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Original Article

Voice Handicap Index after Hyaluronidase Injection in Minimal Associated Pathological Lesions of the Vocal Fold

Sara Elkilany Abdelmonem Tantawy^{1*}, Amal Saeed Quriba ¹, Elham Magdy Hassan ¹, Mohamed kamal mobashir²

¹Phoniatrics Department, Faculty of Medicine, Zagazig University, Egypt.

²Otolaryngology Department, Faculty of Medicine, Zagazig University, Egypt.

Corresponding author:

Sara Elkilany Abdelmonem
Tantawy

E-mail:

sarahelkilany9454@gmail.com

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ABSTRACT

Background: Voice disorders, resulting from structural or functional changes in the larynx, affect about 30% of the population. Larynx structural or functional changes that affect the speaker's functional requirements can be the cause of these disorders. In this study we aim assess voice after hyaluronidase injection in MAPLs of the vocal fold by voice handicap index. **Methods:** This prospective cohort research involved 24 cases diagnosed as benign vocal fold lesions who underwent vocal fold injection of the hyaluronidase (HAase) enzyme in the phoniatric unit, ENT department, faculty of medicine, Zagazig University, from June 2022 until December 2023. **Results:** There was significant distinction among voice handicap index scores at different periods. There wasn't a statistically significant distinction among the two studied maneuvers with regarding the voice handicap index at baseline. There was a statistically significant distinction among the two maneuvers studied with regarding the voice handicap index at 1 month. There wasn't a statistically significant distinction among the two studied maneuvers with regarding the voice handicap index at 3 months. **Conclusion:** In minimally associated pathological lesions (MAPLs) (Reinke's edema, polyps, & asymmetrical nodules), HAase enzyme injection is effective in improving voice, according to the results of the vocal handicap index.

Keywords: VFI, Hyaluronidase enzyme, MAPLs, Reinke's edema

INTRODUCTION

Voice disorders can arise due to alterations in the structure and/or function of the larynx that prevent the voice from fulfilling the speaker's functional requirements. Around thirty percent of the population experiences dysphonia at some point in their lives [1].

The MAPLs, which are also referred to as benign vocal fold lesions, comprise a collection of small benign lesions that impact the vocal folds. Laryngeal cysts, vocal fold nodules, polyps, polypoid degeneration, contact granuloma and Reinke's edema are among these lesions [2].

As a minimally invasive procedure, vocal fold injection (VFI) administers a variety of substances or medications into the laryngeal structures. The technique in concern has made a reemergence due to advancements in endoscopic technology and material science, thus its use in laryngology has been highlighted [3, 4].

An essential extracellular matrix (ECM) protein, hyaluronic acid (HA), is crucial to the biomechanics of the vocal fold. Under certain conditions, excessive production and retention of HA in the superficial lamina propria of the vocal folds (SLP) can lead to the HA becoming lodged in the SLP, therefore reducing the qualities of the voice [5, 6].

The hyaluronidase enzyme (HAase) breaks down HA by means of enzymatic cleavage. HA levels are decreased and the permeability of connective tissues is increased via HAase-mediated degradation [5]. The study's purpose was to determine changes in voice handicap index scores after hyaluronidase injection in Minimal Associated Pathological lesions of the vocal fold.

METHODS

This prospective cohort research involved 24 cases diagnosed as benign vocal fold lesions who underwent vocal fold injection of the hyaluronidase enzyme in the phoniatic unit, ENT department, faculty of medicine, Zagazig University, from June 2022 until December 2023.

Inclusion criteria: All patients with Minimal Associated Pathological Lesions of the Vocal Fold (MAPLs), enlarged polyps, Reinke's edema, or asymmetrical nodules with age more than 18 years of both sexes. **Exclusion criteria:** Patients with any other laryngeal, speech or voice disorders, patients having any neurological disorders, patient having allergy to the material on doing intradermal patch test, patients having abnormal bleeding profile, patients with previous neck surgery or irradiation, history of malignant laryngeal swellings.

Ethical considerations: All participants provided written informed consent, and the research ethical committee of the Faculty of Medicine, Zagazig University, approved the study. Research was carried out in accordance with IRB#:10072/2-11-2022, which is the code of ethics for studies involving human subjects as established by the World Medical Association (Declaration of Helsinki).

Each individual involved in this research was exposed to the voice assessment protocol [7] as well as the voice handicap index [8] before & after 1 and 3 months of HAase injection in the vocal fold.

The Voice Handicap Index-30 was initially devised as a self-reported psychometric instrument for the assessment of voice disorders [9]. The instrument is a self-administered, 30-item scale with physical, functional and emotional subscales. Every individual item is evaluated using a five-point equal-appearing interval scale, ranging from "zero" to "four"; the maximum possible score is 120. There has also been the production of a condensed version of the iteration known as VHI-10, which consists of ten items selected from the initial thirty items [10]. Several validity & reliability tests have been

conducted on both the VHI-30 and VHI-10, and both have been consistently deemed to possess good psychometric characteristics [11]. Furthermore, it has demonstrated positive discriminant validity in multiple investigations [12] when comparing individuals with and without voice disorders. Due to their favorable psychometric characteristics and straightforward administration, the VHI-30 & VHI-10 are extensively utilized in clinical and research environments across the globe [13]. Their validity has been established in a minimum of eighteen distinct languages. According to Malki et al. [8] the Arabic version of the Vocal Health Inventory (VHI) is a valid & dependable self-evaluation instrument for determining the severity of vocal illnesses in Arabic-speaking cases.

Intervention Procedure Technique:

A vocal fold injection will occur subsequent to a comprehensive evaluation, during which the patient is informed of the procedure. The injection is administered via the transoral or transcutaneous (via the cricothyroid membrane) route. Trans-cutaneous VFI is an easy method utilized to administer a variety of substances or medications into the vocal folds. Intradermal injection of four to eight units of hyaluronidase into the forearm (patch test), followed by thirty minutes of observation of the results to identify the presence of hypersensitivity to the substance. Determine the appropriate position of the needle tip within the vocal fold after localizing the site of injection (via the cricothyroid membrane). Subsequently, inject the substance into the vocal fold while ensuring proper needle tip positioning. By utilizing flexible laryngoscopy, the needle point is identified. A proficient application of flexible laryngoscopy is critical in order to obtain a sufficient clear visual field, including the vocal folds. Furthermore, patient adherence is critical for the proper identification and maintenance of the needle tip. Unintentional gag reactions, coughing or swallowing could disrupt the procedure. Therefore, for office-based vocal fold injection to ensure good visibility, patient compliance and adequate anesthesia is required (topical lidocaine continues to be utilized for VFI).

Statistical analysis: The computation was conducted utilizing the IBM SPSS software program version 20.0 on the inputted data. (IBM Corp., Armonk, New York) Qualitative data were described in terms of percentages and numbers. The Kolmogorov-Smirnov test was employed to assess the distribution's normality. The range (minimum & maximum values), standard deviation, mean,

median, & interquartile range (IQR) were employed to characterize the quantitative data. At the 5% significance level, the derived results were deemed significant. The tests utilized were: The chi-square test is utilized to compare categorical variables across distinct groups. ANOVA in which measures are repeated (F): To compare quantitative variables that follow a normal distribution across more than two periods or stages. The Friedman test (Fr) is utilized to compare quantitative variables that have an abnormal distribution across more than two periods or stages. The student t-test (t) is utilized to compare two groups of studies for quantitative variables that have a normal distribution. The Mann-Whitney test (U) is utilized to compare two

groups of subjects for quantitative variables that have an abnormal distribution.

RESULTS

The cases that were examined had a mean age of 43.11(±8.61 SD) with a range (30-65) & among the studied cases, there were 5 (20.8%) females and 19 (79.2 %) males (**Table 1**).

There was a significant distinction among voice handicap index scores at different periods (**Table 2**).

There was a significant positive association among the voice handicap index score & size of the lesion and a significant negative association among the voice handicap index score & phonation time (**Table 3**).

Table 1: Distribution of the studied cases according to demographic data

| Subjects (n = 24) | | |
|-------------------|--------------|--------|
| Age | | |
| Range. | 30 – 65 | |
| Mean ± SD. | 42.75 ± 7.74 | |
| Sex | | |
| Female | 5 | 20.8 % |
| Male | 19 | 79.2 % |

Table 2: Comparison between voice handicap index score at different periods

| | Baseline (n = 24) | 1 month (n = 24) | 3 months (n = 24) | Test of sig. | P |
|-----------------------------------|---------------------------------|------------------|-------------------|--------------|---------|
| voice handicap index score | | | | | |
| Range. | 26 – 103 | 23 – 74 | 10 – 69 | F= 27.685 | <0.001* |
| Mean ± SD. | 76.33 ± 19.51 | 53.83 ± 16.68 | 43.92 ± 19.23 | | |
| Post-hoc | p1=0.004*, p2=0.043*, p3<0.001* | | | | |

p1: p value for comparing between baseline & 1 month, p2: p value for comparing among baseline & 3 months, p3: p value for comparing between 1 month & 3 months.

Table 3: Correlation among voice handicap index score & different parameters

| | voice handicap index score | |
|-----------------------|----------------------------|---------|
| | r | P |
| Size of lesion | 0.505 | <0.001* |
| Frequency | 0.085 | 0.476 |
| Jitter | -0.060 | 0.619 |
| Shimmer | 0.226 | 0.057 |
| HNR | 0.021 | 0.863 |
| phonation time | -0.609 | <0.001* |
| f0tremor | -0.054 | 0.650 |

DISCUSSION

A crucial extracellular matrix (ECM) protein, hyaluronic acid (HA), is essential for vocal fold biomechanics. HA plays a crucial role in regulating inflammation and wound healing [14].

HA levels increase in particular conditions, including polyps and Reinke edema. Another case of excessive HA occurs when hyaluronic acid is administered via injection laryngoplasty. This may lead to the HA settling within the SLP, which can result in a deterioration of voice quality as normal vibratory function is lost [5]. A surgical procedure is employed in order to eliminate the extracellular matrix. Surgical intervention may be obviated if the hyaluronidase enzyme is injected instead of this [15].

Hyaluronidase (HAase) is a proteolytic enzyme preparation. Unknown is the precise chemical structure of this enzyme. Injection HAase is provided in the form of a colorless sterile non-preserved solution. The mechanism of action involves hyaluronic acid (HA) degradation by enzymes. For the purpose of obtaining hydration, hyaluronidase injection is recommended as an adjunct to subcutaneous fluid administration. The administration of hyaluronidase injections enhances the absorption and dispersion of injected medications [16].

Correction and rapid decrease of hyaluronic acid over injection in the vocal fold; polypoid cordites without microphonosurgical removal, correction of Reinke edema, possible reduction of the period of voice disturbance due to acute vocal fold bleeding as well as avoidance of complications associated with vocal bleeding through the use of HAase [5] are all conditions in which its adjunctive application may prove beneficial.

In our research, there was significant variance among voice handicap index scores at different periods (improvement or reduction) postoperatively and this was explained by development in voice quality. There was a significant positive association among the voice handicap index score and size of the lesion, beside a significant negative association among the voice handicap index score and phonation time.

Recommendations: Hyaluronidase injection of MAPLs (VFPs, RE, and VFNs) is a safe and effective procedure. More studies should be addressed to monitor long term follow up and recurrence rates.

CONCLUSIONS

In minimally associated pathological lesions (MAPLs) (Reinke's edema, polyps, and asymmetrical nodules), HAase enzyme injection is effective in improving voice, according to the results of the vocal handicap index.

Conflict of interest statement: The authors declared that there were NO conflicts of Interest.

Disclosure: The authors have no financial interest to declare in relation to the content of this article.

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REFERENCES

1. Ren QW, Lei G, Zhao YL, Zhou L, Luo XL, Peng SL. Laryngopharyngeal Reflux and Benign Vocal Fold Lesions: A Systematic Review and Meta-analysis. *Otolaryngology–Head and Neck Surgery*. 2024 Feb;170(2):309-19.
2. Abdelhamid A, Hassan M, Youssef G. The nature and risk factors of minimal associated pathological lesions of vocal folds at two hospitals in the gulf area. *Journal of Voice*. 2022 May 1;36(3):438-e25.
3. Kim J, Seo HS, Na HS, Son HY, Lee DK, Jeong WJ, et al. Real-time light-guided vocal fold injection as a simulation-based training tool. *Auris Nasus Larynx*. 2021 Feb 1;48(1):124-30.
4. Son HY, Kim S, Mohammad RT, Huh G, Kim H, Jeong WJ, et al. Real-time light-guided vocal fold injection: an in vivo feasibility study in a canine model. *Clinical and Experimental Otorhinolaryngology*. 2021 Aug 1;14(3):338-46.
5. Woo P. Hyaluronidase injection in the vocal folds for vocal hemorrhage, Reinke edema, and hyaluronic acid over injection: a novel application in the larynx. *Journal of Voice*. 2018 Jul 1;32(4):492-8.
6. Chan RW, Gray SD, Titze IR. The importance of hyaluronic acid in vocal fold biomechanics. *Otolaryngology–Head and Neck Surgery*. 2001 Jun;124(6):607-14.
7. Kotby MN, Abou Ras Y, Saleh M, Khidr A, Hegazi M, El Adawy A, et al. Non-organic voice disorders and the syndrome of vocal fatigue. *Clin Vocol*. 2016; 1:92-123.
8. Malki KH, Mesallam TA, Farahat M, Bukhari M, Murry T. Validation and cultural modification of Arabic voice handicap index. *European*

archives of oto-rhino-laryngology. 2010 Nov; 267:1743-51.

9. Jacobson BH, Johnson A, Grywalski C, Silbergleit A, Jacobson G, Benninger MS, et al. The voice handicap index (VHI) development and validation. *American journal of speech-language pathology*. 1997 Aug;6(3):66-70.

10.Higginson IJ, Carr AJ. Using quality of life measures in the clinical setting. *Bmj*. 2001 May 26;322(7297):1297-300.

11.Branski RC, Cukier-Blaj S, Pusic A, Cano SJ, Klassen A, Mener D, et al. Measuring quality of life in dysphonic patients: a systematic review of content development in patient-reported outcomes measures. *Journal of voice*. 2010 Mar 1;24(2):193-8.

12.Behlau M, Madazio G, Oliveira G. Functional dysphonia: strategies to improve patient outcomes.

Patient related outcome measures. 2015 Dec 1:243-53.

13.Seifpanahi S, Jalaie S, Nikoo MR, Sobhani-Rad D. Translated versions of Voice Handicap Index (VHI)-30 across languages: a systematic review. *Iranian journal of public health*. 2015 Apr;44(4):458.

14.Gaston J, Thibeault SL. Hyaluronic acid hydrogels for vocal fold wound healing. *Biomatter*. 2013 Jan 1;3(1): e23799.

15.Jung H. Hyaluronidase: An overview of its properties, applications, and side effects. *Archives of plastic surgery*. 2020 Jul;47(04):297-300.

16.Khan N, Niazi ZR, Akhtar A, Khan MM, Khan S, Baloch N, et al. Hyaluronidases: a therapeutic enzyme. *Protein and Peptide Letters*. 2018 Jul 1;25(7):663-76.

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