

Fat Versus Hyaluronic Acid Injection Laryngoplasty for Unilateral Vocal Fold Paralysis: Efficacy and Results

Original
Article

Aya Raouf Sheikhany, Youssef Mohamed Abdel Moniem, Mo'men Ali Ameen Hamela, Louay El Sharkawy, Adel El-Antably, Tareq Muhammad Algarf

Department of Otorhinolaryngology, Faculty of Medicine, Cairo University, Egypt.

ABSTRACT

Objectives: To compare the use of autologous fat versus hyaluronic acid in injection laryngoplasty for unilateral vocal fold paralysis. The efficacy of the materials regarding voice outcomes (voice handicap index, computerized speech lab) and duration will be statistically analyzed.

Patients and Methods: A prospective study conducted on 38 randomly selected patients with unilateral vocal fold paralysis presented to ORL outpatient clinic at faculty of medicine – Cairo University randomized to receive either hyaluronic acid (HA) perfecta deep® group A and autologous fat for group B. Postoperative evaluations were made based on Auditory Perceptual Assessment of Voice (APA), Computerized Speech Lab (CSL), jitter, shimmer, noise to harmonic ratio, patient satisfaction, phonatory gap and the need for another injection.

Results: One month postoperatively, both groups showed significant improvement in CSL, APA and phonatory gap while six months postoperatively there was significant improvement in favor of group B. No serious adverse events were observed. 18 patients had been re-injected in group A while only 5 had been re-injected in group B due to insufficient voice.

Conclusion: No side-effects were found for either hyaluronic acid or fat groups after injection. Both treatments after one month resulted in significantly improved voice as rated by the patients and significantly improved glottal closure. Resorption was noted for both substances, but mainly for hyaluronic acid/treatment.

Key Words: Autologous fat, Hoarseness, Hyaluronic acid, Injection laryngoplasty, Vocal fold paralysis.

Received: 13 April 2022, **Accepted:** 30 July 2022

Corresponding Author: Youssef Mohamed Abdel moniem, PhD, Department of Otorhinolaryngology, Faculty Of Medicine, Cairo University, Egypt. **Tel.:** 01022712877, **E-mail:** youssefmohamed22222@gmail.com

ISSN: 2090-0740, 2022

INTRODUCTION

Unilateral vocal fold paralysis/palsy (UVFP) is not an uncommon finding in ENT practice. It is not a diagnosis by itself. The exact incidence of unilateral vocal fold paralysis is difficult to clarify for different reasons. Many cases are not diagnosed due to spontaneous recovery or compensation by the opposite cord^[1]. Unilateral vocal fold paralysis causes glottic insufficiency, affecting phonation and respiration^[2]. Many procedures are present to treat UVFP; this includes injection laryngoplasty for vocal cord medialization, medialization thyroplasty, arytenoid adduction, adduction arytenoidopexy, and reinnervation procedures. Selecting which one is appropriate depends on the onset and duration of symptoms, degree of impairment, presence of surgical defect, and possibility for recovery. Regarding injection laryngoplasty, many substances can be used for augmentation of vocal folds such as teflon, collagen, hyaluronic acid, autologous fat and fascia. The ideal substance should be nonallergenic, non-immunogenic, easy to inject, resistant to resorption and have optimal viscoelastic properties in order to enhance vocal fold vibration^[3]. Hyaluronic acid (HA), a sulfated glycosaminoglycan, is one of the main components of the

extracellular matrix of the vocal folds. It is biocompatible, bioactive and non-immunogenic, which explains why it is currently widely used in clinical practice as an injectable material^[4]. Autologous fat has been used as a lateral vocal fold injection agent. It has the advantages of being autologous, readily available, and being an excellent match of the biomechanical properties for replacement of tissue^[5].

The objectives of this prospective study were to evaluate clinical performance (vocal fold function) and safety of hyaluronic acid compared with autologous fat in the treatment of patients with glottal insufficiency.

PATIENTS AND METHODS:

Subjects

All of the study patients had unilateral vocal fold paralysis with dysphonia and/or aspiration and are not candidate for further voice therapy. They had been examined by three professional voice listeners.

38 patients were enrolled in the study. All patients (21 females, 17 males; mean age 42.50 years; range 19 to 63 years) had unilateral vocal fold paralysis and vocal symptoms of minimum 6 to 12 months duration. 19 patients were randomized to treatment with hyaluronic acid (Perfecta deep®) and 19 were randomized for injections with autologous abdominal fat. The patients were blinded as to which substance they received.

All patients were treated and follow up was carried out at the outpatient clinic, faculty of medicine – Cairo University.

The local Research Ethics Committees at Cairo University approved the study. It was conducted and monitored in accordance with good clinical practice.

Assessments, recordings and injection treatment

Assessments and recordings were made before treatment (baseline), at 1st and 6th months after injection. Medical history (including medications and any chronic illness) was obtained. Full head and neck examination was done. The patients rated their voice function and quality by filling the Arabic version of the Voice Handicap Index (VHI)^[6]. Auditory perceptual assessment was done by three professional voice listeners and dysphonia was graded as: 1(mild), 2(moderate), 3(severe).

Diagnostic flexible laryngoscopy was done for all patients at the time of initial evaluation in the outpatient clinic and the findings were recorded (Fig.1). Phonatory gaps were recorded and graded as mild, moderate and severe where mild when the paralyzed cord is close to midline, moderate if midway between adduction and abduction and severe gap if the paralyzed cord is almost fully abducted.

Acoustic analysis using CSL (computerized speech lab) to evaluate Jitter, Shimmer and harmonic to noise ratio. Voice recording and auditory perceptual assessment was done. All voice samples were recorded in a quiet acoustically treated room, using a high quality microphone placed about 15 cm and with an angle about 45 degrees from the subject's mouth.

Injection procedures

The patients were treated with either 5 mg/ml hyaluronic acid (Perfecta deep®) or autologous fat. The surgeon was not blinded as to which substance the patient received. The injections were given into the paraglottic space of the paralyzed vocal fold under rigid laryngoscopic control (Fig. 2). All injections were given under general anesthesia to obtain optimal results. Over injection was done in both groups due to the expected resorption of the material. The mean total volume given was 0.7 ml of hyaluronic acid (perfecta deep®) and 0.8 ml of fat.

Fat harvesting technique, patients were in supine position with the abdomen exposed, local subcutaneous injections of 20 cc saline in the region of left lower abdomen were done to help softening of the subcutaneous fat harvesting by liposuction (Fig. 3), the skin was first punctured by infiltration cannula mounted on a 20cc syringe into the subcutaneous fat level (Fig. 4), liposuction cannula then introduced and negative suction pressure applied through pulling the syringe piston backwards and maintaining that negative pressure (Fig. 5), the liposuction cannula is moved back and forth in the subcutaneous fat plan so as to loosen the lipocytes, after collecting an adequate amount of subcutaneous fat, the cannula was removed and the collected amount of fat was evacuated into a sterile container lined by a piece of gauze to filter the blood, the fat was generously rinsed with saline several times to wash away blood and fatty acids, the harvested amount of fat was mounted to a 5 cc syringe then crushed by fat processors into macro, micro and nano particles (Fig. 6).

Postoperatively patients were evaluated at the first and the sixth postoperative months later to assess improvement in dysphonia. Voice assessment was done using Auditory Perceptual Assessment of Voice (APA) and Voice Analysis was done using CSL, jitter, shimmer, noise to harmonic ratio were obtained. Patients filled the Arabic version of the Voice Handicap Index at the first and sixth postoperative months to obtain reliable impression about patient's perspective of his/her voice. Patient satisfaction, phonatory gap were evaluated. The type and degree of possible side effects of treatment were evaluated during this period. The need for another injection was considered in patients with persistent dysphonia or aspiration after six months postoperative.

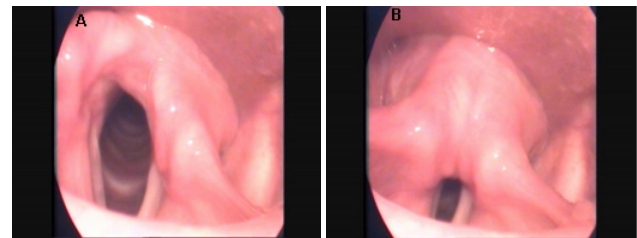


Fig. 1: Flexible laryngoscopy showing left vocal fold paralysis during respiration (A), during phonation (B).



Fig. 2: Needle introduced for injection



Fig. 3: Injecting saline into lower abdomen to aid softening of fat.



Fig. 4: Snip incision before harvesting fat from lower abdomen



Fig. 5: Harvesting abdominal fat.



Fig. 6: Harvested abdominal fat & fat processors.

RESULTS:

38 patients (21 females, 11 males; mean age 42.5 years; range 19 to 63 years) completed the follow-up. 19 patients had been treated with hyaluronic acid (perfecta deep®) (Group A) and 19 with autologous abdominal fat (Group B). There were no immediate or delayed side-effects of both treatments.

The most common cause of unilateral vocal fold paralysis in the patients under study was thyroid surgeries (44.7%) of patients. Other causes are non-surgical trauma (23.7%) and (23.7%) of unknown cause.

Voice handicap index

Each VHI parameter provided a statistically significant level of reliability ($p < 0.001$) when compared with the same parameter before and after the surgery in both groups as well as postoperative VHI scores at the first and sixth months postoperatively.

Although different materials of injection used, there was a significant reduction in VHI scores in both groups. Therefore, a comparison of the degree of improvement between obtained results was done.

One month postoperatively, there was no significant difference in the mean values of functional, physical, emotional and total VHI scores in the patients of group (A) (Table 1) as compared to scores of group (B), (Table 2) While after six months there was statistically significant difference in the mean values of functional, (Table 3) physical, emotional and total VHI scores in the patients of group (A) as compared to scores of group (B) in favor of group (B) (Fig. 7).

Computerized speech lab (CSL)

Jitter

One month postoperatively, there was no significant difference in the mean values of jitter scores in the patients of group (A) (Table 4) as compared to scores of group (B), (Table 5) While after six months there was statistically significant difference in the mean values of jitter scores in the patients of group (A) as compared to scores of group (B) in favor of group (B) (Fig 8).

Shimmer

One month postoperatively, there was no significant difference in the mean values of shimmer scores in the patients of group (A) as compared to scores of group (B), While after six months there was statistically significant difference in the mean values of shimmer scores in the patients of group (A) as compared to scores of group (B)

in favor of group (B) (Fig. 9).

Noise to harmonic ratio (N/H)

One month postoperatively, there was no significant difference in the mean values of noise to harmonic ratio scores in the patients of group (A) as compared to scores of group (B), While after six months there was statistically significant difference in the mean values of noise to harmonic ratio scores in the patients of group (A) as compared to scores of group (B) in favor of group (B) (Fig. 10).

Phonatory gap

As regards group A, one month after injection, 13 patients (68.4%) had no gap and 6 patients (31.6%) had mild gap while, after six months 13 patients (68.4%) had mild gap, 6 patients (31.6%) had moderate gap and no patients had no gap while, as regards group B, one month after injection, 12 patients (63.2%) had no gap and 7 patients (36.8%) had mild gap while, after six months 10 patients (52.6%) had no gap, 9 patients (47.4%) had mild gap.

One month postoperatively, there was no significant difference in the phonatory gap of group (A) as compared to group (B), while after six months there was statistically significant difference in the phonatory gap of group (A) as compared to scores of group (B) in favor of group (B) (Fig 11).

Auditory Perceptual Assessment (APA)

As regards group A, one month after injection, 13 patients (68.4%) had no dysphonia and 6 patients (31.6%) had mild dysphonia while, after six months 13 patients (68.4%) had mild dysphonia, 6 patients (31.6%) had moderate dysphonia while as regards group B, one month after injection, 12 patients (63.2%) had no dysphonia and 7 patients (36.8%) had mild dysphonia while, after six months 10 patients (52.6%) had no dysphonia and 9 patients (47.4%) had mild dysphonia.

One month postoperatively, there was no significant difference in the auditory perceptual assessment (APA) score of group (A) as compared to group (B), while after six months there was statistically significant difference in the auditory perceptual assessment (APA) score of group (A) as compared to scores of group (B) in favor of group (B) (Fig. 12).

Patient satisfaction

As regards group A, one month after injection, 17 patients (89.5%) were satisfied but 2 patients (10.5%) were not while, after six months 4 patients (21.1%)

were satisfied but 15 patients (78.9%) were not while as regards group B, one month after injection, 16 patients (84.2%) were satisfied but 3 patients (15.8%) were not while, after six months 11 patients (57.9%) were satisfied but 8 patients (42.1%) were not.

One month postoperatively, there was no significant difference in patient satisfaction of group (A) as compared to group (B), while after six months there was statistically significant difference in patient satisfaction of group (A) as compared to scores of group (B) in favor of group (B) (Fig 13).

Need for a second injection

18 patients (94.7%) of group A needed another injection while, 5 patients (26.3%) of group B needed another injection. There was a significant difference

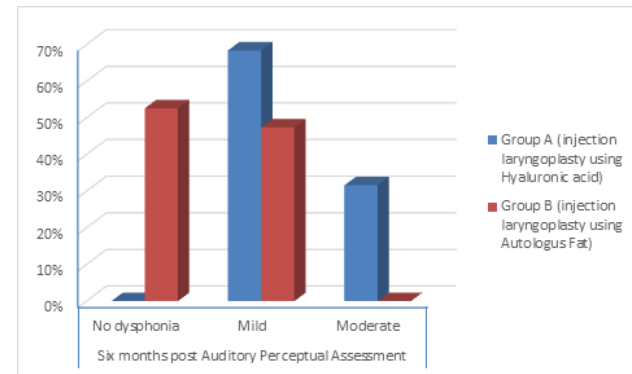


Fig. 7: Comparison of auditory perceptual assessment (APA) scores between the two groups after six months from injection.

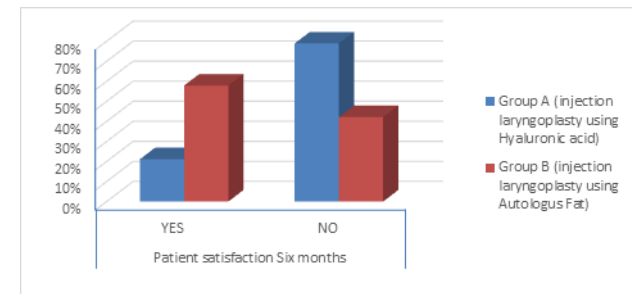


Fig. 8: Comparison of patient satisfaction of both groups six months after injection

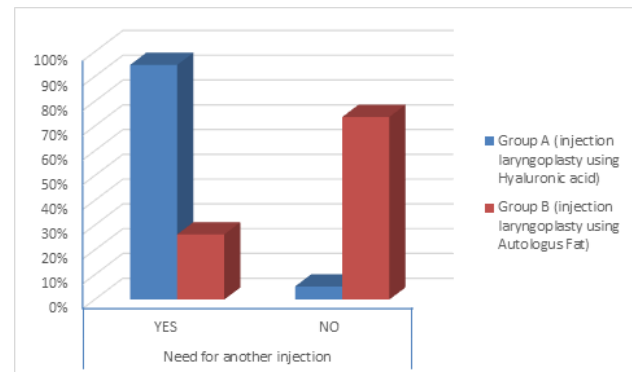


Fig. 9: Comparison of the need for second injection.

Table 1: Pre, one and six months post VHI scores for group A

	Group A (injection laryngoplasty using Hyaluronic acid)					<i>P value</i> compared to pre
	Mean	SD	Median	Minimum	Maximum	
Pre-operative VHI scoring functional	21.89	7.68	21.00	12.00	36.00	---
Post-operative VHI one month functional	11.11	6.61	10.00	3.00	30.00	< 0.001
Post-operative VHI six months functional	18.95	7.71	18.00	9.00	33.00	< 0.001
Pre-operative VHI scoring physical	22.00	7.21	21.00	12.00	38.00	---
Post-operative VHI one month physical	11.26	5.84	12.00	2.00	21.00	< 0.001
Post-operative VHI six months physical	19.00	7.21	18.00	9.00	35.00	< 0.001
Pre-operative VHI scoring emotional	17.26	7.38	16.00	8.00	29.00	---
Post-operative VHI one month emotional	9.68	5.63	10.00	2.00	20.00	< 0.001
Post-operative VHI six months emotional	14.26	7.38	13.00	5.00	26.00	< 0.001
Pre-operative VHI scoring total	61.16	19.28	58.00	33.00	103.00	---
Post-operative VHI one month total	32.16	16.92	31.00	9.00	70.00	< 0.001
Post-operative VHI six months total	52.16	19.28	49.00	24.00	94.00	< 0.001

Table 2: Pre, one and six months post VHI scores of group B

	Group B (injection laryngoplasty using Autologus Fat)					<i>P value</i> compared to pre
	Mean	SD	Median	Minimum	Maximum	
Pre-operative VHI scoring functional	20.79	5.92	21.00	9.00	31.00	---
Post-operative VHI one month functional	10.16	5.11	9.00	2.00	24.00	< 0.001
Post-operative VHI six months functional	9.21	5.03	8.00	2.00	23.00	< 0.001
Pre-operative VHI scoring physical	21.89	5.67	21.00	14.00	32.00	---
Post-operative VHI one month physical	10.74	5.29	8.00	4.00	18.00	< 0.001
Post-operative VHI six months physical	9.74	5.29	7.00	3.00	17.00	< 0.001
Pre-operative VHI scoring emotional	16.58	7.43	14.00	8.00	29.00	---
Post-operative VHI one month emotional	8.00	4.61	7.00	2.00	18.00	< 0.001
Post-operative VHI six months emotional	7.05	4.54	6.00	2.00	17.00	< 0.001
Pre-operative VHI scoring total	59.26	14.36	58.00	39.00	92.00	---
Post-operative VHI one month total	29.11	13.84	31.00	8.00	60.00	< 0.001
Post-operative VHI six months total	26.32	13.81	28.00	7.00	57.00	< 0.001

Table 3: Comparison of functional VHI scores between the two groups

	Group A (injection laryngoplasty using Hyaluronic acid)					Group B (injection laryngoplasty using Autologus Fat)					<i>P</i> value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Pre-operative VHI scoring functional	21.89	7.68	21.00	12.00	36.00	20.79	5.92	21.00	9.00	31.00	0.773
Post-operative VHI one month functional	11.11	6.61	10.00	3.00	30.00	10.16	5.11	9.00	2.00	24.00	0.863
Post-operative VHI six months functional	18.95	7.71	18.00	9.00	33.00	9.21	5.03	8.00	2.00	23.00	< 0.001

Table 4: Pre, one and six months post CSL scores for group A

	Group A (injection laryngoplasty using Hyaluronic acid)					<i>P</i> value compared to pre
	Mean	SD	Median	Minimum	Maximum	
Pre jitter	247.32	104.94	280.10	101.20	390.40	---
One m jitter	196.23	92.80	162.40	87.80	370.50	< 0.001
Six m jitter	237.86	102.24	270.70	98.40	387.50	0.006
Pre shimmer	0.92	0.29	0.90	0.52	1.35	---
One m shimmer	0.60	0.24	0.54	0.27	1.19	< 0.001
Six m shimmer	0.84	0.28	0.82	0.50	1.25	0.001
Pre N/H ratio	0.32	0.11	0.31	0.14	0.54	---
One m N/H	0.18	0.09	0.14	0.06	0.46	< 0.001
Six m N/H	0.30	0.10	0.31	0.14	0.46	0.009

Table 5: Pre, one and six months post CSL scores for group B

	Group B (injection laryngoplasty using Autologus Fat)					<i>P</i> value compared to pre
	Mean	SD	Median	Minimum	Maximum	
Pre jitter	407.12	229.23	340.20	156.80	982.10	---
One m jitter	200.72	90.69	200.40	88.40	400.80	< 0.001
Six m jitter	196.94	101.82	205.80	57.00	410.30	< 0.001
Pre shimmer	1.42	0.39	1.35	0.70	2.10	---
One m shimmer	0.66	0.25	0.70	0.23	1.10	< 0.001
Six m shimmer	0.76	0.31	0.80	0.25	1.28	< 0.001
Pre N/H ratio	0.59	0.31	0.47	0.18	1.32	---
One m N/H	0.28	0.13	0.27	0.11	0.59	< 0.001
Six m N/H	0.33	0.14	0.29	0.13	0.59	< 0.001

DISCUSSION

This randomized, controlled clinical study compared the effects of two injection substances, hyaluronic acid (perfecta deep®) and autologous fat. The results showed that, after 6 months of the injections, the patients' self-ratings were significantly improved after treatment with both hyaluronic acid and fat. However, fat showed less resorption than hyaluronic acid; this difference was significant at the 6-month but not at the 1st month follow-up. Disappearance of the hyaluronic acid derivative may depend on several factors, such as mechanical forces and type of hyaluronic injected^[7].

Patients included in the study were aged above 18 with unilateral vocal fold paralysis for more than six months to give time for potential spontaneous recovery. Patients with history of previous injection were excluded.

In this study, causes of unilateral vocal fold paralysis are variable; 44.7% were due to thyroid surgeries, 23.7% non-surgical trauma and 23.7% of idiopathic cause. A study in 2014 reported that thyroidectomy was the most common iatrogenic cause of unilateral vocal fold paralysis^[8], this agrees to the etiological profile of the subjects enrolled in this study. Another study reported 42% of cases were due to iatrogenic cause and 30% of idiopathic cause^[9], while Loughran *et al.*, 2002 reported that malignancy (lung or thyroid) is the most common cause 42% of cases followed by surgical trauma and idiopathic cause^[10].

Both sides of the vocal folds were equally affected (50%) in the patients under study, of all 38 patients, 19 patients (50%) have left side paralysis and 19 patients (50%) have right side paralysis. In a study by Al-Khtoum *et al.* 2013, out of 53 cases, in 41 cases (77.4%) left vocal fold was involved while the right vocal fold was involved in 12 cases (22.6%)^[11].

Arabic VHI can be reliably applied to the Arabic speaking population as it can help in estimating the degree of severity of the voice problem^[6]. One month postoperatively, there was no significant difference in the mean values of functional, physical, emotional and total VHI scores respectively in the patients of group (A) as compared to scores of group (B). While after six months there was statistically significant difference in the mean values of functional VHI scores in the patients of group (A) as compared to scores of group (B) in favor of group (B). This could be explained by the absorption of hyaluronic acid after six months.

A study done by Khadivi and his colleagues reviewed the results of autologous fat injection laryngoplasty in unilateral vocal fold paralysis and

reported significant improvement in all parameters of voice analysis in both short and long-term follow up^[12]. There is agreement with results obtained in this study.

Another study by Upton and his colleagues reported the efficacy of hyaluronic acid in injection laryngoplasty and in agreement with this study; they noticed short-term improvements in VHI outcome measures of vocal function in patients with glottic insufficiency^[13].

Parameters of CSL improved for both groups after one and six months, with no significant difference after one month and a significant difference after six months in favor of group (B).

In agreement to this study, Fang *et al.*, 2010 detected improvement of jitter, shimmer and noise to harmonic ratio parameters of CSL after fat injection laryngoplasty^[14].

On contrary to this study, Bertroche *et al.*, (2019) detected that the mean longevity of hyaluronic acid injection was 10.6 months^[15]. Also Rudolf *et al.*, (2012) detected a 12 months of acceptable quality of voice was achieved by augmentation using hyaluronic acid. This could be explained by using different types of hyaluronic acid with larger molecular size, compensation by other vocal fold and small preoperative gap^[4].

Phonatory gaps were recorded and graded as mild, moderate and severe where mild when the paralysed fold is close to midline, moderate if midway between adduction and abduction and severe gap if the paralysed fold is almost fully abducted.

Some authors studied the preoperative phonatory gap as a good predictor for better voice outcomes after injection laryngoplasty, the smaller the preoperative gap the better the voice outcomes and patient satisfaction^[16].

Patient satisfaction was evaluated at the first and the sixth months postoperative. In group A 89.5% were satisfied after one month and only 21.1% were satisfied at sixth months while in group B it was 84.2% at the first month and 57.9% after six months. This difference in satisfaction after six months pointed to the short term effect for hyaluronic and the long term effect of autologous fat.

In contrary, Stellan Hertegard MD, (2009) showed that both hyaluronic B gel and collagen can be safely used for injection treatment of unilateral vocal fold paralysis. Both treatments resulted in significantly

improved voice as rated by the patients. However, the patients treated with hylan B gel showed better vocal fold status and longer maximum phonation time at 12 months after treatment as compared with patients treated with collagen^[17].

Wen *et al.*, (2013) studied the outcomes and prognostic factors of injection laryngoplasty (IL) in unilateral vocal fold paralysis using cross-linked porcine collagen (PC) and hyaluronic acid (HA) in unilateral vocal fold paralysis (UVFP), there was significant improvement in voice outcomes but, no significant difference between both groups in a 6 month follow up period^[18].

None of the patients under study developed adverse effect due to injection in both groups. In contrary, Enver *et al.*, (2021) detected inflammatory complications in 2% of cases injected with hyaluronic acid^[19]. Zapanta *et al.*, (2004) reported a case of laryngeal abscess after alloderm injection^[20].

CONCLUSION

Both fat and hyaluronic acid are safe methods for injection laryngoplasty with no adverse reactions. Injection Laryngoplasty gives similar voice outcomes and patient satisfaction of voice on short term basis if it is performed using either Hyaluronic acid or autologus fat. Autologus fat injection offers best long term results, easy to be harvested, with no allergic reactions and save money costs. Hyaluronic acid injection offers good short term results and would be of great benefit as early injectable material for patients with potential recovery. Vocal fold injection under general anesthesia offers good visualization with more costs.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Myssiorek, D. (2004). Recurrent laryngeal nerve paralysis: anatomy and etiology. *Otolaryngologic clinics of North America*, 37(1), 25-44.
2. Périé, S., Chaigneau-Debono, G., Roubeau, B., Bruel, M., Liesenfelt, I., & St Guily, J. L. (2002). Role of medialization in the improvement of breath control in unilateral vocal fold paralysis. *Annals of Otolaryngology, Rhinology & Laryngology*, 111(11), 1026-1033.
3. Hertegård, S., Hallén, L., Laurent, C., Lindström, E., Olofsson, K., Testad, P., & Dahlqvist, Å. (2004). Cross-linked hyaluronan versus collagen for injection treatment of glottal insufficiency: 2-year follow-up. *Acta oto-laryngologica*, 124(10), 1208-1214.
4. Rudolf, R., & Sibylle, B. (2012). Laryngoplasty with hyaluronic acid in patients with unilateral vocal fold paralysis. *Journal of Voice*, 26(6), 785-791.
5. Hsiung, M. W., Woo, P., Minasian, A., & Schaefer Mojica, J. (2000). Fat augmentation for glottic insufficiency. *The Laryngoscope*, 110(6), 1026-1033.
6. Malki, K. H., Mesallam, T. A., Farahat, M., Bukhari, M., & Murry, T. (2010). Validation and cultural modification of Arabic voice handicap index. *European archives of oto-rhino-laryngology*, 267(11), 1743-1751.
7. Lapcik Jr, L., Lapcik, L., De Smedt, S., Demeester, J., & Chabreck, P. (1998). Hyaluronan: preparation, structure, properties, and applications. *Chem. Rev*, 98(8), 2663-2684.
8. Kupfer, R. A., & Meyer, T. K. (2014). Evaluation of unilateral vocal fold immobility. *Current Otorhinolaryngology Reports*, 2(2), 105-113.
9. Havas, T. E., & Priestley, K. J. (2003). Autologous fat injection laryngoplasty for unilateral vocal fold paralysis. *ANZ journal of surgery*, 73(11), 938-943.
10. Loughran, S., Alves, C., & MacGregor, F. B. (2002). Current aetiology of unilateral vocal fold paralysis in a teaching hospital in the West of Scotland. *The Journal of laryngology and otology*, 116(11), 907.
11. Al-Khtoum, N., Shawakfeh, N., Al-Safadi, E., Al-Momani, O., & Hamasha, K. (2013). Acquired unilateral vocal fold paralysis: retrospective analysis of a single institutional experience. *North American journal of medical sciences*, 5(12), 699.
12. Khadivi, E., Akbarian, M., Khazaeni, K., & Salehi, M. (2016). Outcomes of autologous fat injection laryngoplasty in unilateral vocal cord paralysis. *Iranian journal of otorhinolaryngology*, 28(86), 215.
13. Upton, D. C., Johnson, M., Zelazny, S. K., & Dailey, S. H. (2013). Prospective evaluation of office-based injection laryngoplasty with hyaluronic acid gel. *Annals of Otolaryngology, Rhinology & Laryngology*, 122(9), 541-546.

14. Fang, T. J., Li, H. Y., Gliklich, R. E., Chen, Y. H., Wang, P. C., & Chuang, H. F. (2010). Outcomes of fat injection laryngoplasty in unilateral vocal cord paralysis. *Archives of Otolaryngology–Head & Neck Surgery*, 136(5), 457-462.
15. Bertroche, J. T., Radder, M., Kallogjeri, D., Paniello, R. C., & Bradley, J. P. (2019). Patient-defined duration of benefit from juvederm (hyaluronic acid) used in injection laryngoplasty. *The Laryngoscope*, 129(12), 2744-2747.
16. Choi, J., Son, Y. I., So, Y. K., Byun, H., Lee, E. K., & Yun, Y. S. (2012). Posterior glottic gap and age as factors predicting voice outcome of injection laryngoplasty in patients with unilateral vocal fold paralysis. *The Journal of laryngology and otology*, 126(3), 260.
17. Hertegård, S., Hallén, L., Laurent, C., Lindström, E., Olofsson, K., Testad, P., & Dahlqvist, Å. (2004). Cross-linked hyaluronan versus collagen for injection treatment of glottal insufficiency: 2-year follow-up. *Acta oto-laryngologica*, 124(10), 1208-1214.
18. Wen, M. H., Cheng, P. W., Liao, L. J., Chou, H. W., & Wang, C. T. (2013). Treatment outcomes of injection laryngoplasty using cross-linked porcine collagen and hyaluronic acid. *Otolaryngology–Head and Neck Surgery*, 149(6), 900-906.
19. Enver, N., Azizli, E., Akbulut, S., Tatar, E. C., YELKEN, M. K., ÖZTÜRK, K., & OĞUZ, H. (2021). Inflammatory complications of vocal fold injection with hyaluronic acid: a multiinstitutional study. *Turkish Journal of Medical Sciences*, 51(2), 819-825.
20. Zapanta, P. E., & Bielamowicz, S. A. (2004). Laryngeal abscess after injection laryngoplasty with micronized AlloDerm. *The Laryngoscope*, 114(9), 1522-1524.