

Efficacy of Adjunctive Intralesional Steroid Injection After Laryngeal Microsurgery of Benign Vocal Fold Lesion

Arif Surgana¹, Rizka Fathoni Perdana^{1*}, Diar Mia Ardani¹

Department of Otolaryngology, Head and Neck Surgery Faculty of Medicine Universitas Airlangga/Dr. Soetomo General Academic Hospital Surabaya¹

Corresponding author: 1*

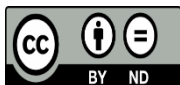


Keywords:

intralesional steroid injection, benign vocal fold lesion, GRBAS, VHI-10, tobacco use, human & health.

ABSTRACT

Benign vocal fold lesion cause alteration of lamina propria epithel then lead to dysphonia. Voice therapy is the first line treatment of benign vocal fold lesion. Low compliance affect increasing number of recurrences. Intralesional vocal fold steroid injection could be alternate adjuvant in management of benign vocal fold lesion. To assess efficacy intralesional steroid injection in benign lesion vocal fold patient those after underwent laryngeal microsurgery. Data collected from RSUD Dr. Soetomo medical records. Design of this study is retsospetive descriptive analytic. We reviewed 8 medical records patients who underwent laryngeal microsurgery removal of benign vocal fold lesion and acquire intralesional steroid injection for consecutive periode Jan 2017 until Des 2018. Score assessment of VHI-10, GRBAS & fiberoptic laryngoscope reviewed before and after intralesional steroid injection. We obtain 8 medical records of patients those underwent intralesional steroid injection following laryngeal microsurgery. VHI-10 scores show significant alteration after 1 month following intralesional steroid injection (p 0.001) and 6 month (p 0.002). GRBAS scores show significant change after 1 month following intralesional steroid injection (p 0.011) and 6 month (p 0.012). Fiberoptic laryngoscopy evaluation shows 2 patients (25 %) have recurrence after 1 month. Adjuvant therapy of intralesional steroid injection have significant effect in relieving dysphonia symptoms that assessed by VHI-10 and GRBAS score. Further study is required to get better objective measurement as such as MDVP assessment and stroboscopy imaging.



This work is licensed under a Creative Commons Attribution Non-Commercial 4.0 International License.

1. Introduction

Benign vocal fold lesion is the lesion in lamina propria that might changes its' outer epithelial structure. This abnormality affects the vocal fold layer, causing the reduction of mucosal wave that occurs due to phonation. Benign vocal fold lesion decreases the efficiency of voice production. Those with benign vocal fold lesion abnormality will experience hoarseness, tension and fatigue in phonation. Benign vocal fold

lesion such as vocal nodules, polyp, cyst, and Reinke's edema can be caused by phonotrauma, chronic inflammation, and Reinke's space tissue remodelling [1], [2].

Diagnosis for this abnormality can be established through fiberoptic laryngoscopy (FOL) and stroboscopic examination [2]. Objective perceptual analysis is required to assess the voice quality. Acoustic analysis and stroboscopic examination are not included in routine examination for dysphonia due to limited facilities. Voice Handicap Index (VHI)-10 examination is used to measure the quality of life people with dysphonia. This questionnaire contains 10 questions that are subjective and specific to dysphonia patients. Dysphonia can also be examined using Grade Roughness Breathiness Asthenic Strain with scale 0 for normal and 3 for extreme in each variable. VHI-10 and GRBAS are the subjective perception examinations for patients and examiner considered the easiest to use on a daily basis to evaluate dysphonia [1- 3].

Voice therapy is still considered the first line of benign vocal fold lesion treatment. Patient's low compliance during the conservative therapy causes failure in healing response. Vocal fold intralesional steroid injection can be used as an alternative for inflammation management in larynx. This procedure is tolerable and low-risk compared to surgery with general anesthesia [4]. There have been 182 microscopic laryngeal surgeries carried out in Dr. Soetomo General Hospital within January 2017 to December 2018, there were about 20 patient of benign vocal fold lesion yearly and there have been nine procedures of intralesional steroid injection [5], [6].

Corticosteroids are a potential anti-inflammatory regimen that can treat disorders in ENT-Head and Neck. Systemic administration of steroids can cause more adverse effects than local intralesional steroids. The steroid concentration is also higher if directly administered to the lesion. Intralesional steroid injection can also be conducted under local anesthesia and thereby reducing the cost of surgery. Vocal fold intralesional steroid injection procedure is reported in several studies to provide a good response, assessed subjectively and objectively. However, further research is required on symptom recurrence after intralesional steroid injection [7].

This study aims to evaluate the effect of adjunctive intralesional steroid injection based on the scores of VHI-10, GRBAS, and FOL.

2. METHODS

This is a retrospective analytical descriptive study. The sample of this study is the medical records of patients with benign vocal fold lesion treated with intralesional steroid injection during the period of January 2017-December 2018 at GBPT of Dr. Soetomo General Hospital. Diagnosis of benign vocal fold lesion were established using FOL at Inpatient Unit of ENT-Head and Neck Surgery. Examinations on voice perception using VHI-10 and GRBAS were recorded before and after steroid injection. Benign vocal fold lesions include vocal nodules, polyp, and vocal fold cyst as well as laryngeal granulomas.

The data included age, sex, duration of hoarseness, and history of tobacco use as well as VHI-10 scores were gathered during patients' visit at Outpatient Unit of ENT-Head and Neck. The degree of voice quality was examined using GRBAS by the doctor in-charge in Outpatient Unit of ENT-Head and Neck. The patients were scheduled for flexible laryngoscopy for vocal fold evaluation. Vocal nodules were diagnosed based on the appearance of edema or epithelial thickening in 1/3 anterior of vocal fold, bilateral, and symmetric. Vocal fold polyp appeared as unilateral lesion, focal, transparant or reddish stroma in the superficial lamina propria layer. Vocal fold cyst appeared as subepithelial lesion, translucent to yellowish, and containing fluid. Laryngeal granuloma appeared as unilateral lesion, focal, and occurring due to

inflammation or post-trauma.

Intralesional steroid injection is an adjunctive alternative to standard therapy in benign vocal fold lesions. Patients with vocal nodules received steroid injections if the patient does not respond well to standard therapy, vocal hygiene and voice therapy. Patients with vocal fold polyps and cysts received intralesional steroid injection as an additional therapy following microscopic laryngeal surgery. Intralesional steroid injection was performed under general anesthesia at the Integrated Surgical Center Building (GBPT) of Dr. Soetomo Surabaya. The injection solution was a mixture of triamcinolone acetate (10 mg/ml) and dexamethasone sodium phosphate (5 mg/ml) with a 1:1 ratio of 0.1 ml for each injection. All post-vocal fold steroid injection patients had a voice rest for 7-10 days. Examination through the scores of VHI-10, GRBAS and fiberoptic laryngoscope evaluation were performed one month post-injection. VHI and GRBAS scores six months post-injection were also measured to assess the recurrence of benign vocal fold lesions.

Data was collected through medical records at Outpatient Unit of ENT-Head and Neck Surgery with ethical approval from Dr. Soetomo Hospital. Data collection was carried out from May to June 2019. The data were processed using the excel program version 2013 descriptively and the p value was calculated using SPSS v25.

3. RESULT

According to the medical record data, nine patients received intralesional steroid injection from January 2017 to December 2018 at Inpatient Unit of ORL-Head and Neck Surgery Dr. Soetomo General Hospital. One patient was excluded from the study due to diagnosed by subglottic stenosis. We evaluated eight patients who had received intralesional steroid injection. All patients were subjected to history taking to assess the VHI-10 score, GRBAS examination and flexible laryngoscopy. The data also included age, sex, duration of hoarseness, and history of tobacco use as seen on Table 1.

Table 1. Characteristics Distribution

Characteristics	Amount	
	N	(%)
Sex		
Male	3	37.50
Female	5	62.50
Age (y.o)		
15 – 25	1	12.50
26 – 35	5	62.50
36 – 45	1	12.50
46 – 55	1	12.50
History of Dysphonia		
≤ 1 year	6	75.00
> 1 year	2	25.00
History of Tobacco use		
Yes	1	12.50
No	7	87.50
Total	8	100

In this study, the data were obtained from eight patients with gender distribution of three male patients (37.50%) and five (62.50%) female patients. The distribution of the age ranges from 16 years to 54 years. The age range between 26-35 years has five patients (62.50%). Six patients (75%) was experienced dysphonia for less than 1 year and two others (25%) had it for more than one year. One patient (12.50%)

had a tobacco use habit and seven others (87.50%) did not smoke.

Table 2. Distribution of benign lesion diagnosis

Diagnosis	Amount	
	N	(%)
Vocal nodules	1	12.50
Vocal fold cyst	3	37.50
Vocal fold polyp	1	12.50
Vocal fold granuloma	3	37.50
Total	8	100

Most diagnoses in this study were vocal fold granulomas and vocal fold cysts. There were three patients. Another diagnosis is vocal nodules and vocal fold polyps only one patient.

VHI-10 scores decrease in all patients 1 month after intralesional steroid injection. The mean of pre-injection VHI-10 score was 18.25 (± 2.92), while in the first month of post-injection the mean was 8.75 (± 2.71) and in the sixth month there was a mean decrease of 8.50 (± 3.66). This data is described on Table 3.

Table 3. VHI -10 Scores

Diagnosis	VHI-10				
	Pre-Injection	Month 1	p*	Month 6	p*
Vocal nodules	17	5		4	
Vocal fold granuloma	23	6		5	
Vocal fold cyst	16	9		12	
Vocal fold cyst	19	6		9	
Vocal fold granuloma	18	12		15	
Vocal fold cyst	15	11		9	
Vocal fold polyp	22	10		6	
Vocal fold granuloma	16	11		8	
Mean	18.25 \pm 2.92	8.75 \pm 2.71	0.001	8.50 \pm 3.66	0.002

* p-value difference between pre-injection and post-injection scores

The VHI-10 scores decreased in the first month after injection in all patients with a mean difference of significant value (p-value 0.001). There was a lowering in the VHI-10 score 6 months post-treatment compared to the score in the first month in five patients. There was an increment in VHI-10 score six months post-treatment compared to the first month in three patients. The decrease in VHI-10 score pre injection and 6 months post-injection was significantly different (p-value 0.002).

Score of GRBAS 1 month after injection decreased in all patients. The mean pre-injection GRBAS 10 score was 6.00 (± 1.07), first month post-injection mean value was 3.38 (± 1.19) and sixth month mean decreased to 2.25 (± 1.28). The GRBAS score decrease in the first month after injection in all patients with a mean difference of significant reduction (p-value 0.011). This data is described on Table 4.

Table 4. GRBAS score

Diagnosis	GRBAS				
	Pre-Injection	Month 1	p*	Month 6	p*
Vocal nodules	7	3		1	
Vocal fold granuloma	6	2		1	
Vocal fold cyst	7	3		4	
Vocal fold cyst	5	4		2	
Vocal fold granuloma	6	3		4	

Vocal fold cyst	7	6	3
Vocal fold polyp	6	3	1
Vocal fold granuloma	4	3	2
Mean	6.00 ± 1.07	3.38 ± 1.19	0.011
			2.25 ± 1.28
			0.012

* P-value difference between pre-injection and post-injection scores

There was an increment in GRBAS scores from month to month 6 in two patients. GRBAS score decrease in between 1st month and 6th month in six patients. There were three patients with GRBAS scores of more than 3 points at 6th month. Score of VHI-10 from pre injection to 6th months post-injection had a significant difference (p-value 0.012).

Benign lesions were still found in two patients (25%) after treatment, and no lesions were found in six patients (75%).

Table 5. Benign Lesion in FOL post-injection

Benign Lesion	Amount (patient)	%	
Decrease	2	25	
Increase	6	75	
Total	8	100	

The following is a picture of FOL in a patient with vocal fold granuloma who improved with intralesional steroid injection. Post-injection FOL showed a decrease in lesion size and an improvement in patient's complaints (Figure 1).

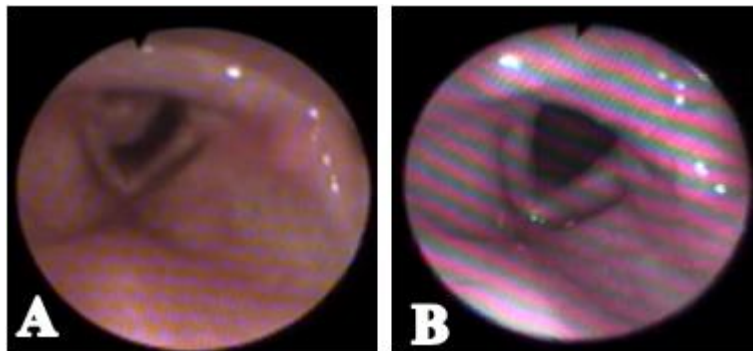


Figure 1. A) FOL image of vocal fold granuloma before intralesion steroid injection. B) FOL image of vocal fold granuloma 1 month after injection.

The following is a picture of FOL in a patient with vocal fold cysts who improved with intravenous steroid injection. In post-injection FOL, there were no cystic lesions and there was an improvement in the patient's complaints (Figure 2)

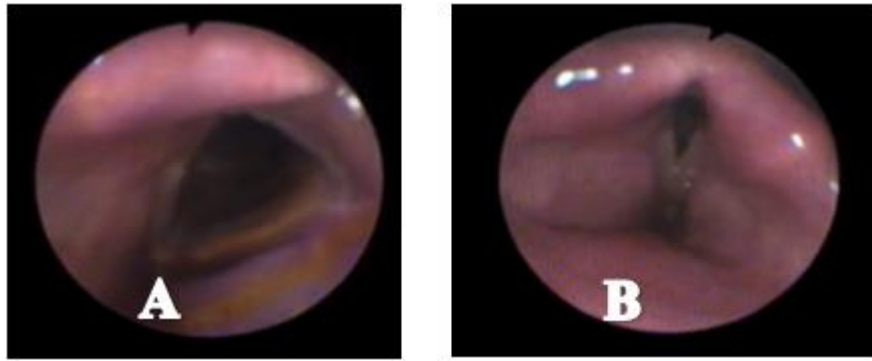


Figure 2. A) FOL image of vocal fold cyst before intralesion steroid injection. B) FOL image of vocal fold cyst 1 month after injection.

The following is a picture of FOL in patients with vocal fold granulomas who experienced recurrences after intralesional steroid injection. On the post-injection FOL images the lesion changes were not significant. This patient found a slight improvement in complaints 1 month post-injection and worsened again after 3 months post-injection (Figure 3).

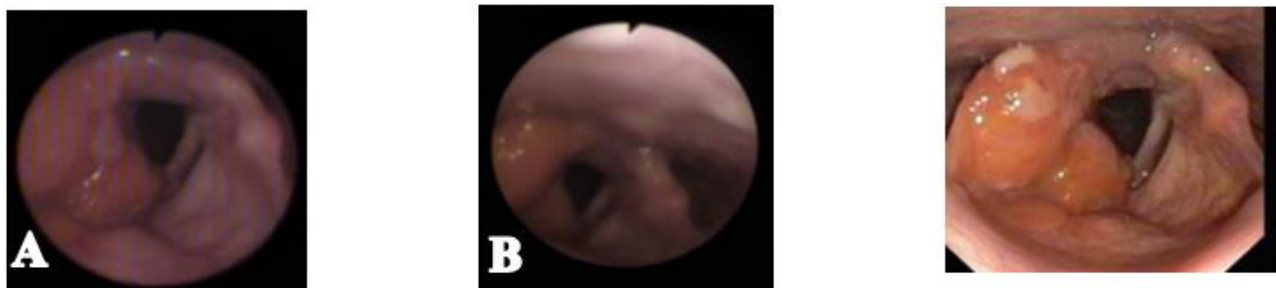


Figure 3. A) FOL image of vocal fold granuloma before intralesion steroid injection. B) FOL image of vocal fold granuloma 1 month after injection. C) FOL image of vocal fold granuloma 3 months after injection.

4. DISCUSSION

Based on the results in table 1 obtained at Inpatient Unit of ORL-Head & Neck Surgery Dr. Soetomo Hospital, more women (62.5%) than men among the patients received intralesional steroid injection therapy. Women are more likely to be reported to experience benign vocal fold lesions than men. This might be due to a higher frequency of female voices, increasing the risk of phonation trauma. In the study by [8] it was reported that there is a larger percentage of women than men (up to 64.9%) who received intralesional steroid injection. In another study, Alisa et al. (2014) with a larger sample size ($n = 641$) women had a 61.8% percentage of the incidence of benign vocal fold lesions [9].

Table 1 shows the largest age range, i.e. round 26-35 years, with 62.5%. This age is in the range of young adults. Cysts and vocal nodules are associated with a younger age range. This is due to higher sound intensity and phonotrauma, that might lead to edema, micro-vascular trauma and mucosal thickening, which in turn is associated with the development of vocal nodules. Cysts can also occur due to ductal obstruction of the mucous glands due to these epithelial changes. Insufficient posterior vocal fold closure is found in the range of young adults rather than the elderly. This is in accordance with a research by Alisa et al. (2014) suggesting that the largest age range is aged between 18-39 years old with 54.4% ($n = 641$) [9], [10].

In this study, there were 75% of patients with a history of dysphonia for less than 1 year and 25% for more

than 1 year. The duration of dysphonia complaints is one of the prognostic factors for the effectiveness of intralesional steroid injection therapy. Patients with dysphonia of longer than 1 year had less effective response than those with complaints of less than 1 year. This is because chronic lesions of the vocal fold have a lot of fibrin deposition, inflammation and amyloid-like material in the tissue. Chronic lesions also cause reactive nodules contralateral to the vocal fold which make post-treatment healing longer. In [7] study, 65% of patients had the history of dysphonia for less than 1 year. In another study, there were two cases of vocal fold polyps with dysphonia duration of more than 1 year and poor response after injection [4].

In this study, there were only 12.5% of patients with a history of tobacco use and 87.5% of patients with a history of not tobacco use. This result slight different in prevalence of adolescent smoker in Surabaya [11]. But this result is in accordance with the study of [4] where 87.3% of the patients with no history of tobacco use. In another study by [8], there were 87.5% of patients with a history of not tobacco use. One of the prognostic factors in patients with benign vocal fold lesions receiving intralesional steroid injection therapy is a history of tobacco use. This is because the histopathological structure of the vocal fold can change in smokers. Superficial keratinization of the epithelium and thinning of the basement membrane are common in smokers. This results in the accumulation of vocal fold epithelium which is often found in benign lesions of the vocal fold [12].

In table 2 of this study, the percentage of diagnosis of cysts and granulomas of the vocal fold is 37.5%, respectively. The diagnosis of vocal nodules and vocal fold polyps was 12.5%, respectively. This is different from the diagnosis profile of [13], where most of the vocal nodules and vocal fold polyps can be caused by the choice of patients for steroid injection, patients with micro-laryngeal surgical extraction plans followed by postoperative steroid injection].

Table 3 shows the VHI-10 score in the first month post-treatment. It was found that the VHI-10 score was reduced at all diagnoses with the pre-injection VHI-10 score of 18.25 (\pm 2.92) to 8.75 (\pm 2.71). At month 6, the mean VHI-10 decreased to 8.5 (\pm 3.66). The paired t test obtained p 0.001 (α =0.05), meaning that there was a significant difference in the VHI-10 score before and after the treatment at month 1 and p 0.002 at month 6. This shows that there is an improvement in dysphonia symptoms based on the patient subjective perception of the emotional, functional and physical aspects. This clinical improvement due to steroids has the effect of reducing tissue granulation and accelerating healing. Steroids also reduce the formation of hypertrophic scar tissue and reduce inflammation. Steroids can inhibit the inflammatory infiltrate response for 12 days and inhibit vasculogenesis for 21 days, and therefore can improve the dysphonia complaints found in patients. This is consistent with the study of [15] that there is a decrease in the VHI-10 score after laryngeal surgery and intralesional steroid injection [14].

Table 4 shows the GRBAS score before treatment has a mean of 6.00 (+ 2.92). One month after treatment there was a decrease in the mean of GRBAS score of 3.38 (\pm 1.19) and a decrease of 2.25 (\pm 1.28) in the following 6 months. The Wilcoxon test obtained p 0.011 (<0.05), which means that there was a significant difference in GRBAS scores before and after the action at month 1 and p 0.012 at month 6. This suggests that intralesional steroid injection can reduce dysphonia symptoms according to the examiner's perception. A histopathological study on rabbit vocal fold after vocal fold surgery and steroid injection resulted in decreased fibroblast proliferation, decreased extracellular matrix deposition, decreased regulation of the inflammatory response and decrease of the AKT pathway to prevent hypertrophic scar in muscle. This can lead to a reduction in dysphonia symptoms [16]. A research by [4] reported that there was a decrease in the GRBAS score at 1 month after injection compared to the pre-injection GRBAS score. The mean of GRBAS

score at the pre-injection of the study was 3.35. The mean score at 1 month after injection was 2.03 [17].

Table 5 also states that the lesions are still found in 25% of patients. It indicates that intralesional steroid injection can reduce the symptoms of dysphonia and the anti-inflammatory effect can be felt from 1-2 weeks post-injection. However, the triamcinolone given can undergo spontaneous absorption in the body for 1-2 months. This can increase the risk of recurrence. Intralesional steroid injection has a fairly high risk of recurrence, namely 4-30% in the meta-analysis study. The incidence of recurrence ranged from 4 weeks to 9 months post-injection. Recurrence can also occur due to vocal abuse by the patients. In this case of recurrence, repeated steroid injections can be performed with adjunctive voice therapy [16].

Figures 1 and 2 show the clinical improvement of patients with granulomas and vocal fold nodules. This suggests that the anti-inflammatory response of steroids reduces the size of the lesions. The effect of steroids reduces lesions from 2 weeks to a maximum of 12 weeks. This is in accordance with the research of [18] showing that the size of the lesion was reduced in 12 weeks by 1.11 (+ 1.45) mm. This study also obtained complete regression in 7 patients from a total of 29 patients.

Figure 3 shows a quite large granuloma lesion with steroid injection to reduce the mass slightly at the beginning of the week but 3 months after injection the complaints worsen again. Figure 3C shows the recurrence of lesions following intralesional steroid injection. This can occur because the anti-inflammatory effect begins to decrease at 4 weeks post-injection. In addition, the triamcinolone deposit will be absorbed by the body within 1-2 months, thereby increasing the risk of recurrence [16].

5. CONCLUSION

A retrospective descriptive analytic study was carried out on eight medical records of patients with benign lesions after intralesional steroid injection. The results showed a significant difference in the effect of steroid injection on reducing dysphonia symptoms as measured by the VHI-10 and GRBAS scores. Recurrence occurs at 25%. Further researches with objective measurements in the form of a Multi-Dimensional Voice Program (MDVP) and a more accurate stroboscopy as well as a longer controlled evaluation are needed to assess the reliability of this measure.

6. References

- [1] Rosen CA, Simpson CB. Pathological conditions of the vocal folds. In : Rosen CA, Simpson CB, eds. *Operative Technique in Laryngology* 1st ed. Berlin: Springer Berlin Heidelberg; 2008. p. 24–6
- [2] Naunheim MR, Carroll TL. Benign vocal fold lesions : update on nomenclature , cause , diagnosis , and treatment. *Curr Opin Otolaryngol Head Neck Surg* 2017;25(1):1-6
- [3] Muslih I, Herawati S, Retno D. Association between voice handicap index and praat voice analysis in patients with benign vocal cord lesion before and after microscopic laryngeal surgery. *Indian J Otolaryngol Head Neck Surg* [Internet]. 2018; Available from: <https://doi.org/10.1007/s12070-018-1363>
- [4] Wang CT, Lai MS, Hsiao TY. Comprehensive Outcome Researches of Intralesional Steroid Injection on Benign Vocal Fold Lesions. *J Voice* 2014;16(1):1-10
- [5] Rekam Medis RSUD Dr Soetomo. EMR Poli THTKL RSUD Dr. Soetomo. Surabaya: RSUD Dr. Soetomo; 2018. p. 1

- [6] Hardianingwati LM, Ardani DM. Prevalence of Benign Vocal Cord Disorder at Dr . Soetomo General Hospital Surabaya Indonesia in June 2015-June 2016. *Indian Journal of Forensic Medicine & Toxicology* 2020;14(2):2289–93
- [7] Wang CT, Lai MS, Cheng PW. Long-term Surveillance Following Intralesional Steroid Injection for Benign Vocal Fold Lesions. *JAMA Otolaryngol Head neck Surg* 2017;143(6):589-94
- [8] Wu PH, Cheng PW, Lin FC, Wang CT. Intralesional Steroid Injection as An Alternative Treatment for 57 Patients of Vocal Fold Mucus Retention Cysts. *Wiley Clinical Otolaryngology* 2018;43(5):1375–84
- [9] Zhukhovitskaya A, Battaglia D, Khosla SM, Murry T, Sulica L. Gender and Age in Benign Vocal Fold Lesions. *Laryngoscope* 2015;125(1):191–6
- [10] Helena R, Martins G, Abrantes H, Lara E, Tavares M, Garcia M, et al. Voice Disorders : Etiology and Diagnosis. *J Voice* 2015;18(6):1-9
- [11] Setyowati L, Widyawati IY, Wahyuni SD. Perceived Behavioral Control and Intention Related to The Smoking Behavior of Early Adolescents in North Surabaya. *Jurnal Ners* 2020;15(2):193–6
- [12] Effat KG, Milad M. Comparative histopathological study of vocal fold polyps in smokers versus non-smokers. *The Journal of Laryngology & Otology* 2015;129(4):484–8
- [13] Siddapur GK, Siddapur KR. Comparative study of benign vocal fold lesions in a tertiary health centre. *Int J Otolaryngol Head Neck Surg* 2015;1(2):65–8
- [14] Campagnolo AM, Tsuji DH, Sennes LU, Imamura R. Steroid injection in chronic inflammatory vocal fold disorders, literature review. *Braz J Otorhinolaryngol* 2008;74(6):926–32
- [15] Cho J, Kim S, Joo Y, Park Y, Hwang W, Sun D. Efficacy and safety of adjunctive steroid injection after microsurgical removal of benign vocal fold lesions. *J Voice* 2017;26(3):1-6
- [16] Wang CT, Liao LJ, Cheng PW, Lo WC, Lai MS. Intralesional Steroid Injection for Benign Vocal Fold Disorders : A Systematic Review and Meta-Analysis. *The Laryngoscope* 2013;123(1):197–203
- [17] Sofiyanti S, Goenawan H, Lesmana R, Tarawan VM, Division P, Padjadjaran U, et al. Review Article The AKT pathway and satellite cell activation in skeletal muscle mass regulation. *Fol Med Indones* 2022;58(1):68–73
- [18] Ramavat AS, Tiwana H, Banumathy N, Bakshi J, Panda N. Efficacy of Intralesional Steroid Injection in Small Benign Vocal Fold Lesions. *J Voice* 2018;8(1):1-6