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The impact of platelet-rich plasma enriched nasal pack on postoperative healing after nasal surgeries

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Abstract
Background: Nasal surgeries including turbinectomy and septoplasty are performed to treat chronic obstruction of the nose. The aim of the work was to study the impacts of platelet-rich plasma (PRP) enriched Nasal Pack after Inferior turbinectomy on postoperative healing and tissue recovery.
Methods: This prospective randomized controlled work was performed on 50 individuals who underwent partial bilateral turbinectomy, with or without septal surgery and suffered from nasal obstruction with or without headache. After turbinate reduction, one side was treated with PRP enriched nasal pack and the other side was the control side the pack was enriched with saline.
Results: Pain level in the morning after operation and after pack removal was less in the PRP side compared to the control side and it was significant. The degree of crusting and synechia formation showed, after 1 week: mild crustation and synechia was reported in 25 cases in the test side, and 45 cases in the control side. After 2 weeks: mild crustation and synechia in 5 cases in the test side and control side. After 1-month PRP side is like the control side: absent crustation and synechia was reported in all cases in the test side and control side.
Conclusions: PRP is a promising material, and it was beneficial in the healing process after partial inferior turbinectomy, and it was noted on short term follow up particularly after one week.

Keywords: Platelet-rich plasma, nasal pack, postoperative healing, nasal surgeries

Introduction
Nasal surgeries including turbinectomy and septoplasty are performed to treat chronic obstruction of the nose. The most common causes of chronic nasal obstruction resulting from the enlargement of the inferior turbinate are vasomotor rhinitis and perennial allergic rhinitis. The patients often have bilateral turbinate enlargement, which is attributed to mucosal thickening rather than hypertrophy of the bone structure underneath [1]. Initial medical interventions, such as the administration of antihistamines, topical and systemic steroids, as well as allergen avoidance strategies, are often employed. However, in cases where these interventions remain ineffective, surgical intervention may be recommended [2].
Chronic nasal obstruction often arises from the hypertrophy of the inferior turbinates. Nasal blockage may give rise to several issues, including challenges in nasal respiration and compromised quality of sleep. The presence of these symptoms might potentially have a negative impact on the overall well-being and functioning of individuals, affecting both their mental and physical aspects of life [3, 4].
Multiple surgical methods exist with the purpose of reducing the dimensions of the inferior turbinates. Radiofrequency ablation (RFA), Bilateral partial inferior turbinectomy, and microdebrider-assisted inferior turbinoplasty (MAIT) are the prevalent and extensively researched procedures [5].
Certain patients may have complications during the healing process of nasal wounds following surgery, which may have a negative impact on their quality of life. These complications include discomfort, the formation of crusts, bleeding, and the development of synechia [6].
Platelets are widely recognized for their crucial function in the process of hemostasis. However, it is noteworthy that platelets also play a significant part in the beginning and

control of wound healing. This crucial activity involves the release and modulation of a wide array of cytokines, growth factors, and other bioactive molecules [7, 8].

Platelets possess a recognized role in the process of haemostasis, but they also have the ability to produce several chemicals that facilitate tissue healing, angiogenesis, and inflammation [9].

The presence of growth factors in platelets has been seen to enhance the rate of recovery in injured tissues [10].

Platelet-rich plasma (PRP) is a constituent of plasma that is acquired by the process of centrifugation of whole blood, resulting in a concentration of platelets that is roughly five times more than that seen in regular blood. The concentration of PRP may exhibit variability based on the centrifugation speeds and durations used during its preparation [11].

The utilization of PRP in clinical settings has been a longstanding practice to exploit this particular situation. Currently, there is a widespread utilization of PRP in several domains of medical therapy. For instance, this technology is utilized in many surgical procedures such as (Orthopaedic operations, maxillofacial attempts, and flap shifting operations, etc.), additionally, it is utilized in the treatment of chronic wounds, ulcers, and burns [10].

While several studies have shown the beneficial impact of PRP on wound healing, our literature review has revealed an insufficient number of prospective controlled trials investigating the usage of PRP in nasal surgeries [6].

The purpose of this work was to evaluate the impacts of PRP enriched Nasal Pack after Inferior turbinectomy on postoperative healing and tissue recovery.

Patients and Methods

This prospective randomized controlled work was performed on 50 individuals, aged between 18 and 50 years old, who underwent partial bilateral turbinectomy, with or without septal surgery and suffered from nasal obstruction with or without headache. The study was done from March 2022 till August 2022, after the ethic committee of Tanta university hospital. The participants have provided written informed permission.

Criteria for exclusion were patients with associated inflammatory conditions as acute rhino sinusitis, chronic rhino sinusitis with or without polyposis, nasal masses, previous nasal surgery and with diabetes mellitus (DM), uncontrolled hypertension and any bleeding disorder.

All patients in this study were subjected to history taking, general examination, otorhinolaryngological clinical assessment, anterior rhinoscopy and rigid endoscopy, computer tomography (CT) scans of the nose and paranasal sinuses, laboratory tests [full blood count, clotting time, bleeding time, prothrombin time and activity, partial thromboplastin time, international normalized ratio (INR)].

Partial inferior turbinectomy was done under general anesthesia using classical cold steel method with or without bipolar for hemostasis. Following the completion of the surgical procedure, merocel packs were inserted into both nasal cavities; in one side, merocel pack was soaked and inflated with saline (control side) left side in the other side, it was soaked with 5ml PRP (test side) right side.

Platelet-rich plasma preparation

Throughout the induction of anaesthesia, a volume of 25 milliliters of autologous venous blood was collected from the patient. This blood sample was then processed in a laboratory centrifuge throughout the surgical procedure. The modified curasan method was used to prepare PRP. Throughout the anesthetic induction, a total volume of 25 mL of blood was intravenously extracted from patients. This blood was then gathered in a sterile vacuum tube that was coated with an anticoagulant solution including citric acid and dextrose. Subsequently, the obtained blood samples were processed in a laboratory centrifuge throughout the surgical procedure. A centrifuge equipment that operates automatically was utilized to extract PRP at a rotational speed of 1300 rpm for a duration of 10 minutes. Following the process of centrifugation, three distinct layers were observed: an upper layer consisting of straw-colored fluid with a low concentration of platelets, referred to as platelet-poor plasma; a middle layer known as the buffy coat, which exhibited a high concentration of platelets; and a lower layer characterized by a high concentration of red blood cells.

The plasma of a straw-like color was obtained, along with the buffy coat and 1 mL of the layer containing red blood cells. The sample underwent centrifugation at a speed of 2000 rpm for 10 minutes. The PRP was acquired as a red button located at the base of the test tube. The specimen was obtained using a pasteur pipette and thereafter placed into a sterile tube. The platelet-poor plasma was discarded. The precipitated material (PRP) obtained during the second centrifugation step was carefully transferred into a sterile tube. To initiate the activation process, a volume of 0.5 mL of calcium chloride was introduced into the PRP. The patients received equal amounts of either PRP or saline, administered using a sterile 2.5 mL dental injection with a 20 G needle, so order to activate the merocel packs on both sides. The administration of autologous PRP, which was produced via centrifugation and delivered through the merocel pack, was conducted for a duration of up to three hours. Hence, the preservation of the efficacy of PRP was seen [12].

Postoperative

Packs were removed 48 hrs after surgery. Then, Patients were followed one week, two weeks and after one month by rigid endoscopy and anterior endoscopy.

Outcome measures

The study examined the pain levels experienced during the insertion of nasal packs and the subsequent discomfort related with their withdrawal. Participants were instructed to document the intensity of pain encountered using a linear numerical scale, ranging from 0 to 10. A score of 0 indicated the absence of any discomfort, while a score of 10 indicated the most severe agony possible. The scores were recorded at two distinct time points: initially in the morning following the surgical procedure, and subsequently following the removing of the pack.

The management of hemorrhage during the presence of the packs and the extent of hemorrhage subsequent to their removal. The evidence of bleeding was documented with a grading system that included four categories: no bleeding (graded as 0), bleeding lasting for a duration of less than three minutes (graded as 1), bleeding that subsided with the use of ice packs (graded as 2), and bleeding that necessitated repacking (graded as 3).

Additional challenges, such as the removal of packs being difficult or the fragmentation of packs, were also observed. Endoscopic examination of the nasal cavities was conducted at intervals of 1, 2, and 4 weeks in order to evaluate the extent of crusting and synechia development. Each of the aforementioned observations was assigned a numerical

value based on the following criteria: absence was denoted as 0, mild was denoted as 1, and severe was denoted as 2. The presence or absence of synechia formation was documented.

Results

Fifty patients (10 male and 40 female) who underwent partial inferior turbinectomy alone or with septoplasty, aged from 18-50 years were included in this study. In each participant, PRP was utilized in one side "test side" and other side was utilized as a control. The test side was the right side in all patients; the control side was the left side. 10 patients underwent partial turbinectomy alone and 40 patients underwent partial turbinectomy with septoplasty.

Table 1: Distribution of the studied cases according to demographic data and operation (n = 50)

		No.	%
Age (years)		32.28 ± 10.20	
Sex	Male	10	20.0
	Female	40	80.0
Operation	Turbinectomy with septoplasty	40	80.0
	Turbinectomy	10	20.0

Data are presented as mean ± SD or number (%).

Pain level in the morning after operation was fewer in the PRP side compared to the control side and it was significant (*p*-value < 0.001). Pain level in the morning after pack removal is less in the test side than the control side and it was significant (*p*-value < 0.001). Table 2

Table 2: Comparison between test side and control side according to pain score

Pain	Test side (n= 50)	Control side (n= 50)	Z	P
In the morning after operation	6.48±1.15	8.32±1.25	5.919*	<0.001*
In the morning after pack removal	3.32±1.04	4.54±1.22	5.907*	<0.001*
$^{Z}p_1$	<0.001*	<0.001*		

Data are presented as mean ± SD or number (%). Z: Wilcoxon signed ranks test, p: p value for comparing between test side and control side, p1: p value for comparing between the morning after operation and the morning after pack removal, *: Statistically significant at p ≤ 0.05.

Bleeding while the pack *in situ* is less in the test side, no bleeding was seen in 18 individuals in the test side while 0 cases in the control side. Bleeding less than 3 minutes was seen in 30 cases in the test side while 45 cases in the control side. Bleeding that settled with ice packs in 2 cases in the test side and 5 cases in the control side. Bleeding while removing the pack, no bleeding was seen in 35 individuals in the test side while 0 cases in the control side, Bleeding fewer than 3 minutes was seen in 15 cases in the test side while 50 cases in the control side. Table 3

Table 3: Comparison between test side and control side according to Bleeding

Bleeding	Test side (n= 50)		Control side (n= 50)		Test of sig.	P
	No.	%	No.	%		
While the pack *in situ*						
No bleeding	18	36.0	0	0.0	MH= 10.500*	<0.001*
Less than 3 minutes	30	60.0	45	90.0		
Settled with ice packs	2	4.0	5	10.0		
While removing the pack						
No bleeding	35	70.0	0	0.0	McN	<0.001*
Less than 3 minutes	15	30.0	50	100.0		
Settled with ice packs	0	0.0	0	0.0		
p_1	$^{MH}p_1$=0.004*		$^{McN}p_1$=0.063			

Data are presented as number (%). McN: McNemar test. MH: Marginal Homogeneity Test, p: p value for comparing between test side and control side, p_1: p value for comparing between whiles the pack *in situ* and while removing the pack, *: Statistically significant at $p \leq 0.05$.

After 1 week: mild crustation and synechia was reported in 25 cases in the test side, and 45 cases in the control side. After 2 weeks the PRP side is like control side: mild crustation and synechia in 5 cases in the test side and control side. After 1-month PRP side is like the control side: absent crustation and synechia was reported in all cases in the test side and control side. Table 4

Table 4: Comparison between the different periods according to degree of crustation and synechia (endoscopic)

Degree of crustation and synechia (Endoscopic)	After 1 week		After 2 weeks		After 1 month		P
	No.	%	No.	%	No.	%	
Test side							
Absent	25	50.0	45	90.0	50	10.0	<0.001*
Mild	25	50.0	5	10.0	0	0.0	
Sig. bet. periods	p_1<0.001*, p_2<0.001*, p_3=0.221						
Control side							
Absent	5	10.0	45	90.0	50	100.0	<0.001*
Mild	45	90.0	5	10.0	0	0.0	
Sig. bet. periods	p_1<0.001*, p_2<0.001*, p_3=0.361						

Data are presented as number (%). Sig. bet. Periods was done using Post Hoc Test (Dunn's), p: p value for comparing between the studied periods, p1: p value for comparing between after 1 week and after 2 weeks, p2: p value for comparing between after 1 week and after 1 month, p3: p value for comparing between After 2 weeks and after 1 month, *: Statistically significant at $p \leq 0.05$.

Discussion

PRP may be recognized as an autologous non-immunogenic therapeutic approach that facilitates healing. It is characterized by a substantial amount of growth factors (GFs) and cytokines. It assumes significant functions in diverse phases of regeneration and repair of tissues. PRP is a component of whole blood that is enriched with concentrated GFs and proteins [13, 14].

The findings of our study indicate that the use of PRP had a positive impact on the reduction of post-operative discomfort and bleeding.

PRP has been widely recognized as a well-established therapeutic intervention that yields favorable results for a range of clinical problems. Nevertheless, the use of this technique in the field of ENT remains infrequent, and further research is required to explore its potential applications [15]. Despite the limited number of research examining the use of PRP in nasal surgeries. Limited research has shown comparable findings. Research was conducted to examine the therapeutic effects of PRP when administered to the nasal passages subsequent to endoscopic sinus surgeries. A total of 12 subjects were included in the trial, and their progress was monitored for a duration of 6 months. The findings of the research indicate that PRP shown positive effects on healing of wounds in nasal surgeries and may have potential applications in endoscopic sinus surgeries. However, it is important to note that the study had a very restricted sample size [16].

Contrary to the findings of our investigation, the study conducted by Ugur Yildirim *et al*. similarly observed favorable outcomes of PRP on the mucosa of the nose. Based on the findings of their study, the administration of PRP injections to the nasal mucosa affected by injury shown notable benefits in terms of lowering inflammation, softening mucus, and minimizing the occurrence of synechia. Hence, the administration of submucosal PRP injections following endonasal operations may be regarded as an efficacious intervention for preserving nasal physiology [17].

In a study conducted by Salah el din and Hussin [18], a cohort of 30 individuals was subjected to the administration of PRP injections into the inferior turbinates subsequent to submucosal diathermy. The group of recipients who received PRP treatment shown significant enhancements in crusting, bleeding, and mucociliary clearance when contrasted to the control group, which was treated with saline solution (n=30).

The study conducted by Kuzucu *et al*. [19] examined the impact of PRP on the life quality of individuals who underwent endonasal surgeries. Postoperatively, a group of 25 individuals received Merocel nasal packs combined with PRP, whereas another group of 25 individuals received nasal packs soaked in saline solution. The administration of PRP was shown to speeds up the process of wound healing, resulting in quicker healing for patients during the first postoperative period. This accelerated healing was particularly evident in the mucosa of the nasal septum and concha. Additionally, patients reported a reduced number of complaints during this recovery period.

In a study conducted by Rice [20], the application of PRP was administered to one nasal passage, while normal saline was treated to the other nasal passage in a group of 13 volunteers. The findings of this study indicated that there were no statistically substantial variations seen between the two treatments. Nevertheless, it is probable that PRP may have influenced the adjacent nasal passage via systemic absorption. However, the research population in this particular investigation was also restricted in size.

In a comparable manner, Pomerantz and Dutton [16] conducted an assessment on the life quality of a group of 16 individuals who had PRP packing following endoscopic sinus surgeries. And were contrasted with data acquired retrospectively from an additional group of 16 control individuals who received conventional packing. The findings of their study demonstrated a greater degree of improvement in the PRP group. The lack of statistical significance in the variation between the groups was attributed to the limited sample size.

In their study, Friji *et al*. [21] described an approach aimed at alleviating atrophic rhinitis by the autologous transplantation of adipose tissue and PRP. A total of 5 participants had a procedure in which autologous lipoaspirate was administered to both nasal cavities, targeting particular areas such as the inferior and middle turbinates, floor, and septum. The administration of PRP was performed in the same anatomical regions. Each of the 5 participants noticed an improvement in symptoms, characterized by the complete resolution of nasal crusting. The clinical assessment revealed the existence of nasal mucosa that seemed glistening, with no indications of tissue atrophy.

The healing effects of PRP following vocal-fold stripping were assessed by Woo *et al*. [22] in a study conducted on rabbits. The results of the morphological examination indicated a reduction in the presence of granulation tissues, while the histology results revealed a well-organized deposition of collagen on the side that received the PRP injection.

The study conducted by Sidman *et al*. [23] examined the impact of administering PRP to the tonsillar fossae on the outcomes of tonsillectomy in a cohort including 70 children, with 35 children assigned to the group receiving therapy and 35 children assigned to the control group. No statistically substantial variation was observed regarding pain levels, recovery duration, or frequency of post-operative clinic visits among individuals who had PRP therapy. The authors postulated that the duration of PRP retention might have been inadequate to provide therapeutic effects on tissue repair. Additionally, the source of post-tonsillectomy discomfort may be attributed to the inflammatory muscles under the surface and the healing wound's surrounding mucosa. It is improbable that the injection of PRP would have an impact on this aspect.

Platelet concentrates initially appeared in the field of transfusion medicine for the purpose of managing and preventing hemorrhage resulting from severe thrombocytopenia. This condition is often associated with medullary aplasia, acute leukemia, or substantial blood loss throughout prolonged surgical procedures. The platelet concentrates often used for transfusion purposes has been identified as PRP [24].

PRP is a component obtained from an individual's own blood, characterized by elevated levels of platelets. These platelets are rich in various GFs, including platelet-derived GF, transforming growth factor-beta, vascular endothelial GF, and hepatocyte GF. These GFs are widely recognized for their significant contribution to the process of healing of tissues [25].

PRP has many notable benefits. Firstly, it is derived from the patient's own blood, which makes it autologous and biocompatible, so ensuring intrinsic safety. Secondly, PRP is rich in growth factors that facilitate the healing process of damaged tissues. Lastly, when administered *in vivo*, PRP produces a fibrin scaffold that promotes cell migration and facilitates the development of new matrix structures [26, 27].

There are other factors that have been used to hasten healing after nasal surgeries such as hyaluronic acid and growth factors.

HA plays a significant role in the process of healing occurring in the upper airway. The administration of HA subsequent to nasal operations was seen to effectively inhibit significant crust development in the first week of the healing process, reduce adhesions, minimize mucosal edema, and enhance regeneration of mucosa. According to Laurent *et al*. [28], the application of hyaluronic acid packing combined with absorbable gel inside a sponge in human subjects was seen to be linked to a reduced presence of fibrous connective tissue in the middle ear, in comparison to the employment of gelat in sponge alone.

The application of hyaluronic acid subsequent to nasal operations was seen as successfully minimizing the occurrence of substantial crust development within the initial week of the healing process, while also enhancing subjective evaluations of the healing progress [29].

GFs are a category of chemical signaling molecules that elicit cellular growth. The typical fluid involved in the process of wound recovery contains a significant quantity of growth elements. A diverse range of GFs is implicated in the preservation and restoration of nasal mucosa [30].

According to the findings existed in our work we can come to the conclusion that platelet-rich plasma (PRP) enriched nasal pack applied immediately after partial inferior turbinectomy has an effective role in accelerating the healing process and so improving post-operative pain and to some extent decreasing the incidence of bleeding and decreasing crustation and synechia formation.

Our study, supported by literature and search results revealed that PRP is a product that is seen to be entirely safe, since it is carefully manufactured via the process of collecting and concentrating the individual's own blood, to accelerate the healing process after partial inferior turbinectomy.

Limitations of the study where the sample size was relatively small, our study was done in a single center, The period of follow up was relatively short and PRP should be injected in the turbinate itself.

Conclusions

PRP is a promising material, and it was beneficial in the healing process after partial inferior turbinectomy, and it was noted on short term follow up particularly after one week.

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