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Transnasal endoscopic microfractured fat injection in glottic insufficiency

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Abstract. *Transnasal endoscopic microfractured fat injection in glottic insufficiency. Objective*: We evaluated a novel treatment for glottic insufficiency involving the injection of autologous material with direct glottic visualisation in an outpatient setting.
Methods: Three patients with vocal cord palsy underwent laryngoplasty under local anaesthesia using only a flexible endoscope with a working canal for Microfractured Fat Fibre-endoscopic Injection (MFFI). Adipose tissue was processed using the Lipogems® device, which allows optimal purity, fluidity, and mesenchymal stem cell content in the resultant emulsion.
Results: According to the preliminary data, MFFI was well tolerated and no complications were observed. During the 12-month follow-up period, voice improvement was constant in all three patients, hinting at the stem cell-related regenerative potential of the procedure.
Conclusions: MFFI was proven to be a useful and straightforward tool, combining all of the relevant advantages of other known treatments for glottic insufficiency, and is an efficacious and innovative treatment that can be performed on an outpatient basis using only autologous material.

Introduction

Several therapeutic options have been proposed for the treatment of glottic insufficiency and secondary dysphonia. Autologous fat injection, a well-established and safe procedure, has considerable advantages[1,2] and is frequently used to treat glottic insufficiency,[3] but it requires general anaesthesia and exposure of the glottis by direct laryngoscopy.[4] To overcome these limitations, endoscopic techniques with local anaesthesia have been employed successfully with a transthyrohyoid or transcricothyroid injection of various alloplastic materials.[5,6] Another innovation is transnasal laryngoplasty using commercial micronised human dermal tissue[7]. Ricci-Maccarini *et al*.[8] proposed a completely transnasal endoscopic procedure using an injection pistol with autologous fat.

We propose a treatment for glottic insufficiency that uses autologous injection material without the need for an injection pistol using a method that allows direct glottic visualisation on an outpatient basis. Here, we report the preliminary data on three patients.

We used Lipogems® (Lipogems International Srl., Milan, Italy), a novel fat harvesting and processing method. Lipogems®-treated microfractured fat has had promising preliminary results in vitro and for the clinical treatment of scars, scleroderma, and other aesthetic applications due to the fluidity, purity, and high mesenchymal stem cell content of the adipose tissue emulsion.[9] This sterile device employs metal marbles to microfracture fat tissue while a saline solution-irrigated filtering system refines the aspirate. The resultant emulsion is nearly free of blood and connective tissue residue that could elicit an inflammatory reaction. The emulsion also has a smoother consistency and is more fluid than other lipoaspirates and offers lower injection resistance, allowing the use of smaller needles and eliminating the need for an injection pistol. The 80% fat content of the emulsion is particularly effective for this procedure because it provides stability and minimal resorption times. The smaller fat clusters offer a larger overall contact surface, facilitating graft survival and exposing more mesenchymal stem cells from the adipose tissue.

Materials and methods

After receiving approval from our institutional ethics committee, we performed Microfractured

Fat Fibre-endoscopic Injection (MFFI) in three consecutive patients with glottic insufficiency via laryngoplasty under local anaesthesia with a flexible endoscope and a working canal.[10] The minimum follow-up time was 12 months.

Clinical case description

Case 1

A 63-year-old female presented with hoarseness and mild dysphagia following the removal of a left carotid paraganglioma 3 years prior. Endoscopic evaluation revealed complete left vocal cord palsy with inconsistent aspiration of thin liquids. The right vocal cord was normal. Videostroboscopy revealed a complete glottic closure defect during phonation. The left vocal fold was fixed in a paramedian position, and there was no difference in vertical position between the folds.

Case 2

A 72-year-old male presented with hoarseness and severe liquid dysphagia 6 months following a right lung lobectomy for carcinoma with mediastinal lymphadenopathy. Endoscopic examination revealed right vocal fold palsy and laryngovideostroboscopy revealed incomplete glottic closure during phonation. Similar to patient 1, there was no difference in vertical position between the folds. The left vocal cord was fixed in a lateral position.

Case 3

A 65-year-old female presented with hoarseness 7 months after a total thyroidectomy. A complete larynx examination revealed left vocal cord palsy with glottic insufficiency and a posterior glottic chink. There was no difference in vertical position between the folds. The left vocal cord was fixed in a paramedian position.

The maximum phonation time (MPT), Voice Handicap Index (VHI) score, and grade, roughness, breathiness, asthenia, and strain (GRBAS) values for each patient are summarised in Tables 1 and 2.[11,12]

Surgical technique

Abdominal fat was harvested under local anaesthesia using a standard liposuction technique with blunt, small gauge cannulas. The skin incision was sutured and a compressive dressing applied to the donor site. The fat was inserted into the Lipogems® device and processed with gentle shaking and saline solution irrigation to create a fluid emulsion.

The patients were prepared for MFFI as follows. SpO_2 and electrocardiogram (ECG) monitoring was performed while the patient was positioned in an operating bed. Midazolam (2.5 mg) was administered through a venous access port to achieve partial sedation. Local anaesthetic was applied to the nose and throat by spraying a 3% lidocaine solution.

Endoscopy was performed using a 6.2-mm flexible operative endoscope (Olympus Exera II, Olympus Corp., Tokyo, Japan) that was inserted nasally. When the glottic plane was reached, topical anaesthesia was applied through the working canal using a 3% lidocaine solution, followed 5 min later by a 10% solution. The solutions were sprayed directly onto the vocal folds.

The emulsion was injected laterally into the vocal process of the affected fold through the working port of the endoscope using a 21-gauge needle (Figure 1). The defect was over-compensated until 130% of the desired final fold medialisation was achieved (Figure 2). This small overcompensation is required due to the minimal loss of water content from the emulsion and fat loss due to minimal local inflammation after the procedure. The solution flowed easily through the needle, and small-volume syringes (1 mL) allowed more precise control.

No other devices were necessary to perform the procedure, but a second operator was required to control the syringe. The endoscope was retracted after ruling out bleeding or other complications. Vitals were monitored until normal upper airway sensitivity was restored (~30 min). Glottic patency was re-evaluated using a flexible endoscope before discharge.

Follow-up

Patients underwent an ear, nose, and throat exam with flexible endoscopy and videostroboscopy 1 week and 1, 3, 6, and 12 months after the procedure. Voice was assessed according to GRBAS values and MPT during all follow-up examinations. The VHI questionnaire was also administered.

Table 1

MPT, GRBAS, and VHI values at baseline and during short-term follow-up for each patient

Patient	Baseline						1 week follow-up		1 month follow-up					
	MPT	GRBAS	VHI				MPT	GRBAS	MPT	GRBAS	VHI			
			F	P	E	Total					F	P	E	Total
1	6''	2/1/2/2/0	31	29	11	71	10''	1/1/1/2/0	10.5''	1/1/0/1/0	25	20	8	53
2	5''	1/2/3/1/1	36	32	15	83	10.5''	1/1/1/1/0	10.5''	1/0/1/0/0	20	20	9	49
3	7''	2/2/1/1/0	27	20	24	71	11''	1/1/1/1/0	11.5''	1/0/1/0/0	20	10	12	42

MPT: maximum phonation time; GRBAS: grade, roughness, breathiness, aesthenia, strain; VHI: Voice Handicap Index; F: functional; P: physical; E: emotional.

Table 2

MPT, GRBAS, and VHI values during long-term follow-up for each patient

Patient	3 months follow-up						6 months follow-up						12 months follow-up					
	MPT	GRBAS	VHI				MPT	GRBAS	VHI				MPT	GRBAS	VHI			
			F	P	E	Total			F	P	E	Total			F	P	E	Total
1	11''	1/0/0/1/0	22	15	6	43	11''	1/0/0/1/0	18	13	5	36	11''	1/0/0/1/0	15	10	5	30
2	10.5''	1/0/1/0/0	17	20	6	43	11''	0/0/1/0/0	14	15	6	35	12''	0/0/0/0/0	12	12	4	28
3	12''	0/0/1/0/0	19	8	8	35	12.5''	0/0/1/0/0	14	6	7	27	12.5''	0/0/1/0/0	9	5	5	19

MPT: maximum phonation time; GRBAS: grade, roughness, breathiness, aesthenia, strain; VHI: Voice Handicap Index; F: functional; P: physical; E: emotional.

Results

The procedure was well tolerated and no complications were reported. Two of the three patients experienced local pain and one patient had a self-limiting haematoma at the harvesting site (thigh). Voice improvement occurred immediately following the procedure and the patients continued to improve during the follow-up period. In all patients, the vocal folds maintained the same even vertical position. Patients 1 and 3 retained the paramedian positioning of the left vocal cord, whereas patient 2 exhibited vocal fold medialisation that contributed to symptom improvement. Two patients had complete glottic closure visualised by videostroboscopy after 3 months, and the other patient (patient 1) had a residual posterior glottic chink. Such a defect may be considered normal in most female patients and could have gone unnoticed during preliminary examination due to the wide glottal defect and paramedian position of the paralysed vocal fold. The defect was still not closed after 1 year. The lack of posterior chink closure may also be due to the treatment choice: patients with paramedian positioning of the cords and posterior chinks tend to yield poorer results with lipo-injection than with arytenoid rotation or fixation. Dysphagia completely resolved after 3 months. All improvements remained at the 6- and 12-month follow-ups (see patient 1 in Figure 3).

The MPT, GRBAS, and VHI follow-up results are summarised in Tables 1 and 2.

Discussion

Of the numerous treatments for glottic insufficiency, few utilise autologous material on an outpatient basis. MFFI could represent a straightforward, cost-effective, and reliable method of treating this condition. We think that the endoscopic approach is convenient, providing optimal glottic visualisation using a device commonly employed by otolaryngologists. Fat harvesting is accomplished with a well-known standard liposuction technique and requires only brief training with the Lipogems® device. Compared to standard centrifuged fat and most injection materials, the Lipogems® device delivers a more fluid emulsion, allowing the use of

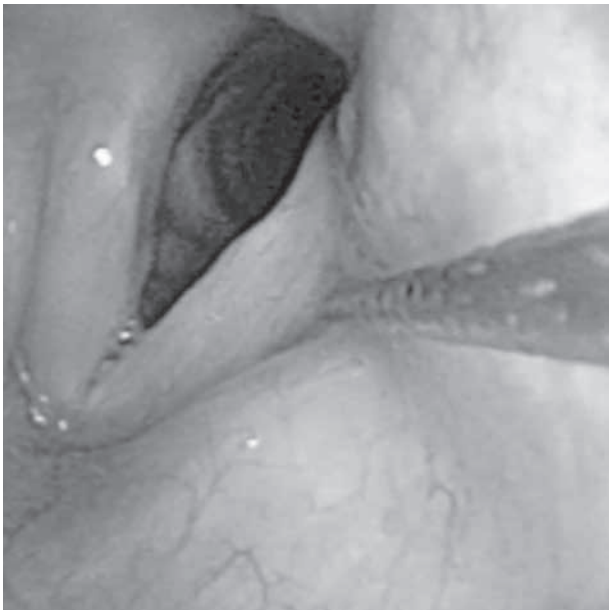

Figure 1
Injection into the paretic left vocal fold using a 21-gauge needle. The needle was inserted into the lateral portion of the vocal fold.

Figure 2
The left vocal fold following the procedure. Similar to traditional fat injection procedures, the vocal fold should be over-injected to compensate for reabsorption.

smaller gauge needles and providing better control during injection.[13] The needle must be at least 21 gauge, as smaller sizes inhibit emulsion flow and may jeopardise adipose cell survival.

Figure 3
One year follow-up of patient 1. The glottal closure stably improved, but a residual glottal posterior chink persisted.

The use of only local anaesthesia for the endoscopic procedure allows the continuous evaluation of glottic patency and phonation with little effort from the patient. Unfortunately, MFFI requires overcorrection of the defect. As a considerable amount of the emulsion consists of water, the volume is partially reabsorbed within hours. This allows a pre-discharge evaluation of glottic patency. The laryngeal anatomy changes minimally in 2 h, likely due to the low content of pro-inflammatory oils and impurities. This provides the surgeon more immediate and realistic results.

Compared to other endoscopic injection techniques, MFFI with Lipogems® causes less inflammation because processed autologous fat is less likely to cause an allergic reaction or local granulomatosis than synthetic materials.[9] This technique does not involve an external injection, which reduces oedematous complications and allows direct access to the surgical site. This approach is useful and provides good functional results but lacks the microscopic magnification and vocal fold immobility provided by microlaryngoscopic techniques. The technique may also be performed in patients with reduced neck extension or abnormal neck anatomy, which are the major contraindications for microlaryngoscopy.

The only endoscopic technique that is directly comparable to MFFI is transnasal laryngoscopy with Cymetra. Trask *et al*.[7] proposed a less traumatic procedure with 23-gauge needles, but their technique does not use autologous material.

Patients tolerated the MFFI procedure extremely well. Discomfort caused by the local anaesthesia was minimised by the two-step lidocaine application, allowing a smooth transition to altered glottic sensitivity. Harvesting autologous fat is more difficult in leaner individuals, such as those with cancer, but it is nearly always present in the inner thigh. Harvesting from the donor site can cause complications (scarring), and an abdominal belt may be required to limit local haematoma formation. If the thigh is the harvesting site of choice, a local compressive dressing is enough to reduce haematoma formation.

The results were encouraging and improvements constant through the 12-month follow-up period. The fluid emulsion obtained with the Lipogems device has been demonstrated to include high concentrations of extremely viable mesenchymal stem cells, which appear to be more apt to multipotency than conventional enzymatically derived adipose stem cells.[14] We might assume that the high stem cell content of the injected material grants considerable regenerative potential, which is mirrored by progressive improvement in the patient's voice. Nevertheless, this hypothesis should be reinforced by comparing the results to control groups of similar patients treated with traditional injection laryngoplasty and laryngoplasty with stem cell-enriched autologous fat. Such improvement is both subjective and objective due to the scale assessment; tough objective measurements, such as electroglottography, could have added more relevant information.[15]

Considerable patient compliance is required. Local anaesthesia cannot be used in patients with major cognitive impairment, panic attacks, and other uncontrolled psychiatric conditions.

Conclusion

MFFI is a useful and straightforward procedure that combines the relevant advantages of other known treatments for glottic insufficiency: local anaesthesia, glottic visualisation, a direct approach to the glottic plane, reliable outcomes, autologous material, regenerative potential, and an easy revision procedure. MFFI is a promising procedure allowing outpatient treatment of glottic insufficiency using only autologous fat. Nevertheless, due to the preliminary nature of these results and limited follow-up monitoring, further studies are required. Moreover, our case series lacks patient with wide glottal gaps, whose defects react radically differently to injection laryngoplasty. Therefore, further studies are required.

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