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Impact of Platelet-Rich Plasma on Healing of Wound in Vocal Folds

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Patients who presenting with hoarseness mostly show benign vocal folds (VFs) changes which required a combination of conservative and interventional treatment. Scarring during healing of vocal folds can lead to lifelong impairment of the vocal performance and decrease the quality of life. The aim of this study was to compare between the outcomes in healing of VFs wound with Platelet-rich plasma (PRP) and without PRP injection as regard restoration of vocal fold and voice. A total of 40 patients who presented with VFs benign tumor and admitted to surgical removal of tumor. Patients divided into two groups in equal numbers: groups (A) who had operated with sub epithelial injection of PRP, and group (B): who had operated without sub epithelial injection of PRP. All patients were subjected to the following: preoperative and surgical management, and postoperative follow up were evaluated. In our study, there was statistically significant difference between the two studied groups regarding healing (100% in group A and 60% in group B). There was a significant improvement all acoustic parameters and dysphonia in group A compared with group B who not injected with PRP. Injection of PRP for injured vocal folds during surgical benign tumor removal lead to improved wound healing and a fewer scar formation. Also, PRP was act as growth factor causing increased vocal fold regeneration.

Keywords: Vocal fold injury, PRP, Vfsbengin tumor, scars, dysphonia.

INTRODUCTION

Vocal folds (VFs) act by a symmetrical vibrations for production of voice which have ultimate role in different occupations. Unpredicted dysphonia may affect individuals in their jobs and considerably decline their quality of life (Friedrich et al., 2013). Scarring of VFs is the major reason for permanent dysphonia and resulting from trauma or inflammatory injury in layered of VFs structure. VFs scars may leading to pliability loss of VF lamina propria and a depressing changes of VFs viscoelasticity and thus impair vibration of VFs significantly (Graupp et al., 2016). In some cases dealing with VFs wound and scar, significant improvements in the voice have occurred after speech therapy. However, speech therapy alone is unlikely to result in histological improvements in VF scars (Mortensen, 2010; Wang et al., 2013). Injection laryngoplastyis existing a common and appropriate treatment for VFs. The injection materials includs steroids as estradiol or dexamethasone, bovine collagen, autologous collagen, autologous fat have proven due to their reputation for improving voice quality (Sataloff, 2010; Yildiz et al., 2018). Other materials have been injected to completed healing process and soften VF scars as Hyaluronic acid (HA) (Gaston and Thibeault, 2013). However, this effect remains un confirmed and there is no standard modality for the or treatment of VF

wounds with scarring prevention(Kumai,2019).
format references as per journal style(xyz et al.2012).

Other approach of injection biomaterials as polyethylene glycol (PEG) which established biocompatible polymer approved by the US Food and Drug Administration (Karajanagi et al.,2011). Platelet-rich plasma (PRP) referred to as platelet-enriched plasma, platelet-rich concentrate, autologous platelet gel, and platelet releasate. PRP consist of the plasma fraction portion of autologous blood containing a concentrated number of platelets. PRP has mitogenic and chemotactic properties, serves as a clotting and growth factor agonist (Mehta et al., 2008; Lacci et al., 2010). In addition to use in the treatment of chronic skin and soft tissue wound, publications regarding the use of PRP Including periodontal and oralsurgery, maxillofacial surgery and trauma surgery (Nikolidakiset al.,2008; Mishra et al.,2009). Also, Platelet-rich plasma injection to VF wound has been demonstrated as effective on improvement of wound healing using animal models in vivo (Woo et al.,2014; Cobden et al.,2016). As there is currently no definitive regenerative medicineused for treatment for VF wound healing with fibrosis, and biomaterials have become increasingly important research areas within otolaryngology (Kumai, 2019). Therefore, the aim of this study to compare between the outcomes in of VFs wound healing with PRP injection and without PRP injection as regard restoration of vocal fold and voice.

MATERIALS AND METHODS

A comparative prospective study was performed on 40 patients with vocal folds benign tumor were carried out in the otolaryngology department in Zagazig University Hospitals. All Patients were admitted for surgical remove of benign VF lesions after obtaining Institutional Review Board (IRB) approval and patient written informed consent. Patients were divided into two equal groups, Group (A) who had sub-epithelial injection of PRP during operation. Group (B) who hadnot injected with PRP during operation.

Inclusion and Exclusion criteria:

All patients included in this study have proved to clinically diagnosed vocal benign lesions and fit for surgery and general anesthesia. Meanwhile, patients with malignant lesions of vocal folds, history of previous laryngeal operations and patient who contraindicated for general anesthesia were excluded.

I- Preoperative evaluation:

All participants of the study were exposed to the voice assessment protocol applied in our phonetic unit which was done preoperatively passing through two levels:(1) elementary Diagnostic Procedures: which included auditory perceptual assessment of the patient's voice, (2) clinical and additional diagnostic aids : which includes documentation of laryngeal examination by laryngoscope using either flexible nasal-fibro-scope, connected to a camera with aerodynamic measures and acoustic analysis.

Hearing assessment:

Hearing assessmentwas evaluated by Tuning fork tests, Pure tone audiometry (PTA) Speech discrimination score (SDS) and Eustachian tube function (ETF) was assessed by tympanometry. Appropriate masking was performed throughout frequencies (250Hz to 2000Hz). The recordings were done in a sound-treated room to minimize environmental noise, the recorded materials for all patients were rated using the modified GRBAS scale which scaled from (0 to 3) according to severity of dysphonia.

Preparing the platelet rich plasma:

5ml of peripheral venous blood was drawn from the patient after general anesthesia with a 16 or 18 gauge butterfly needle, this blood was kept in a 5 ml plain vacuum tubes, then immediately centrifuged using a tabletop centrifuge for 12 minutes at 3200 rpm. This causes the blood to be separated out into the three layers, the middle layer consisted of PRP.

II - Operative Technique:

Following general anesthesia and oral intubation using the possible smallest size of endotracheal tube which is preferred. After accurate visualization of the glottis, under high magnification using an operative microscope with a 400-mm objective lens (Zeiss, Germany). An incision was made on the upper surface of the vocal fold lateral to the lesion and flap was elevated followed by dissection of the wall of the lesion from the surface mucosa and the vocal ligament, the lesion was removed. Elevation of the flap and dissection of the wall of the lesion from the surface mucosa and the vocal ligament. After, complete removal of the lesion, PRP injected in the sub epithelial layer at the site of lesion excision in group (A).

III. Post operative follow up:

The first follow up one week after operation to cheek any complication. Documentation of laryngeal examination by video laryngoscope and voice assessment protocol applied in our phonetic unit which was done two months after surgery. Subjective assessment of vocal quality parameters were done including: Pitch, Loudness and Presence of hoarseness, straining and breathiness.

Statistical analysis:

Data analyses were performed using SPSS version 17.0 (SPSS Inc, Chicago, IL). Quantitative data were expressed as mean± standard deviation (SD).The Wilcoxon signed-rank test was used to compare continuous variables. P value < 0.05 was considered statistically significant.

RESULTS

This study included forty patients with ages ranging from 33 to 55 years and divided to group (A) who injected with PRP and group (B) who not injected with PRP. There was no statistically significant difference between the two studied groups regard sex of patients (Figure 1). Percentage of males were (45%) in group A and (55%) in group B, while females were (55%) in group A and (45%) in group B.

Concerning type of lesions (including: Polyp, Nodule, Cyst and Rinken edema) among the studied patients, there was no statistically significant difference between both groups. Moreover, there was statistically significant difference between the two studied groups regarding healing. Patient of group (A) were healed completely without scar formation after PRP injection, however, patient of group (B) were healed with 40% scar formation as shown in Table (1).

Infigure 2 showed a statistically significant reduction in average fundamental frequency (AFF.F0) in group (A) which were (185.9±29.2 and169.5±26.1) for pre- and post- intervention versus group (B) which were (195.9±46.5 and 190.1±46.4) for pre- and post- intervention.

Regarding dysphonia shown in figure (3), there was statistically significant improvement in dysphonia post intervention than pre-intervention in group (A). 15% of the patient who injected with PRP and didn't have dysphonia after surgery, 60% of patient had grade I dysphonia and 25% of patient had grade II dysphonia.

Even more, there was statistically significant improvement in dysphonia post-intervention than pre-intervention with (15%) of the group B of patients who not injected with PRP and didn't have dysphonia after surgery ,(55 %) had grade I dysphonia and (30 %) had grade II dysphonia infigure (4).

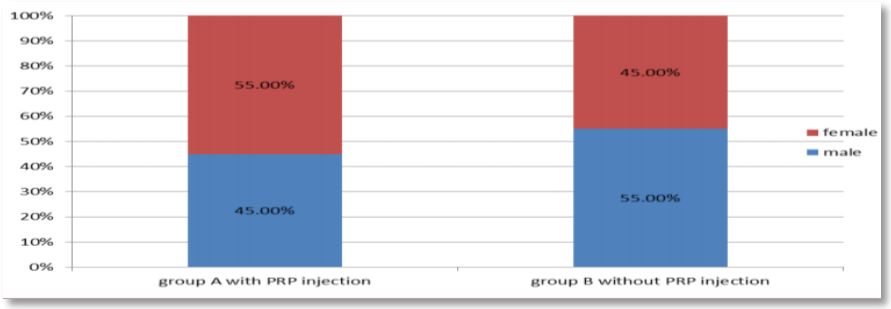

Figure1: Bar chart for sex distribution in the studied groups.

Table 1: Comparing type of lesion and healing in the studied groups

	Group A No(20)	%	Group B No(20)	%	χ^2	p-value
Type of lesion:						
Polyp	9	45.0%	5	25.0%		
Nodule	6	30.0%	7	35.0%	4.9	0.1
Cyst	2	10.0%	7	35.0%		
Rinken edema	3	15.0%	1	5.0%		
Healing:						
Scar	0.0	0.0%	8	40.0%	11.6	**0. 001***
Complete	20	100.0%	12	60.0%		

** Statistically highly significant difference (P ≤ 0.001)

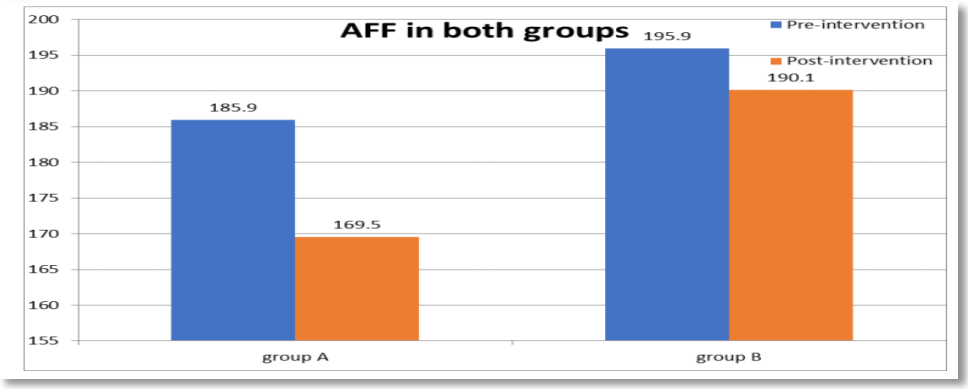

Figure2: Bar chart for comparing AFF before and after surgery in both groups.

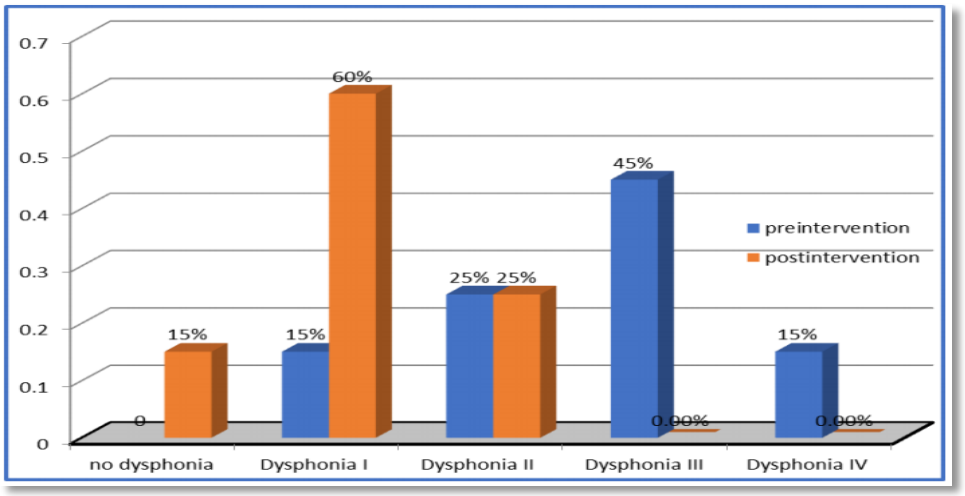

Figure 3: Bar chart for comparing dysphonia grade before and after surgery in group (A).

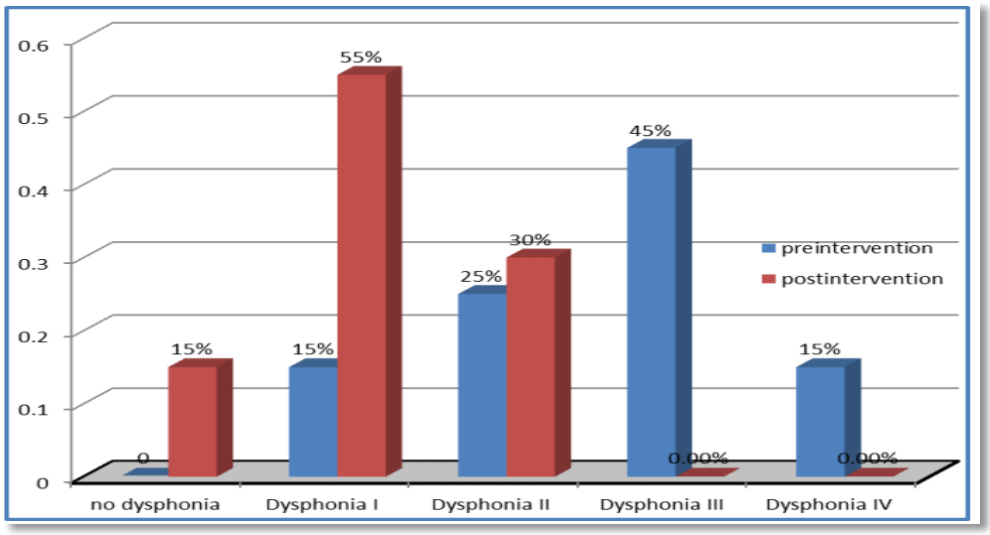

Figure 4: Bar chart for comparing dysphonia grade before and after surgery in group (B).

DISCUSSION

A major challenge in vocal folds lesions for the treating physician are: (1)phonosurgery and the risk of scarring,(2)Diagnosis and treatment of existing scars and Postoperative wound healing (Bohlender,2013). Platelet-rich plasma is a novel material that is being used more frequently in many surgical specialties (Stavrakas et al., 2016).This study was conducted to compared between patients who had operated with VFs sub epithelial injection of PRP (group A) and patients who had operated without sub epithelial injection of PRP (group B) for assessment of healing process after surgical removal of benign VFs tumor and its reliable effect on the restore of voice.

The present study revealed a significant difference between the two studied groups regarding healing with (100.0%) of the 1stgroup were healed without scaring while (60.0%) of the 2nd group were healed without scaring.As regard grades of dysphonia in the 1stgroup (with PRP injection), there was statistically significant improvement in dysphonia grades. Concerning the acoustic parameters in the 1st group (with PRP injection), there was statistically significant reduction in the Average fundamental frequency. AFF(F0),Jitter, Shimmer and dysphonia after surgery with PRP injection and there was statistically significant increase in Harmonic to noise ratio(NHR) HNR and the Maximal phonation time(MPT)post intervention with high improvement post-intervention.

This results was explained by Tang et al.(2015) who recorded that, activated PRP can release several growth factors, including connective tissue growth factor (CTGF), fibroblastic growth factor-2 (FGF-2), bone morphogenetic protein (BMP-2), and transforming growth factor-beta 2 (TGF-β2). These growth factors may play a synergistic action in the cell proliferation in the vocal folds. As well, this results are inagreement with Bless et al.(2010) who previously reviewed various VF scarring animal models in detail, providing a basis for the development of antifibrotic therapies. Obviously, animal models can be used to systematically address scarring issues that cannot be examined in patients (Yamashita et al.,2010).

Moreover, our results are concur with Cobden et al.,(2016) who evaluated that effectiveness of PRP application on scar tissue of acute vocal fold injury. They showed a significant difference between control and study groups for epithelial growth factor receptor ($P < 0.05$).the authors concluded that PRP accelerates epithelization of injured rat vocal folds and useful to prevent scar formation.

Platelet-rich plasma is an autologous concentrate of human platelets in a small volume of plasma containing biologically active factors responsible for hemostasis, synthesis of new connective tissue and revascularization (Sommeling et al., 2013).PRP play a role in host defense mechanism at the wound site by producing signaling proteins that attract macrophages; suppress cytokine release and limit inflammation, improve tissue regeneration, promote new capillary growth and accelerate epithelialization in chronic wounds. PRP also may contain a small number of leukocytes that synthesize interleukins as part of a non-specific immune response (Stavrakas et al., 2016).

Our results are harmonize with Volakakis et al.,(2019) who conducted that, treatment with autologous PRP accelerates wound healing as measured objectively. Compared with conventional treatment, a significantly higher reduction in surface area, diameter, and circumference of the wound was observed by PRP application.

Further studies, preferably larger randomized multicenter, and necessary to confirm the PRP efficacy in wound healing, as well as to define the optimal PRP application method.

CONCLUSION

It appears operatively injected with Platelet-rich plasma (PRP) accelerates wound healing of vocal folds with fewer scar formation. So, PRP has beneficial effects on VFs wound healing.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

AUTHOR CONTRIBUTIONS

All author contributed in all parts of the paper.

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