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Role of platelet rich plasma in improving quality of life in patients with atrophic rhinitis

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Abstract

Introduction: An atrophy of the nasal mucosa, gradual atrophy of the turbinate supporting bone, excessive enlargement of the nasal chambers, sticky secretion, and dry crusts that form a peculiar fetor are all characteristics of atrophic rhinitis (AR), a chronic debilitating nasal mucosal condition.

Aim of the study: To evaluate the effectiveness of platelet rich plasma (PRP) in improving the quality of life in patients with atrophic rhinitis.

Subjects and Methods: 30 patients with primary atrophic rhinitis attended the ENT outpatient clinics of the Fayoum University Hospital within 18 months. They were divided into two equal groups (A and B), each consisting of 15 patients. Group (A) received a nasal platelet-rich plasma submucosal injection after providing their informed consent, while Group (B) (the control group) received conservative management in the form of irrigation and douches like glucose glycerin nasal drops for six months. The SNOT 25 score was used to evaluate results 1, 2, 3, and 6 months after the intervention.

Results: The PRP group showed a statistically significant difference between the initial score and scores at 1, 2, 3, and 6 months, as the mean initial score was 22.4 (SD = 3.0), while the mean SNOT 25 score after one month was 22.2 (SD = 3.2), after two months was 17.9 (SD = 2.9) after 3 months was 15.3 (SD = 3.8), and finally after 6 months was 12.7 (SD = 4.9), ($P<0.001$). On the other hand, the control group showed no statistically significant difference between the measurements and the baseline measurements.

Conclusion: Through autologous PRP injection, this study offered a novel regenerative approach for atrophic rhinitis treatment that can help atrophic rhinitis patients.

Keywords: Atrophic Rhinitis; Allergic Rhinitis; Platelet-Rich Plasma; Platelet Rich Plasma.

1. Introduction

The symptoms of atrophic rhinitis (AR), a severe chronic nasal mucosal disease with an unknown cause, include nasal mucosal atrophy, loss of the turbinates'

underlying bone, abnormal nasal cavity widening (with paradoxical nasal congestion), viscid secretions, and dry crusts, which give the patient the appearance of a fetus (ozaena) [1]. Coryza foetida, rhinitis atrophicans, atrophic catarrh, rhinitis chronica foetida, and acute necrotizing rhinitis are all terms used to describe AR [2].

It is common in tropical countries like India, China, the Philippines, Greece, Malaysia, Egypt, Central Africa, Latin and South America, Eastern Europe (Poland), Pakistan, the Mediterranean, and Saudi Arabia [3].

Respiratory epithelium metaplasia results in ciliary atrophy and atrophy of the mucosal and submucosal glands, followed by stratified squamous or cuboidal epithelium with or without keratinization. The mucosa dries, turns pale, and secretes thick, viscid, sparse secretions before producing crusts and scabs that are greenish or grayish-yellow in color. Lamina propria displays chronicity and fibrosis [4]. There are two types of atrophic rhinitis; primary and secondary atrophic rhinitis [5, 6].

Treatment for atrophic rhinitis is to moisturize the nasal mucosa, get rid of the nasal crusts, and improve the function of the paranasal sinuses and nasal mucosa [7]. This issue is addressed using a variety of therapeutic approaches, including topical medications, systemic therapy, and surgical procedures [8].

Since there is a high concentration of platelet growth factors in small volumes of plasma that works to provide a "perfect environment" for tissue regeneration and is considered biological therapy, platelet-rich plasma (PRP) is a revolutionary therapeutic technique that was developed in the 1950s and is now used in many fields of medicine [9].

Platelet rich plasma (PRP) is now universally acknowledged as a powerful means for accelerating tissue regeneration and wound healing [10]. Injection and extraction of autologous PRP are not linked to allergic responses or other issues brought on by iso- or hetero-antigens. PRP has recently been used to help individuals with atrophic rhinitis regenerate their nasal mucosa [11, 12].

In our study, we aim to evaluate the effectiveness of PRP in improving the quality of life in patients with atrophic rhinitis.

2. Subjects and methods

2.1. Subjects

In the current randomized clinical trial (RCT), thirty patients with primary atrophic rhinitis attended the ENT outpatient clinics of the Fayoum University Hospital within 18 months.

They were divided into two equal groups (A and B), each group consisting of 15 patients, where:

- Group (A) (Case group): who received a nasal PRP submucosal injection after giving their informed consent.
- Group (B) (control group): who received conservative management through

irrigation and douches like glucose glycerin nasal drops for six months.

Inclusion and exclusion criteria

The patients included in this study were aged between 10 and 60 with primary atrophic rhinitis. Exclusion criteria included patients aged less than 10 years old and patients who had previous nasal surgery.

Primary outcomes

The SNOT-25 score at 1, 2, 3, and 6 months after the intervention in terms of comparison mattered between the two groups.

2.2. Methods

The goal of the procedure was fully described, and all patients provided informed consent. All patients should have the fundamental triad of encrustations, a spacious nose, and a fetus bilaterally. All patients had given a full medical history and had undergone a full clinical examination and endoscopic examination. Before the intervention, all patients were evaluated subjectively using the Sino nasal outcome test (SNOT-25) questionnaire and were asked to use the scale below to indicate how severely the different aspects outlined in the questionnaire impacted them. A nasal platelet-rich plasma injection was given to the group (A) three times: once at zero days, once after a month, and finally after two months. All 30 patients were assessed using the Sino-Nasal Outcome Test-25 (SNOT-25) and endoscopically for color and appearance of nasal mucosa at 1, 2, 3, and 6 months during the follow-up.

The injection was held at the outpatient clinic, under endoscopic control with the following steps:

1. Lidocaine pledges were applied in each nostril for 15 minutes. During that, the PRP was prepared by taking twenty-five milliliters of the patient's blood using a laboratory centrifuge (Heraeus labofuge 200, Germany).
2. 4 ccs of PRP were injected in every side from inside outward at the following sites:
   - Inferior turbinate: two injections (1 cc) at the inferior turbinate along its medial and inferior surfaces.
   - Middle turbinate: one injection (1 cc) in the body of the middle turbinate.
   - The septum: Sub-mucoperichondrial injection (1cc) at the caudal end.
   - The floor: (1cc) was related to the vestibular area.
3. If any bleeding occurs, a pack of ephedrine was placed on the bleeding side for 10 minutes.

PRP preparation

Venipuncture in acid citrate dextrose (ACD) tubes was used to collect whole blood. Blood were not cooled before or during platelet separation. The blood was centrifuged using a 'soft' spin, which allows the blood to be divided into three layers: the bottom RBC layer, the top cellular plasma (plate-let-poor plasma [PPP]) layer, and the buffy coat, which is an intermediate PRP layer. The soft spin lasted 3 minutes. The platelet-containing supernatant plasma was

transferred to another sterile tube (without anticoagulant). To get a platelet concentrate, the tube was centrifuged at a greater speed (a hard spin). PRP was in the lowest third, while platelet-poor plasma was in the top two-thirds (PPP). Platelet pellets developed at the bottom of the tube. After removing the PPP, the platelet pellets were suspended in a little amount of plasma (2 _4 mL) by gently shaking the tube. About 2–2.5 cc of the PRP was put into a sterile tube using a 5-cc syringe. The prepared syringe was immediately transported to the injection site, where the PRP was injected.

2.3. Statistical analysis

The statistical program SPSS version 26 was used to code and input the data. The mean and standard deviation for numerical variables and percentage for categorical categories were used to summarize the data variables. The independent sample t-test for numerical variables and the Chi-square test for categorical variables are used to compare groups. The paired sample t-test was used to compare the SNOT 25 score in both groups at the start and after six months. It is statistically significant if the *P-value* is less than 0.05.

3. Results

Thirty patients were classified into two groups: the case group (A) and another control group (B). Statistical analysis of the age of the patients using an independent sample t-test

showed no significant difference between the two groups, as the mean age in the PRP group is 22.8 (SD = 5.9) and in the control group is 32.1 (SD = 5.7), with *P = 0.876.*

The study group included 12 females and 3 males in each group, which showed no statistical significance in sex distribution (Table 1).

Table 1: Comparison of the two groups regarding age, sex, and initial SNOT score.

Variable		**PRP group**	**Control group**	***P-value***
Age year (Mean±SD)		22.8±5.9	23.1±5.7	0.876
Sex N(%)	Male	3 (20)	3 (20)	>0.999
	Female	12 (80)	12 (80)	
SNOT 25 score, Initial		22.4±3	22.3±2.6	0.949

At one-month assessment, the SNOT 25 score was lower for the PRP group, indicating better functionality (22.2±3.2), than for the control group (22.4± 2.7). At two months' assessment, the SNOT 25 score was lower for the PRP group, indicating better functionality (17.9±2.9), than for the control group (22.2±3.0). At three months of assessments, the SNOT 25 score was lower for the PRP group, indicating better

functionality (15.3±3.8), than for the control group (22.7±3.0). At six months of assessment, the SNOT 25 score was lower for the PRP group, indicating better functionality (12.7±4.9), than for the control group (22.9± 3.1) (Table 2).

Table 2: Comparison of the two groups regarding different SNOT scores.

Variable (Mean±SD)	PRP group	Control group	*P-value*
SNOT 25 score, Initial	22.4±3	22.3±2.6	0.949
SNOT 25 score, 1m	22.2±3.2	22.4±2.7	0.052
SNOT 25 score, 2m	17.9±2.9	22.2±3	<0.001*
SNOT 25 score, 3m	15.3±3.8	22.7±3	<0.001*
SNOT 25 score, 6m	12.7±4.9	22.9±3.1	<0.001*

* Significant.

The comparison of the SNOT 25 score initially and after 1, 2, 3, and 6 months in both groups was done using a paired sample t-test. The PRP group showed a statistically significant difference between the initial score and scores at 1,2,3, and 6 months, as the mean initial score was 22.4 (SD=3.0), while the mean SNOT 25 score after 1 month was 22.2 (SD=3.2) after 2 months was 17.9 (SD=2.9) after 3 months was 15.3 (SD=3.8), and finally, after 6 months was 12.7 (SD=4.9), *P<0.001*. On the other hand, the control group showed no statistically significant difference between any of the measurements and the baseline measurement (Table 3).

Table 3: Comparison of the SNOT 25 score initially and after 1,2,3,6 month.

	Variable	Mean±SD	Mean difference	*P-value*
PRP	SNOT 25 score, Initial	22.4±3	-	-
	SNOT 25 score, 1m	22.2±3.2	0.5	0.001*
	SNOT 25 score, 2m	17.9±2.9	0.8	<0.001*
	SNOT 25 score, 3m	15.3±3.8	1.2	<0.001*
	SNOT 25 score, 6m	12.7±4.9	1.5	<0.001*
Control	SNOT 25 score, Initial	22.3±2.7	-	-
	SNOT 25 score, 1m	22.4±2.7	0.2	0.751
	SNOT 25 score, 2m	22.2±3	0.3	0.685
	SNOT 25 score, 3m	22.7±3	0.4	0.288
	SNOT 25 score, 6m	22.9±3.1	0.5	0.272

* Significant.

4. Discussion

Atrophic rhinitis (AR) is a chronic debilitating nasal mucosal illness characterized by atrophy of the nasal mucosa, gradual atrophy of the turbinate underlying bone, excessive widening of the nasal chambers, and viscous secretion and dry crusts resulting in distinctive fetor (ozaena) [13].

Patients often present with fetal symptoms, such as nasal crusting, anosmia, nasal blockage, nasal discharge, or epistaxis [14].

Primary AR is characterized by slow, cumulative degeneration of the nasal mucosa that develops spontaneously. It is the typical type of the disease, although several infectious agents have been hypothesized as etiologies, as well as other variables such as genetics, hormonal factors, nutritional insufficiency, or autoimmune disorders [4].

Syphilis, lupus, leprosy, rhinoscleroma, chronic sinusitis, a deviated septum, or major nasal surgery can all cause secondary atrophic rhinitis [15].

Different treatment methods have been explored with four basic approaches: decreasing the nasal cavity with various substances and implants, encouraging natural nasal mucosal regeneration, lubricating the nasal mucosa, or enhancing the nasal cavity's vascularity [16].

Nasal irrigation and flushing, glucose-glycerin nasal drops, liquid paraffin, anti-ozaena solution, antibiotics, iron, zinc, protein, vitamin supplements, vasodilators, prostheses, vaccinations, placental extract, or acetylcholine with or without pilocarpine are all used to treat atrophic rhinitis. However, these techniques have different efficacies [16].

Many surgical methods were tried; the Young procedure or its modified form is the most popular surgical therapy for atrophic rhinitis. This procedure aids in the regeneration of healthy nasal mucosa as well as the development of mucus strands. Furthermore, once the nostril is closed, the disease's unpleasant characteristics, such as fetor and crusting, vanish [17–20]. Auto-grafts (cartilage, bone, and fat), as well as biomaterials such as blastopore and silastic, were utilized to reconstruct the patient's defective anatomy [21]. In addition, several injectable materials, like collagen and fat, have been proven to be suitable for restoring structure and nasal function [22].

Plasma concentrations in PRP are greater than platelet concentrations in whole blood. PRP increased factors that influence tissue development, differentiation, and scar repair, such as platelet-derived growth factor, transforming growth factor, fibroblast growth factor, endothelial growth factor, and insulin-like growth factor, which improved wound healing and tissue regeneration [23].

In this study, we investigated PRP injection into the atrophic nasal mucosa, with atrophic rhinitis symptoms during 6 months of follow-up.

A group of 30 patients with atrophic rhinitis was randomized into two cohorts, Group (A) who received the nasal platelet-rich plasma, and the other control group (B) received the traditional treatment (glucose glycerin drops) for six months

Patients in group A improved within two months of PRP injection and further

improvement was noted 6 months after, and this was noted in the endoscopic picture and reflected in the SNOT-25 scores during follow-up.

While in group B there was no improvement obtained at the start of the study and minimal improvement was noticed six months later after traditional treatment.

SNOT-25 scores in group (A) averaged 22 at first before PRP, improving to 12 months later, but in group (B), SNOT-25 scores were 22 with no improvement later.

Our results in comparison with previous studies like Friji *et al.*, 2014 [12], who used platelet-rich plasma in the treatment of atrophic rhinitis in five patients with autologous lipoaspirate administered bilaterally to the inferior, middle turbinate, floor, and septum, with simultaneous injections of platelet-rich plasma into the same regions as a biogenic activator to enhance adipocyte survival and graft absorption decrease. He found all five patients reported that their nasal crusting had disappeared, and their other symptoms had improved six months following the procedure. Also, he found by endoscopic examination that no signs of atrophy, and the normal glistening of the nasal mucosa had returned. Also, he used the Sino nasal outcome test-20 and found that the Sino-Nasal Outcome Test-20 decreased from 36 to 8.

According to Friji *et al.*, 2014 [12], the explanation for that improvement referred to the stimulatory impact of mesenchymal stem cells within the fat graft. However, Friji *et al.*, 2014, study was unable to prove or exclude any alternative non-mesenchymal mechanisms for their findings. On the other side, the main weak points in their study were the limited number of patients and the fact that the findings were not backed up by histopathological examination [12].

Our study proved that using PRP only in the treatment of primary atrophic rhinitis had improved the nasal symptoms in comparison to Friji *et al.,* 2014 [12], who used fat graft and PRP (to exclude mesenchymal stem cell role).

Although secondary atrophic rhinitis was excluded from our study Kim *et al.,* 2021, studied the impact of PRP injection in patients with secondary atrophic rhinitis following rhinoplasty [24].

A total of 22 patients in 2019 and divided into two groups (12 in the PRP group A and 10 in the traditional saline spray group B). Nasal bacterial cultures were collected after PRP was injected bilaterally into the inferior turbinate. Symptoms were assessed using the Nasal Obstruction Symptom Evaluation (NOSE) and the Sino-Nasal Outcome Test-22 (SNOT-22), where nasal mucociliary clearance was assessed using the saccharin transit time (STT). The results were encouraging since the PRP group (group A) showed improvement in symptoms, and NOSE and SNOT-22 scores were significantly decreased. However, no substantial improvement in the nasal symptoms and no obvious changes in scores of NOSES and SNOT-22 were shown in the saline spray group (group B) [24].

Also, the Kim *et al.,* 2021, prospective research shared certain similarities with ours in that it was a comparison of PRP vs. saline

spray and employed the same method, but their assessment included NOSE and STT [24].

This prompted us to look at the clinical image improvement by nasal endoscopy, and with SNOT-25 symptoms, our study showed comparable outcomes as with the adipocyte-derived stem cell dermo fat grafts acquired from Friji *et al.,* 2014 [12] study, and also similar to Kim *et al.,* 2021, study [24].

Conclusion

Through autologous PRP injection, this study offered a novel regenerative approach for atrophic rhinitis treatment that can help atrophic rhinitis patients.

Although the improvement in our study was proved endoscopically and by the nasal symptoms, we suggest further investigations to use histopathological examination and mucociliary clearance using saccharine transient time with a greater number of patients and a longer follow-up to validate these findings.

Ethical considerations

The study was approved by the ethical committee of the faculty of medicine at Fayoum University.

Availability of data and materials

The data sets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Patient consent

Informed written consents for participation were taken and signed by the eligible relatives before recruitment and randomization.

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Conflicts of Interest: All authors declare no conflict of interest.

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