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LARYNGOLOGY

Office-based blue laser therapy for dyspnea in patients with type 3 Reinke's edema

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Abstract

Purpose To investigate the effectiveness of in-office blue laser therapy on dyspnea in patients with type 3 Reinke's edema.

Methods The medical records and video-recordings of patients with Reinke's edema type 3 who had undergone office-based blue laser therapy between March 2022 and January 2023 were reviewed. The primary outcome measures assessed before and after surgery were dyspnea severity, risk of obstructive sleep apnea (OSA), and disease regression. The severity of dyspnea was measured using the Dyspnea Severity Index (DSI), the risk of OSA was assessed using the STOP-BANG questionnaire, and disease regression was assessed by reviewing the laryngeal examination before and after surgery. The Voice Handicap Index-10 (VHI-10) was used as a secondary outcome measure.

Result A total of 10 patients were included. The mean age of the study population was 58.9 ± 4.2 years. The male-to-female ratio was 2:3. In total, 20 vocal fold lesions were treated among which 18 were reviewed. Eight lesions regressed completely and 10 partially. There was a statistically significant drop in the mean score of DSI after surgery (16.1 ± 10.2 pre-operatively vs 2.3 ± 2.3 post-operatively, p-value < 0.001). The mean STOP-BANG score decreased from 4.8 ± 1.47 to 3.1 ± 1.28 (p-value $= 0.001$). There was also a significant improvement in VHI-10 score (22.7 ± 7.0 vs 4.4 ± 5.6, p-value < 0.001).

Conclusion Office-based blue laser therapy offers a safe and effective treatment for shortness of breath in patients with type 3 Reinke's edema.

Keywords Laryngology · Dyspnea · Breathing · Voice disorders · Benign lesions

Introduction

Vocal Fold Reinke's edema is an exudative lesion of the lamina propria commonly encountered in women [1]. Risk factors include smoking, laryngopharyngeal reflux disease and phonotrauma [2]. Patients usually present with an alteration in pitch and/or loudness secondary to the polypoid degeneration of the vocal folds. Professional voice users may also complain of a contracted vocal range, difficulty in sustaining a note, and/or problems in transition between vocal registers [3]. In advanced cases, symptoms such as dyspnea and snoring can prevail. In a prospective study on the pathogenic role of Reinke's edema in snoring, Hamdan et al. noted a higher prevalence of obstructive sleep apnea (OSA) in their study group in comparison to a control group matched according to age, gender, and body mass index (36 vs. 4%, respectively) [4]. The authors stressed the need to consider vocal fold Reinke's edema as a risk factor for OSA among other structural and neurologic disorders of the larynx.

Treatment of patients with Reinke's edema is challenging. Vocal hygiene therapy and vocal exercises are always recommended as a start. Failure to improve following conservative treatment is an indication for surgical intervention, particularly in patients who rely on their voice to make a living. The surgery is traditionally performed in the operating room using the microflap [5] or mini-microflap technique [6] in order to preserve part the mucosal lining and minimize damage to the deep structures of the vocal fold. With the advances in technology and the introduction of the flexible endoscope with a working channel, office-based treatment of vocal fold Reinke's edema has markedly evolved over the last two decades [7–12]. Among the various in-office treatment options is laser therapy. In a recent

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systematic review and meta-analysis on the effectiveness of office-based laser therapy for Reinke's edema, the authors asserted the improvement in subjective and objective voice outcome measures following treatment [13].

No previous study looked at the impact of office-based laser therapy on dyspnea in patients with type 3 vocal folds Reinke's edema. Type 3 Reinke's edema is characterized by extensive edema of the upper and lower lip of the vocal folds, with the open airway space being limited only to the posterior glottis [14]. The purpose of this investigation is to examine the effect of office-based blue laser therapy on dyspnea in patients with type 3 Reinke's edema. The blue laser is a new photoangiolytic laser (wavelength 445 nm) with superior hybrid properties in comparison to the old photoangiolytic lasers [9, 13, 15, 16]. The hypothesis set forth by the authors is that in-office blue laser therapy is effective in treating dyspnea in patients with type 3 Reinke's edema.

Materials and Methods

After having obtained the Institutional Review Board approval of the American University of Beirut Medical Center (IRB ID: BIO-2022-0280), the medical records and video-recordings of patients with vocal folds Reinke's edema type 3 who had undergone office-based blue laser therapy at the Voice Unit in a tertiary referral center between March 2022 and January 2023 were reviewed. All patients who had undergone office-based laser therapy using other types of lasers or who had their office-based procedure aborted due to poor tolerance were excluded.

A total of 10 patients were included. This patient series has not been reviewed or reported previously. Demographic data include age, gender, history of smoking, laterality and type of lesion. The primary outcome measures assessed before and after surgery were dyspnea severity, risk of OSA, and disease regression. The severity of dyspnea was measured using the Dyspnea Severity Index (DSI) described by Gartner-Schmidt et al. A DSI score above 10 was considered abnormal [17]. The risk of OSA was assessed using the STOP-BANG questionnaire described by Chung et al. The total score of the STOP-BANG questionnaire categorizes patients into subjects at low risk for OSA if the score is 0–2, intermediate risk for OSA if the score is 3–4, and high risk for OSA if the score is 5 or more [18]. Disease regression was assessed by reviewing the laryngeal examination before surgery and 6–12 weeks after. The laryngeal examination is usually performed using the flexible nasopharyngoscope with a distal chip camera (HD Video Rhino-Laryngoscope from KARL STORZ) with or without video-stroboscopic evaluation using the 70-degree telescope (The 9310HD PENTAX Medical Digital Video Capture Module). The size of the lesion was graded as type 1 if the edema was on the upper surface of the vocal folds with a preserved glottic patency, type 2 if the edema extended from the upper to the lower surface of the vocal folds, which are partly in contact with each other, and type 3 if the edema was so advanced that the glottic opening is only seen posteriorly or if the bulge was sac-like extending into the subglottic space during inspiration [14]. Decrease in mucosal waves and/or presence of an adynamic segment on video-stroboscopic examination following surgery were also noted.

The video-recordings were reviewed by two otolaryngologists independently who rated disease regression following laser therapy. The inter-rater variability was computed to assess the reliability of the reported findings. The VHI-10 score described by Rosen et al. was also reported as a secondary outcome measure [19].

This study conforms to the regulations and standards established by the Declaration of Helsinki of the World Medical Association.

Statistical method

Categorical and continuous variables were described using frequencies and means (± standard deviation), respectively. Paired t test was used to analyze continuous variables. Interrater reliability was computed using Cohen's kappa coefficient. The interquartile range (IQR) for the VHI-10 scores was calculated as the difference between the 75th (Q3) and 25th percentiles (Q1). All analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 24 software package. A two-tailed p-value < 0.05 was considered statistically significant.

Surgical technique

Office-based blue laser therapy of vocal fold Reinke's edema was performed on all patients via the trans-nasal approach using a flexible nasopharyngoscope (Pentax Medical FNL-15RP3) with a working channel. An intramuscular injection of glycopyrrolate (200 mg/1 ml) was administered prior to the procedure in some patients to reduce the pooling of secretions in the larynx. With the patient fully awake and in the upright sitting position, sponges soaked with 1% lidocaine HCL with 1:100,000 Epinephrine and 0.1% Xylometazoline Hydrochloride were inserted in the nasal cavities to achieve local anesthesia and decongestion. The oropharynx and hypopharynx were anesthetized using 2–3 puffs of xylocaine spray (2%). An aliquot of 5 cc of 2% lidocaine HCL was dripped on the vocal folds via the working channel of the fiberoptic endoscope while the patient was asked to sustain a vowel (laryngeal gargle). Following the successful application

of the local anesthetic to the larynx and pharynx, the blue laser 400 nm glass fiber (TrueBlue; A.R.C. Laser Company) was advanced through the working channel of the fiberoptic laryngoscope toward the vocal fold lesion. Using a power setting of 10 Watts, pulse duration of 40 ms, and pulse pause of 300 ms, the laser beam was applied in non-contact and contact mode until there was blanching of the lesion. Note that all the patients were instructed to have complete voice rest after surgery for 3–5 days based on their vocal occupational demand. They were also advised cessation of smoking, good hydration and were kept on a proton pump inhibitor twice daily for a period of at least 3 months. The patients were also informed that potential worsening of the voice may occur in the first few days after surgery due to the post-operative inflammation as a result of laser-induced thermal injury. See Fig. 1.

Results

Demographic data

Ten patients who underwent office-based blue laser treatment for vocal fold Reinke's edema (type 3) were included in this study. The procedure was well tolerated by all patients and no complications were noted. The mean age of the study population was 58.9 ± 4.2 years, and the mean BMI was 31 ± 3.2 kg/m^2. The male-to-female ratio was 2:3. All patients were smokers. Two patients reported history of reflux disease (20%). Table 1.

Fig. 1 An endoscopic view of the larynx showing the blue laser glass fiber in non-contact mode in a patient with type 3 Reinke's edema

Table 1 Demographic characteristics of the study population

Demographic data	Cases ($N = 10$)
Gender (Male:Female ratio)	2:3
Age in years (mean ± SD)	58.9 ± 4.2
BMI in kg/m^2 (mean ± SD)	31 ± 3.2
Smoking (n (%))	10 (100)
Reflux (n (%))	2 (20)

SD standard deviation

Disease regression after office-based blue laser therapy

All patients except for one had a single treatment session during which unilateral or bilateral vocal fold lesions were treated in-office using the blue laser. In total, 20 vocal fold lesions were treated. The duration of surgery ranged between 7 and 17.57 min with a mean of 10.11 min. The mean number of Joules delivered was 240.4 J and it ranged from 112 to 367 J (n = 5). Follow-up video-recordings was available for 9 out of 10 patients, i.e. 18 vocal fold Reinke's edema were reviewed. Out of these 8 regressed completely and 10 regressed partially. Table 2 and Fig. 2a and b. Review of the laryngeal video-stroboscopic examinations following surgery which were available in 7 patients showed good mucosal waves in 12 of the 14 vocal folds, and mild impairment in the remaining two. There was no worsening of the mucosal waves in any of the cases post-laser therapy and no vocal fold scaring or stiffening were noted.

Inter-rater reliability analysis revealed an intra-class correlation coefficient (ICC) of 0.847 indicating excellent reliability between the two otolaryngologists who evaluated the endoscopic laryngeal findings.

Table 2 Grading of Reinke's edema lesions before and after treatment with Blue Laser

Patient	Disease laterality	Grade before	Grade after
1	Bilateral	3 (R); 3 (L)	1 (R); 2 (L)
2	Bilateral	2 (R); 3 (L)	Normal (R); 1 (L)
3	Bilateral	2 (R); 3 (L)	1 (R); Normal (L)
4	Bilateral	1 (R); 3 (L)	N/A
5	Bilateral	3 (R); 3 (L)	1 (R); Normal (L)
6	Bilateral	3 (R); 2 (L)	1 (R); Normal (L)
7	Bilateral	3 (R); 3 (L)	2 (R); 1 (L)
8	Bilateral	3 (R); 3 (L)	1 (R); Normal (L)
9	Bilateral	3 (R); 3 (L)	Normal
10	Bilateral	3 (R); 3 (L)	1 (R); Normal (L)

R right; *L* left; *N/A* not applicable

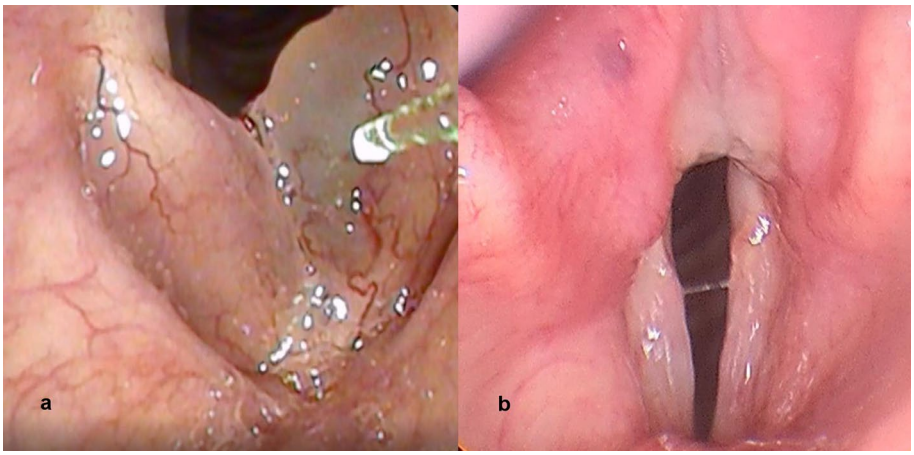

Fig. 2 **a** An endoscopic view of a patient with type 3 Reinke's edema before undergoing in-office blue laser therapy. **b** A laryngeal view six weeks after office-based blue laser therapy of bilateral type 3 Reinke's edema showing type 1 Reinke's edema on the right side and complete regression of the disease on the left

Table 3 Mean ± standard deviation of dyspnea severity index and STOP-BANG score before and after blue laser treatment ($n = 10$)

	Before	After	p-value
DSI	16.1 ± 10.2	2.3.0 ± 2.31	< 0.001*
STOP-BANG	4.8 ± 1.47	3.1 ± 1.28	0.001*

DSI dyspnea severity index

*Statistically significant (p < 0.05)

Dyspnea severity index (DSI) and STOP-BANG scores before and after blue laser therapy

Six patients out of 10 had an abnormal DSI, i.e., above 10, prior to surgical intervention. All patients had a decrease in their DSI score after surgery. None of the patients had an abnormal DSI after surgery. The mean score of the study group decreased significantly from 16.1 ± 10.2 to 2.3 ± 2.3 (p-value < 0.001).

With respect to the STOP-BANG score, five patients had intermediate risk of OSA, and 5 patients had high-risk of OSA. Eight patients out of 10 had a decrease in their STOP-BANG score after surgery. The mean STOP-BANG of the study group decreased from 4.8 ± 1.47 to 3.1 ± 1.28 (p-value = 0.001). In summary, post-operatively four patients had low risk of OSA, five had intermediate risk of OSA and only 1 had high risk of OSA. Table 3.

Voice handicap 10-score (VHI-10) before and after laser therapy

All patients had a decrease in their voice handicap index-10 score. The mean score of the total group dropped from 22.7 ± 7.0 (IQR, 17.5–30.5) to 4.4 ± 5.6 (IQR, 1.5–11) after surgical intervention (p-value < 0.001).

Discussion

There are numerous studies on the use of lasers for the treatment of vocal folds' Reinke's edema. In a review of 443 cases of office-based laryngeal surgery, which included 10 cases of Reinke's edema, Koufman et al. reported near-total disease regression in all treated subjects [11]. Pitman et al. reported improvement in physicians' perceptual evaluation following KTP laser therapy in 7 patients. The subjective improvement in voice quality substantiated by a decrease in the VHI score by 9 points was accompanied by an increase in the fundamental frequency, albeit not significant [10]. Koszewski et al. noted an increase in phonatory range in addition to a decrease in the VHI score in a cohort of patients with Reinke's edema who underwent office-based photoangiolytic laser therapy [20]. In a recent publication, Hamdan et al. also reported a significant decrease in the VHI-10 score and a non-significant increase in the fundamental frequency in 8 patients treated in-office using the blue laser [12].

In all the above reports, the outcome measures used were voice-related. The subjective and objective improvement in voice quality after laser therapy was ascribed to disease regression secondary to selective photo-angiolysis of the lesion's vasculature, and/or to thermogenesis A careful review of these reports shows that dyspnea and/or sleep-related breathing symptoms were not noted although patients with vocal folds Reinke's edema type 3 have a decrease in glottic aperture that invariably improves after surgery. In one study that included 25 patients, Hamdan et al. highlighted the increased prevalence of snoring and risk of OSA in patients with Reinke's edema in comparison to healthy controls [4]. The results of this investigation corroborate these findings. Sixty percent of the study group had an abnormal DSI score and 50% were at a high risk of OSA. The results of this investigation also showed that a large percentage of patients with type 3 Reinke's edema who suffered from dyspnea and/or were at a moderate to severe risk of OSA, improved

following office-based blue laser therapy. The improvement in respiratory symptoms is not self-evident given the well-known pulmonary morbidities associated with smoking which was common in all the subjects of our study group.

OSA is a morbid condition associated with many systemic diseases. The etiology is multifaceted and the most common sites of airway obstruction are the nose, velopharynx, and hypopharynx. Laryngeal dysfunction is gaining attention as a new site of upper airway obstruction in patients with OSA. Both structural and neurologic disorders in affected subjects have been described [21]. Neurologic disorders include unilateral and bilateral vocal fold paralysis, whereas structural abnormalities included adult laryngomalacia, laryngeal cysts, glottic, and subglottic stenosis. This investigation suggests that vocal fold Reinke's edema is also one of many potential causes of OSA. It also suggests that this structural abnormality is amenable to office-based laser therapy. The respiratory symptoms and high risk of OSA in affected patients are often masked by the phonatory disturbances and should be addressed cautiously. The resurge in office-based laryngeal surgery offers a new treatment opportunity to patients with dyspnea and/or at risk of having OSA and spares the patient the need for admission and the morbidity of suspension microlaryngeal surgery [21].

This study has its limitations. One is its retrospective nature and second is the limited number of subjects. Another limitation is the lack of objective measure of dyspnea and or OSA such as polysomnography. Nevertheless, this is the first study to highlight the usefulness of office-based laser therapy in treating dyspnea and reducing the risk of OSA in patients with type 3 Reinke's edema. Respiratory symptoms in smokers are invariably attributed to lower airway diseases and not to the upper airway as shown in this study. This information is valuable to primary care physicians and otolaryngologist engaged in the treatment of airway symptoms in smokers, particularly in dysphonic patients.

Conclusion

The risk of OSA in patients with type 3 Reinke's edema is often underestimated. The results of this investigation indicate that a significant percentage of patients with type 3 Reinke's edema have dyspnea and are at moderate to significant risk of having OSA. Office-based blue laser therapy offers a safe and effective treatment for the respiratory symptoms in affected patients. The authors of this manuscript advocate surgical intervention in patients with type 3 Reinke's edema who suffer from dyspnea and/or are at moderate risk of having OSA, in addition to their phonatory complaints.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by PARF, JH, CAZD and AG. The first draft of the manuscript was written by A-LH and Patrick ARF and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials The data that support the findings of this study are available upon request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval The study has been approved by American University of Beirut Institutional Review Board, Approval Number: BIO-2022-0280.

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