Intracordal platelet rich plasma injection protocol

Original Article

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Abstract

Introduction: Vocal fold atrophy, scarring and sulcus vocalis are benign pathologies characterized by inadequate remodeling of the lamina propria, affecting vocal fold vibration. The treatment of these conditions is complex and often results in unsatisfactory outcomes, which has led to increasing research into the regenerative potential of biological therapies, such as platelet-rich plasma (PRP). Intracordal injection of this autologous product has proven to be safe and effective in optimizing vocal quality.
Objectives: To propose a protocol for preparation and intracordal injection of PRP, and subsequent evaluation of its safety and efficacy.
Material and Methods: Literature review.
Results: The protocol defines the selection criteria for the target population, describes the PRP preparation and application technique, and the monitoring method after the intervention.
Conclusion: It is important to innovate the treatment of these pathologies in order to optimize vocal quality. Given the promising results of intracordal PRP injection, the implementation of this protocol will allow its systematic integration into clinical practice and the development of scientific research in this area.
Keywords: laryngology; dysphonia; vocal cord; atrophy; groove; scar; injection laryngoplasty; platelet rich plasma

Introduction

Vocal fold atrophy, sulcus, and scarring are benign lesions that are characterized by extracellular matrix deficit and inadequate remodeling at the level of the lamina propria (LP).[1,2] Atrophy is characterized by thinning and bowing of the vocal folds, accompanied by ventricle enlargement due to reduced muscle tone.[1,2] Sulcus is defined as a longitudinal depression along the free edge of the vocal fold, caused by epithelial invagination into the other layers of the LP.[1,3,4] Scar formation results from abnormal deposition of collagen and

fibrous tissue in the LP.[1,5,6] These conditions alter the microarchitecture, viscoelasticity, and vibration properties of the vocal folds, leading to glottic insufficiency, which manifests as dysphonia, vocal fatigue, and vocal tension.[1,2,5,7] The literature supports a sequential therapeutic approach, recommending that speech therapy be first attempted, and when insufficient, complemented by minimally invasive surgical interventions. However, a gold standard method has not yet been established.[4] Surgical approaches are divided into direct techniques, which manipulate the LP to restore vibratory properties of the vocal folds, and indirect techniques, which focus on medialization to correct glottic insufficiency.[4,8] Conventional techniques often yield unsatisfactory and non-durable results with regard to restoring optimal phonation,[2,8–11] prompting increasing exploration of biological therapies,[15,15] including growth factors,[2,14–17] stem cells,[18–20] and platelet-rich plasma (PRP).[7,21-25] PRP is an autologous product obtained by centrifugation of a blood sample, resulting in a high concentration of platelets, growth factors, cytokines, and adhesion molecules.[7,9,21] These bioactive agents exert anti-inflammatory, anti-fibrotic, and regenerative effects on the LP, acting in a paracrine manner on mesenchymal stem cells, endothelial cells, and fibroblasts to promote cell proliferation and migration, angiogenesis, and extracellular matrix synthesis.[7,11–13] The safety and efficacy of this technique in optimizing the short-term vocal quality, measured by a reduction in jitter, shimmer, and the Vocal Handicap Index (VHI), have been demonstrated in several studies[7,11-13,22,25] and confirmed by a systematic review and meta-analysis published in August 2023.[9] No serious adverse effects or significant periprocedural complications have been documented. The reported adverse events included syncope, minor vocal fold hematoma in an anticoagulated patient, transient cough, throat clearing, and odynophagia.[7,11,21,22,25]

Recently, Peak Woo[25] and Georgia Mackay[13] reported for the first time the long-term benefits of intracordal PRP injections on the vocal quality, particularly on the maximum phonation time; Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) classification; VHI; and acoustic parameters. This study aimed to develop a protocol to facilitate the pioneering, systematic integration of PRP into clinical laryngology practice in Portugal.

Materials and methods

This protocol was based on a literature review, with particular emphasis on the method described by Peak Woo.[25] The target population includes patients with vocal fold atrophy, sulcus, or scarring, in whom previous medical or surgical interventions had been ineffective. The protocol describes the initial assessment, including the clinical history, stroboscopic evaluation, and assessment of vocal parameters using universally validated scales. It proposes a plan for monitoring and evaluating the results obtained, as well as therapeutic guidance after administration of PRP.

Results

Clinical protocol

Patient selection

The target population includes patients with vocal fold atrophy, sulcus, or scarring, in whom previous medical or surgical interventions had been ineffective.

Voice appointment

- Collection of demographic and clinical data

Clinical information should be collected at the initial appointment, including age, sex, medical history, current medications, and previous medical or surgical treatment for the vocal pathology.

- Voice assessment:

1. Laryngeal endoscopy with videostroboscopy
2. Auditory-perceptual evaluation: GRBAS scale
3. Aerodynamic analysis: maximum phonation time
4. Acoustic analysis: shimmer, jitter, and harmonic-to-noise ratio

5. Self-assessment questionnaire on the functional impact of dysphonia on the quality of life: VHI.

- Informed consent:
Patients are informed about the off-label use of PRP in laryngology. The informed consent form provides a detailed explanation of PRP preparation and administration, and outlines the potential benefits and adverse effects reported in the literature.

PRP preparation
1. Blood collection: 17 mL of venous blood is collected and placed in tubes containing an anticoagulant solution (e.g., dextrose citrate).

2. Double centrifugation:
- First centrifugation: 100x g for 10 minutes to separate the plasma components according to their densities. Plasma is then transferred to a sterile tube.
- Second centrifugation: 200x g for 15 minutes to concentrate the platelets.

3. PRP extraction
- The top 80% of the supernatant solution (platelet-poor plasma) is discarded.
- The remaining 20% (~1 mL) is collected as PRP.

PRP administration
Monthly administration of three PRP injections.
Bilateral subepithelial injections (0.5 mL per vocal cord), targeting the middle portion of the membranous vocal fold, except in cases of unilateral structural pathology.
The route of administration is selected according to anatomical considerations, patient tolerance, preferences of the patient and/or clinician, and logistical capabilities of the institution.
- Transcervical, endoscopy-guided, 25-G needle
- Transoral, endoscopy-guided, 25-G needle
- Suspended microlaryngoscopy, 25-G needle
After the procedure, the patients are observed for two hours or admitted if outpatient conditions are not met.

Figure 1
Schematic representation of platelet-rich plasma (PRP) preparation

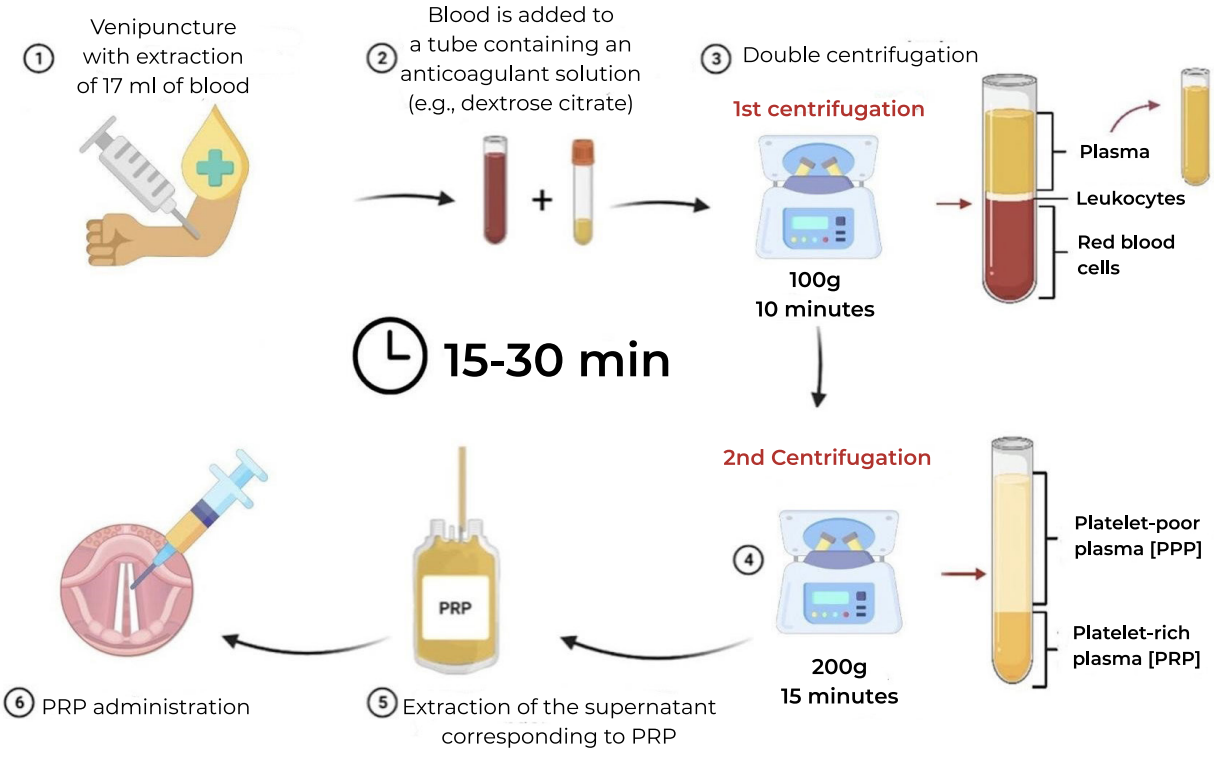
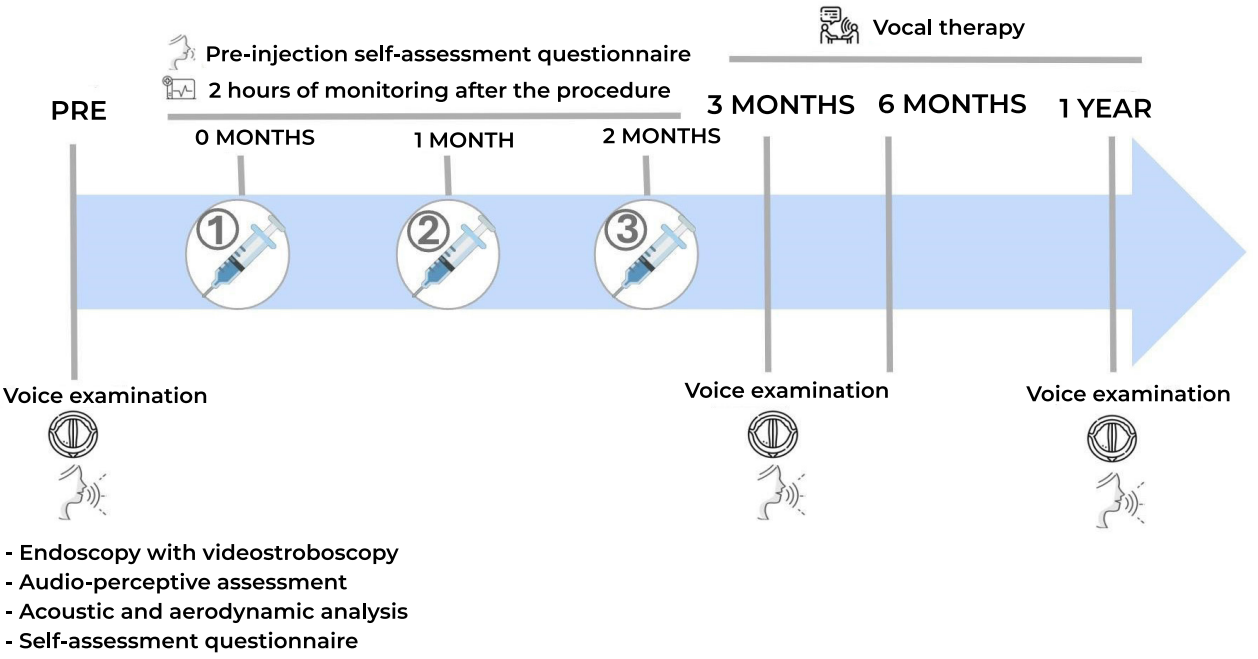


Figure 2
Protocol for administration of platelet-rich plasma (PRP), assessment of results, and post-treatment therapeutic guidance



Evaluation of outcomes

Patients are evaluated three, six, and 12 months after the first PRP injection.

Voice assessment:

1. Laryngeal endoscopy with videostroboscopy
2. Auditory-perceptual evaluation: GRBAS scale
3. Aerodynamic analysis: maximum phonation time
4. Acoustic analysis: shimmer, jitter, and harmonic-to-noise ratio
5. Self-assessment questionnaire on the functional impact of dysphonia on the quality of life: VHI. This questionnaire is administered prior to each PRP injection.

Post-treatment therapeutic guidance: speech therapy sessions are initiated one week after the last PRP injection. This adjuvant therapy aims to correct maladaptive phonatory patterns that cause phonotrauma and may predispose to recurrence of vocal pathology and compromise the effectiveness of PRP injections.

Discussion

The treatment of vocal fold atrophy, sulcus, and scarring remains complex and challenging, as conventional techniques have shown limited effectiveness. This has stimulated growing interest in novel therapies, particularly intracordal PRP injections.[2,4,8–11] This biological product, which is a key component of regenerative medicine, has been widely used in other specialties, including orthopedics, plastic surgery, and ophthalmology, and has gained attention in otorhinolaryngology more recently. Animal models have demonstrated the potential of PRP to promote histological regeneration of the multilayered structure of the vocal folds.[22,23] PRP is an autologous product that can be prepared relatively easily, and no inflammatory reactions or complications have been reported after its injection into vocal cords.[7,11-13,25] Additionally, PRP does not carry the ethical and legislative concerns associated with other biological treatments.[12,13] PRP contributes to the restoration of the viscoelastic and vibratory properties of the vocal folds, improving both the objective and subjective vocal quality outcomes in the

short-term,[7,9,11-13,25] and more recently the long-term.[13,25] Despite these promising findings, the current evidence is limited by the small number of studies and lack of standardization in PRP preparation and administration protocols in laryngology practice.

Conclusion

Given the limited effectiveness of conventional therapeutic interventions for vocal fold atrophy, sulcus, and scarring, there is growing interest in innovative approaches such as intracordal injections of PRP, a biological agent with regenerative and anti-fibrotic properties. Studies have reported promising results, which may represent a paradigm shift in the management of vocal fold pathologies. Nonetheless, further studies are needed to generate more robust results regarding the effectiveness of PRP in treating vocal fold pathologies both in the short- and long-term.

Conflict of Interests

The authors declare that they have no conflict of interest regarding this article.

Data Confidentiality

The authors declare that they followed the protocols of their work in publishing patient data.

Human and animal protection

The authors declare that the procedures followed are in accordance with the regulations established by the directors of the Commission for Clinical Research and Ethics and in accordance with the Declaration of Helsinki of the World Medical Association.

Privacy policy, informed consent and Ethics committee authorization

The authors declare that they have obtained signed consent from the participants and that they have local ethical approval to carry out this work.

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Scientific data availability

There are no publicly available datasets related to this work.

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