).

each participant. The second group underwent excision of the lesion using cold instrumentation by MLS after visualization by rigid laryngoscopy. Both procedures were performed in general anesthesia due to logistic limitations (Figures 2–4).

Postoperative care was same in both groups and included adequate hydration and absolute voice rest for 1 week. In the second week, subjects followed relative voice rest including minimal talking and avoidance of straining activities such as whispering and shouting. Voice therapy was started in the third postoperative week. Subjects received proton pump inhibitors for 2 weeks postoperatively to prevent reflux-associated delay in recovery. None of the subjects received antihistamine agents.

Subjects were followed up at 2, 6, and 12 weeks postoperatively for lesion size, acoustic parameters, and subjective perception. Reduction in size was classified into one of five categories: (1) complete, (2) incomplete (more than 50% reduction in size), (3) partial (less than 50% reduction in size) reduction, (4) no change, and (5) recurrence. For the purpose of analysis, those with partial or incomplete reduction and recurrence were considered as failure. Acoustic parameters measured were (1) frequency of glottal opening and closing (Hertz), (2) maximum phonation time in seconds, and (3) jitter or (4) shimmer, which both indicate instability of voice fold vibration. Perceptual analysis was performed using the VHI, which is a 30-item questionnaire that assesses functional, emotional, and physical aspects of voice disorders.¹⁷ GRBAS, a four-point grade of dysphonia using roughness, breathiness, asthenia, and strain, was used ranging from zero (indicating normal) to three (indicative of severe deviance).

Subjects who did not show response to ILS injection in the first group 3 months after procedure were advised excision of lesion by microlaryngeal surgery.

Statistical analysis was performed using *Statistical Package for Social Sciences* (SPSS version 20 for Windows, IBM Corp., Armonk, New York). The categorical variables are presented as frequency distributions and percentages. Continuous variables are presented as mean and standard deviation. Student *t* test for unpaired data was used to compare means. Skewness was assessed using Kolmogorov test and skewed data are presented as median and interquartile range. Mann-Whitney *U* test was used to compare distributions between groups. Wilcoxon signed-rank test was used to compare ordinal data within each group over time. Two-tailed *P* value of less than 0.5 was considered significant in all tests for interpretation. A *post hoc* power analysis to detect a difference of 1.32 (\pm 1.88) mm in the original lesion size of 2.63 (\pm 1.28) mm revealed a power of 80% with alpha of 0.5 with 15 subjects in each group.

RESULTS

A total of 29 subjects were included in the study and 15 (nine men and six women) of them were randomized to receive ILS injection. Fourteen (13 men and one woman) were randomized to the second group to receive initial MLS. The baseline comparison of the two groups is presented in Table 1. All subjects had unilateral lesions except one, who presented with bilateral Reinke edema and was randomized to the MLS group. There

were no significant baseline differences between the individuals receiving ILSs and those undergoing microlaryngeal surgery.

The distribution and comparison in the outcome parameters have been presented in Table 2 and Table 3. The difference between the measurements at follow-up and baseline have been calculated in the two groups undergoing different procedures, and these differences in means have been compared using a paired *t* test. The results indicate a significant increase in habitual frequency of glottal opening and closing in both groups following procedure. A significant increase in maximum phonation time is similarly noted, especially for the subjects undergoing MLS. A significant decrease in shimmer and jitter is noted only in the MLS group. There is a significant reduction in the VHI in both groups irrespective of the procedure used for treatment. The results of the ILS group with regard to VHI are comparable to the MLS group. A significant reduction in GRBAS group is noticed only in the MLS group.

DISCUSSION

In the current study on 29 subjects with benign vocal cord lesions randomized to receive ILS injection or MLS, we found that steroid injection with methylprednisolone is a simple procedure and results in significant and comparable improvement in habitual *f*₀, mean phonation time (MPT), and VHI after 12 weeks of follow-up.

ILS injections for benign vocal cord lesions hailed as conservative procedures have been demonstrated to improve voice parameters and to delay surgery. In addition, they may lead to regression of the lesion and spare the patient from undergoing a surgical procedure. The procedure affords a possibility of recurrent injections at different times to achieve desired results, which may not be possible with a cold instrument intervention.

At this point, a discussion on the agents used for injections is prudent. Researchers have reported using several agents such as triamcinolone acetonide, methylprednisolone, and a mixture of dexamethasone sodium phosphate and triamcinolone.^{8,9,13,18} Triamcinolone, due to its long-acting nature, has been associated with vocal cord atrophy and formation of plaques.^{11,19} Meanwhile, a very low risk of postoperative complications has been reported with the use of methylprednisolone.⁸

Most researchers have previously reported the use of steroid injections as a procedure that can be administered in office settings under local anesthesia.^{8–10,13,14} Mathison et al showed that although voice-related quality-of-life outcomes in subjects undergoing steroid injections under topical anesthesia were similar to those receiving general anesthesia for the procedure, the rate of perioperative complications were higher among subjects receiving topical or local anesthesia.²⁰ We felt that in addition to a lower complication rate, better precision could be achieved if the procedure was accomplished under general anesthesia. Further, this yielded better comparison of anesthesia-related complications in our study groups.

Reduction in size

We noted significant reduction in the size of the lesion among subjects undergoing ILS injection at 12 weeks (1.11 + 1.45 mm)

TABLE 1.
Baseline Preoperative Comparison of the Subjects in Two Groups

Characteristic	Group 1 (Intralesional Steroid)	Group 2 (Microlaryngeal Surgery)	
Age	39.27 (26–60)	44.36 (32–67)	0.2
Sex distribution			
Male	9 (40.9)	13 (59.1)	
Female	6 (85.7)	1 (14.3)	
Presenting complaints			
Reduced loudness	12 (63.2)	7 (36.8)	
Increased effort	5 (55.6)	4 (44.4)	
Vocal tiredness	4 (66.7)	2 (14.3)	
Throat clearing	4 (80.0)	1 (20.0)	
Roughness	4 (66.7)	2 (33.3)	
Pitch break	1 (50.0)	1 (50.0)	
Duration of symptoms	5.3 months	5.4 months	0.9
Exposure to environmental irritants	4 (26.7%)	6 (42.9%)	0.5
Nasal allergies	4 (28.6)	2 (13.3)	0.4
Vocal abuse	10 (71.4%)	8 (53.3%)	0.3
Laryngopharyngeal reflux	7 (46.7%)	8 (57.1%)	0.7
Perioperative size of lesion	2.75 (+1.39) mm	3.23 (+0.83)	0.4
Habitual f0 (frequency of glottal opening and closing in Hertz)	185.86 (15.71)	148.86 (8.61)	0.05
MPT0 (maximum phonation time in seconds)	8.53 (1.28)	7.93 (0.85)	0.7
Jitter	1.19 (0.23)	1.03 (0.16)	0.5
Shimmer	1.78 (0.2)	1.46 (0.21)	0.3
VHI	20.27 (2.91)	25.14 (3.08)	0.26
GRBAS	5.8 (0.56)	7.07 (0.35)	0.07
Preoperative diagnosis			0.3
Vocal polyps	8 (42.1)	11 (57.9)	
Vocal cyst	5 (71.4)	2 (28.6)	
Vocal nodule	1 (100.0)	0	
Reinke edema	1 (50.0)	1 (50.0)	
Lesion side			0.5
Right	8 (57.1)	7 (46.7)	
Left	6 (42.9)	8 (53.3)	

Notes: This table presents the baseline comparison of the groups according to the procedure performed in each. The values presented indicate mean (\pm standard error) or frequency (percentage) as applicable.

Abbreviation: Habitual f0, frequency of glottal opening and closing in Hertz.

as compared to baseline (2.63 + 1.28 mm) with no recurrence. Complete regression of lesion was noted in seven patients, whereas partial response was noted in eight subjects in the first group. Obviously, all lesions showed complete regression in the microsurgery group. In 2013, Wang et al included 30

subjects with polyps and cysts, injected them with dexamethasone, and reported complete and partial resolution in 10 and 19 subjects, respectively.¹⁰ In another study, the same authors included 176 subjects with vocal polyps and cysts in 2014, 92 of whom received intralesional and 84 received educational

TABLE 2.
Distribution of Outcome of Individual Lesion Types in Two Groups

Lesion	MLS		ILS		Total	
	Success	Failure	Success	Failure	Success	Failure
Cyst	2	-	3	2	5	2
Polyp	11	-	4	4	15	4
Nodule	0	-	1	-	1	-
RE	1	-	1	-	2	-

Notes: This table presents the distribution and comparison of outcome of individual lesion types in the two groups according to the procedure performed. Statistical tests of significance have not been applied due to small numbers.

Abbreviation: RE, Reinke edema.

TABLE 3.
Comparison of Outcome Parameters

Characteristic	Group 1 (Intralesional Steroid Injection)	Group 2 (Microlaryngeal Surgery)
Acoustic parameters		
(1) Habitual f0 (Frequency of glottal opening and closing in Hertz)		
FU1	-0.23 (4.16, $P=0.96$)	-4.65 (4.3, $P=0.3$)
FU2	-10.6 (2.6, $P=0.003$)*	-11.9 (5.5, $P=0.05$)
FU3	-13.5 (4.1, $P=0.009$)*	-14.4 (5.6, $P=0.03$)*
(2) MPT0 (maximum phonation time in seconds)		
FU1	-1.5 (0.65, $P=0.03$)*	-4.4 (0.6, $P<0.01$)*
FU2	-3.2 (2.1, $P=0.2$)	-9.8 (0.6, $P<0.01$)*
FU3	-3.9 (2.7, $P=0.2$)	-10.8 (0.8, $P<0.01$)*
(3) Jitter		
FU1	0.2 (0.08, $P=0.02$)*	0.3 (0.06, $P<0.01$)*
FU2	0.06 (0.09, $P=0.5$)	0.5 (0.13, $P<0.01$)*
FU3	0.08 (0.09, $P=0.4$)	0.6 (0.13, $P<0.01$)*
(4) Shimmer		
FU1	0.2 (0.3, $P=0.4$)	0.4 (0.11, $P=0.003$)*
FU2	0.7 (0.5, $P=0.17$)	0.8 (0.21, $P=0.002$)*
FU3	0.9 (0.42, $P=0.05$)	1.04 (0.25, $P=0.001$)*
Perceptual analysis		
Voice Handicap Index (VHI)		
FU1	3.9 (1.5, $P=0.02$)*	10.1 (1.5, $P<0.01$)*
FU2	7.3 (2.3, $P=0.01$)*	16 (2.7, $P<0.01$)*
FU3	7.1 (2.4, $P=0.01$)*	19 (3.1, $P<0.01$)*
GRBAS (dysphonia)		
FU1	1.1 (0.7, $P=0.13$)	3.0 (0.3, $P<0.01$)*
FU2	1.1 (1.2, $P=0.4$)	4.7 (0.3, $P<0.01$)*
FU3	2.0 (1.1, $P=0.1$)	5.6 (0.3, $P<0.01$)*

Notes: This table compares the means for the difference between the measured value at follow-up and the baseline using a paired *t* test. The values represent difference in means (standard error, significance level). Where the difference in the means is significant with *P* values <0.05, this has been indicated by *.

Abbreviations: FU, follow-up; Habitual f0, frequency of glottal opening and closing in Hertz.

advice on vocal hygiene and reported regression in 39% of the subjects receiving the steroid intervention at 2 months.¹⁵

Acoustic parameters

We report significant improvement in habitual f0, and MPT was seen at 6 and 12 weeks after intervention in both groups. However, we did not notice similar dramatic findings in shimmer and jitter. Tateya et al evaluated 28 subjects with vocal nodules who received triamcinolone acetate injections in 2004 and reported improved MPTs and flow rates at 3 weeks.⁹

Perceptual analysis

Perceptual analysis using VHI and GRBAS scale showed significant improvement in both groups during each follow-up visit. Similar results in perceptual analysis have been reported in previous studies.^{7,10}

Limitations and strengths

Our study is the first Indian study to address the subject of ILSs for benign vocal cord lesions. In addition, it is the first study that

directly compares the outcome in conservatively managed subjects in terms of voice parameters and perception analysis with those undergoing a surgical intervention. Despite a limited sample size due to logistic considerations, we were able to demonstrate a significant impact of therapy with steroid injections in reducing lesion size and improving voice parameters over 12 weeks. Although blinding was not possible in the current study due to the nature of intervention, it reveals important findings about effectiveness of steroid injections for benign vocal cord lesions in our subjects for further exploration in larger double-blinded trials. Also, it would be interesting to evaluate the stability of the improvement in longer follow-up periods.

We have presented the images before and after the surgery in Figure 5. We note that there is a difference in image quality between the two images as they have been recorded using different cameras. The preoperative picture was captured using Endovision camera with image capture device, whereas the postoperative image was taken directly from the screen of the monitor leading to difference in image quality. It would have been desirable to have captured the images from similar devices.

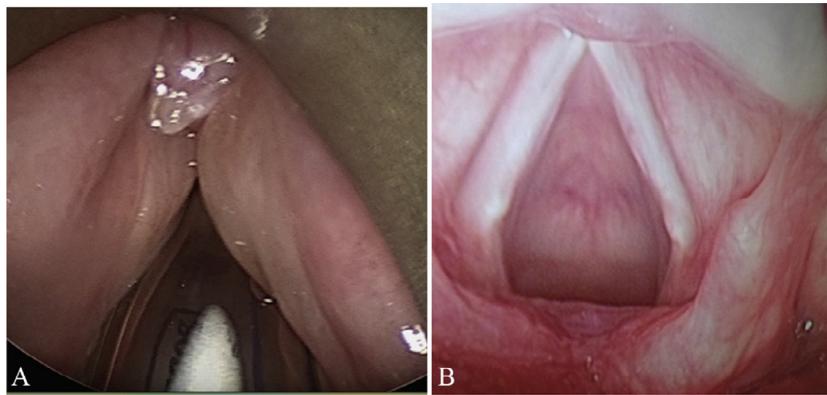


FIGURE 5. (A and B) Vocal cord polyp showing complete resolution after ILS at 3 months of follow-up.

CONCLUSIONS

ILSs are effective in reducing size of lesion and also improve acoustic parameters, perceptual analysis, and grade of dysphonia in patients presenting with benign vocal cord lesions. Although our study may not be adequately powered to determine a direct comparison of steroid injections with MLS in the long term, it reflects on the utility of the procedure in our subjects.

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