

# Role of Platelet Rich Plasma in Mucosal Healing After Nasal Surgeries

Original  
Article

Ahmed Adel Sadek<sup>1</sup>, Mostafa Sayed Hammad<sup>1</sup>, Mostafa Esmael Hassan<sup>1</sup>, Zaki Mohamed Zaki<sup>2</sup> and Mostafa Nasr Zayed<sup>1</sup>

<sup>1</sup>Department of otorhinolaryngology, Faculty of Medicine, Minia University, Minia, Egypt.

<sup>2</sup>Department of Clinical pathology, Faculty of Medicine, Minia University, Minia, Egypt

## ABSTRACT

**Aim:** To Demonstrate Role Of Platelet Rich Plasma In Mucosal Healing After Nasal Surgeries.

**Patients and Methods:** This prospective study was conducted at Otolaryngology, Head and Neck surgery department, The study was approved by the Institutional Review Board at Minia University. During the period from 2021 to 2022, we selected, operated, and followed up 200 patients who had bilateral symmetrical nasal surgery. The study participants were recruited from patients with nasal disease attending outpatient clinic and required nasal surgery. The patients were randomly classified into two groups, with 100 patients in each group.

**Results:** Autologous PRP application accelerates mucosal healing after nasal surgeries. This study included 200 subjects divided into two groups

There was a significant difference in the occurrence of synechia between group 1 (study group) and group 2 (control group) ( $p=0.034$ ). In study group synechia occurred in 8 patients it was mild and relieved by repeated packing, while in control group synechia occurred in 14 and was more length and needed excision under local anesthesia with repeated packing.

**Conclusion:** In conclusion, prp is a simple and effective method, and application of prp mucosal wound can be healed faster in early period after nasal surgeries. It also decrease postoperative early period of pain, bleeding and synechia that enhance the quality of life for patient after nasal surgery.

**Key Words:** Bleeding, pain, platelet rich plasma, synechia, wound healing, .

**Received:** 18 June 2022, **Accepted:** 30 July 2022

**Corresponding Author:** Ahmed Adel Sadek, Department of otorhinolaryngology, Faculty of Medicine, Minia University, Minia, Egypt, **Tel.:** +20 10184 24884, **E-mail:** ahmeda.sadik3030@gmail.com

**ISSN:** 2090-0740, 2022

## INTRODUCTION

Platelet-rich plasma (PRP) is the autologous concentration of a large number of platelets which is obtained by centrifugation of autologous blood in a small volume of autologous plasma<sup>[1]</sup>.

In 1970 PRP was developed and was first used in cardiothoracic by Ferrari in Italy in 1987, in the mid-1990 PRP therapy began gaining popularity and has been applied at many different medical fields such as pain management, cosmetic surgery, sports medicine and dentistry<sup>[2]</sup>.

PRP is thought to work via degranulation of granules in platelets and thought to speed the healing by collagen synthesis, increase cellular proliferation and matrix formation as it contains number of growth factors believed to be influential in early wound healing<sup>[3]</sup>.

Chronic rhinosinusitis (CRS) is an inflammation that lasts more than 12 weeks, this inflammation occurs in the mucosa that covers the nasal sinuses and the surrounding area<sup>[3]</sup>.

Clinical signs of CRS include nasal obstruction, rhinorrhea, postnasal discharges, facial fullness, hyposmia or anosmia, fatigue, headache, toothache, cough, and overpressure in the ear. Without management, it can lead to dangerous complications such as periosteal cellulitis, abscess, and bowler's eye<sup>[5]</sup>.

In general, treatment for chronic sinusitis is based on three rules: reducing mucosal inflammation, decrease the flow of fluid within the sinuses and holding the growth of bacteria. Based on current guidelines, the main pharmacotherapeutic approaches are antibiotics and glucocorticosteroids<sup>[4]</sup>.

Although, these approaches have failed many times, the patient in the following cases should be referred to an otolaryngologist for consideration of sinus surgery: adult nasal polyposis, aspirin-exacerbated respiratory disease, allergic fungal rhinosinusitis, comorbid asthma, and symptomatic patients in whom maximal medical therapy has failed.

Generally, in endoscopic sinus surgery the most important aims are as follow: decrease the recurrence and severity of sinus infections; enhance the symptoms of sinusitis; improving the airflow through nasal passages; and improve the sense of smell of the patient. The recurrence of the disease in CRS is an important challenge and the need for re-surgery<sup>[5]</sup>.

To avoid the recurrence of sinusitis and revision surgery, the following actions have been proposed to avoid return of sinusitis and revision surgery: antibiotics; long-time low-dose antibiotics; longtime low-dose nasal steroids; and unrelated medications such as antihistamine desensitization, antileukotrienes and platelet-rich plasma (PRP)<sup>[6]</sup>.

**PATIENTS AND METHODS**

This prospective study was conducted at Otolaryngology, Head and Neck surgery department, Minia, Egypt. The study was approved by the Institutional Review Board at Minia University. During the period from 2021 to 2022, we selected, operated, and followed up 200 patients who had fess operation for all patients.

The study participants were recruited from patients with nasal disease attending outpatient clinic and required nasal surgery. The patients were randomly classified into two groups, with 100 patients in each group.

**Group A (study group):** who had PRP instilled at the end of the nasal surgery.

**Group B (control group):** who didn't have PRP instilled at the end of nasal surgery.

During induction of anesthetic agents and first steps of nasal operation and under complete sterile technique, 10 ml of peripheral blood (venous) was taken from the patient with a 10 ml syringe to evade damage and irritation of platelets; then collected blood was kept in a 5 ml plain vacuum tubes.

Using a tabletop centrifuge machine the tubes were immediately centrifuged and finally the temperature of the centrifugation was kept at 20° C to 24° C. Then the blood was discreted into the three layers owing to the density of its inner contents: red blood cells formed the bottom layer , PRP formed middle layer (about 1.5 ml3), which is formed of platelets and white blood cells (WBCs; buffy coat) that could be easily obtained, and platelet poor plasma formed the top layer.

**Inclusion criteria**

**1. age of patient 18-60 years**

all of outpatients did not have previous nasal surgery with normal nasopharyngeal examination.

**Exclusion criteria**

- 1-Patients refusing the research procedure.
- 2- Patients who had previous nasal surgery.
- 3- Patients with chronic illness as DM.
- 4- Medical unfit patients.

At the end of each operation prp was sprayed on the merocele and the nose was packed by it for 48 hours and Patients were followed up for one month post operative.

**RESULTS**

This study included 200 subjects divided into two groups: group A which is the study group including 100 subjects and group B which is the control group also including 100 subjects. (Table 1) presents the demographic data of the subjects in each group. In group A the mean age of subjects is 33.8±12.1 years. There are 46 males and 54 females. While in group B the mean age of subjects is 33.85±12.13 years. There are 44 males and 56 females.

**Table 1:** demographic data

Variables	Group A	Group B	p-value
	N=100	N=100	
Age: Mean ±SD	33.8±12.1	33.85±12.13	0.988
Sex:			
Males	46(46%)	44(44%)	0.978
Females	54(54%)	56(56%)	

1- The difference in post-operative pain by visual analogue score between group A and group B:

The statistical results of the patients according to pain scores are shown in Table 2. The VAS score was 4.68±0.88 (mean ± SD) in the study group in the first week and was found to be 7.04±0.86 control group (Table 2). (p<0.001).

**Table 2:** The difference in post-operative pain by visual analogue score between group A and group B 1<sup>st</sup> week

	Group A	Group B	p-value
	N=100	N=100	
Mean ±SD	4.68±0.88	7.04±0.86	<0.001

In the 3<sup>rd</sup> week test, the result was found to be 0.49 ± 0.940 in the study group and 2.37 ± 1.36 in the control group. A statistically significant difference was found between the 3<sup>rd</sup> and 1<sup>st</sup> weeks in both groups (p < 0.05) (Table 3).

**Table 3:** The difference in post-operative pain by visual analogue score between group A and group B 3<sup>rd</sup> week

	Group A	Group B	p-value
	N=100	N=100	
Mean ±SD	0.49 ± 0.940	2.37 ± 1.36	p < 0.05

2- The difference in wound healing duration between group A and group B (Table 4):

There was a significant difference in mean of wound healing duration in days between group A and group B , mean ( $5\pm 0.77$  vs  $7.47\pm 1.10$  respectively) ( $p < 0.001$ ). The mucosal healing was completed within 5 to 6 days post operative, while without using PRP mucosal healing was completed within 7 to 9 days post operative.

**Table 4:** The difference in wound healing duration between group A and group B

	Group A	Group B	<i>p-value</i>
	N=100	N=100	
Mean $\pm$ SD	$5\pm 0.77$	$7.47\pm 1.10$	$< 0.001$

3- The difference in post-operative bleeding between group A and group B (Table 5):

When we compared difference in post-operative bleeding between group A and group B after the removal of the nasal merocele pack and within 2 weeks post operative follow up, we found that in the PRP group bleeding was observed in 3 patients, and no bleeding was observed in 97 patients while in control group bleeding was observed in 12 patients and no bleeding was observed in 88 patients.

There was significant difference in the occurrence of bleeding between group A and group B ( $p = 0.016$ ).

**Table 5:** The difference in post-operative bleeding between group A and group B

		Group A	Group B	<i>p-value</i>
		N=100	N=100	
bleeding	No	97(97%)	88(88%)	0.016
	Yes	3(3%)	12(12%)	

4- The difference in post-operative synechia between group A and group B (Table 6):

There was a significant difference in the occurrence of synechia between group A and group B ( $p = 0.034$ ).

**Table 6:** The difference in post-operative synechia between group A and group B

		Group A	Group B	<i>p-value</i>
		N=100	N=100	
synechia	No	92(92%)	86(86%)	0.034
	Yes	8(8%)	14(14%)	

## DISCUSSION

Chronic rhinosinusitis is a chronic inflammation of mucosa of sinuses and nasal cavities and the symptoms persist more than three months , without significant improvement, inspite of medical treatment as systemic antibiotic, antihistaminic and local nasal steroid.

The diagnostic criteria of CRS include symptoms as nasal obstruction, nasal discharge, and facial pain, also hyposmia or anosmia, headache, chronic cough, and fatigue may be present. Examination by endoscope show discharge ,mucopurulent or purulent, on maxillary sinus ostium and osteomeatal complex. Nasal polyps may be found in mucosa of sinuses or middle meatus. CT nose and paranasal sinuses showing total or partial opacification or inflammation of one affected sinuse or more of the paranasal sinuses<sup>[7, 8]</sup>.

Chronic rhinosinusitis is usually associated with presence of nasal polyps or without nasal polyps(CRSwNP) and CRS (CRSsNP)<sup>[9]</sup>.

The pathogenesis of CRS is controversial. The inflammatory process begins due to interaction between allergens, fungi, virus, bacteria, or inflammatory toxins with host environment.

Defects in the normal functioning of the epithelial barrier as the loss of integrity of the barrier, reduction of the expression of antimicrobial products and colonization which occurred by fungi and bacteria, have a significant effect on chronic inflammation.

The increase in inflammatory cytokines , thymic stromal lymphopoietin and chemokine is the character of the chronic inflammation, by which the chronic inflammatory process is initiated.

Thus, collection of the immune cells, including mast cells, eosinophils, group 2 innate lymphoid cells , and lymphocytes in the chronic inflammatory response that leads to formation nasal polyps<sup>[10]</sup>.

To date, different treatments have been developed to recover CRS. The intranasal steroids and nasal saline irrigation is the most effective nonsurgical treatment. There are incompetent data on using oral steroid in CRS without nasal polyposis. Topical antibiotics do not show any benefit in CRS without nasal polyps.

The treatment by long-term antibiotics for 12 consecutive weeks have shown possible therapeutic response however, there is interest for development of antibiotic resistant bacteria with subsequent infections.

Functioning endoscopic sinus surgery in CRS is safe and effective surgery when medical treatment has failed and in the patients used long-term maintenance medical therapy<sup>[11,12]</sup>.

The high recurrence rate of FESS as recurrence of rhinosinusitis symptoms and nasal polyposis ,was noticed in several patients post operative. To decrease the recurrence rate ,in our study we aimed to use PRP which is characterized by its anti-inflammatory mechanism that reduce the number of FESS revisions and decrease resistance to antibiotics.

Platelet-rich plasma formed of healing factors and multiple growth factors like vascular endothelial growth factor, transforming growth factor and platelet derived growth factor.

Activated platelets release this factors which that can be controlled by a variety of stimulants such as collagen, calcium chloride, adenosine 5cdiphosphat or thrombin.

PRP also contains fibrinogen and a number of viscid glycoproteins that support cell migration antibacterial activity, by increasing the local concentration of antibiotic proteins and white blood cells , resulting in the use of products in postoperative patients, as an additive to standard therapy that aim to prevent infection.

PRP has an dynamic role in proliferation and differentiation of myofibroblasts and human dermal fibroblasts , which accelerates wound healing. According to these properties, PRP has been used in different fields of surgery such as ophthalmology, orthopedic surgery, trauma and dental regenerative surgery<sup>[13,14]</sup>.

In our study, we submit that PRP enhance nasal mucosal wound healing and has a faster mechanism for decreasing edema of mucosa, Following up of nasal mucosal healing , at 3days postoperative, then at 7 days, 14 days till one month, it showed improvement of healing of the nasal mucosa in control group and there was a significant difference in mean of wound healing duration between two groups ( $p < 0.001$ ).

That is agree with Salah El Din *et al*<sup>[15]</sup> performed a randomized single blinded study on 60 patients with inferior turbinate hypertrophy. Submucous diathermy of inferior turbinate was done with topical application of PRP postoperative that showed the clearance of mucocilliary and mucosal healing was improved in PRP group ( $p$  value 0.004) with less bleeding and crust formation.

Another research was done in 2019 12Concentrated Growth Factors Extracted from Blood Plasma Used to Repair Nasal Septal Mucosal Defect After Rhinoplasty.

The membranous CGF film was applied to the surface. While the prepared liquid CGF was injected around the wound.

At intervals from 3 to 5 days, all patients were treated with CGF.

After 3 to 12 treatments, all the patients completed repair of mucosal defect of the the nasal septam , with good function and appearance.

That demonstrated the application of CGF dominated the local infection and promoted healing of the defect of nasal mucosa after rhinoplasty.

Another research was done in 2020<sup>[16]</sup> to detect the effects of submucosal PRP injection on wound healing in

endonasal surgeries: an experimental study. A total of 24 male adult New Zealand rabbits were used in this study. Three equal groups were randomly constituted with all animals. Group A PRP was injected submucosally into the damaged area. Group (S) single dose 0.7 cc 0.9% NaCl submucosal injection was applied to the damaged mucosal. Group (C) no injections were administered. The results of this study showed the positive effects of PRP on the nasal mucosa. According to these results, PRP injection to the injured nasal mucosa showed synechia-reducing effects, mucus-softening and anti-inflammatory effects.

Post-operative pain by visual analogue score between two groups we found that the pain reduced and there was significant difference in mean pain score between study group and control group, the was  $4.68 \pm 0.88$  (mean  $\pm$  SD) in the study group in the first week and was found to be  $7.04 \pm 0.86$  control group ( $p < 0.001$ ).

In the 3<sup>rd</sup> week test, the result was found to be  $0.49 \pm 0.940$  in the study group and  $2.37 \pm 1.36$  in the control group ( $p < 0.05$ ).

That it is agree with<sup>[17]</sup> to determine the impact of platelet-rich fibrin (PRF) on olfactory function and pain after septoplasty operations, that was prospective randomized observational study, with 148 patients who had septoplasty operation.

Patients were divided two groups, 67 patients were put in group A in which PRF did not instilled ,while 74 patients were placed in another group B in which PRF was applied after the completion of septoplasty operation. At 1 and 3 week, using visual analogue scale , Pain scores of patients were measured.

visual analogue scale was  $6.37 \pm 2.26$  (mean  $\pm$  SD) in the group without PRF in the first week and was found to be  $4.10 \pm 2.09$  in the PRF group.

while in the 3<sup>rd</sup> week test, the result was found to be  $2.37 \pm 1.36$  in the group without PRF and  $0.49 \pm 0.940$  in the group with PRF. And there was a statistically significant difference positive between two groups ( $p < 0.05$ ). That showed less painscores were obtained in PRF group in both 1<sup>st</sup> week and 3<sup>rd</sup> week post operative.

Kuzucu *et al*<sup>[18]</sup> (Randomized Controlled Trial) Patients who had nasal surgery according to randomized patient's choice have been classified into two groups ,one group was injected with saline merocele pack and the other group with platelet-rich plasma (PRP) in their nasal path. Patients were followed postoperative for 1 month; Nose Obstruction Symptom Evaluation (NOSE) Scala score, bleeding, pain, and crust rate have been compared between 2 groups. The results showed positive significant difference between two groups and  $p$  value was ( $P < 0.001$ ). This study showed that on postoperative bleeding, pain, crusts and postoperative complaints are lesser

Post operative bleeding, when we compared difference in post-operative bleeding between group A and group B after the removal of the nasal merocel pack. In the PRP group, no bleeding was observed in 89 patients, bleeding less than 3 minutes was observed in 9 patients and bleeding needed ice pack was observed in 2 patients.

While in control group no bleeding was observed in 67 patients, bleeding less than 3 minutes was observed in 27 patients and bleeding needed ice pack was observed in 6.

Significant difference between groups was determined in terms of bleeding (P: 0.031).

That is agree with 18, Bleeding incidence following the removal of the merocel pack was found to be 0.12 in the PRP group and 0.50 in the control group. This difference between 2 groups was statistically significant (P=0.031).

Postoperative synechia was followed and in study group synechia occurred in 8 patients which was mild and relieved by repeated packing, while in control group synechia occurred in 14 which was more length and needed excision under local anesthesia with repeated packing. There was a significant difference in the occurrence of synechia between group A and group B (p=0.034).

Another research was done in 2019,<sup>[19]</sup> Determining the effect of platelet-rich plasma on improving endoscopic sinus surgery: A randomized clinical trial study, In this study, one side of the nose was randomly selected as the control and the other side as the case, and at the end of the surgery, PRP was sprayed onto the surface where the polyp was removed in the side that was intended as the case. Using Meltzer's criteria to grade the nasal endoscopic finding before and after operation, while Lund-Mackay scoring system was used to classify CT finding. All patients were followed for 6 months, and Findings of this study suggested that treatment by PRP may be effective in reducing symptoms of patients showing recurrence of CRS symptoms following endoscopic sinus surgery subjectively but not objectively.

#### CONFLICT OF INTERESTS

There are no conflicts of interest.

#### REFERENCES

1. Lee KS, Wilson JJ, Rabago DP, Baer GS, Jacobson JA, Borrero CG. Musculoskeletal applications of platelet-rich plasma: fact or future? *American Journal of Roentgenology*. 2011;196:628-636.
2. Navarrete Álvaro ML, Ortiz N, Rodriguez L, *et al.* Pilot study on the efficiency of the bio-stimulation with autologous plasma rich in platelet growth factors in otorhinolaryngology: otologic surgery (tympanoplasty type I). *International Scholarly Research Notices*. 2011;2011.
3. Derycke L, Eyerich S, Van Crombruggen K, *et al.* Mixed T Helper Cell Signatures In Chronic Rhinosinusitis with and without Polyps. *PLOS ONE*. 2014;9:e97581.
4. Ghogomu N, Kern R. Chronic rhinosinusitis: the rationale for current treatments. *Expert Review of Clinical Immunology*. 2017;13:259-270.
5. Rahman T, Alam MM, Ahmed S, Karim MA, Rahman M, Wahiduzzaman M. Outcome of Endoscopic Sinus Surgery in the Treatment of Chronic Rhinosinusitis. *Mymensingh Med J*. 2016;25:261-270.
6. Patel GB, Kern RC, Bernstein JA, Hae-Sim P, Peters AT. Current and Future Treatments of Rhinitis and Sinusitis. *The Journal of Allergy and Clinical Immunology: In Practice*. 2020;8:1522-1531.
7. Daramola OO, Lidder AK, Ramli R, *et al.* Patient knowledge and perception of computed tomography scan in the management of chronic rhinosinusitis symptoms. *The Laryngoscope*. 2015;125:791-795.
8. Garneau J, Ramirez M, Armato Iii SG, *et al.* Computer-assisted staging of chronic rhinosinusitis correlates with symptoms. *International Forum of Allergy & Rhinology*. 2015;5:637-642.
9. Hirsch AG, Stewart WF, Sundaresan AS, *et al.* Nasal and sinus symptoms and chronic rhinosinusitis in a population-based sample. *Allergy*. 2017;72:274-281.
10. Hulse KE, Stevens WW, Tan BK, Schleimer RP. Pathogenesis of nasal polyposis. *Clinical & Experimental Allergy*. 2015;45:328-346.
11. Rahman T, Alam MM, Ahmed S, Karim MA, Rahman M, Wahiduzzaman M. Outcome of Endoscopic Sinus Surgery in the Treatment of Chronic Rhinosinusitis. *Mymensingh Medical Journal: MMJ*. 2016;25:261-270.
12. Zhao Q-M, Gao J, Huang X-x, Chen X-p, Wang X. Concentrated growth factors extracted from blood plasma used to repair nasal septal mucosal defect after rhinoplasty. *Aesthetic plastic surgery*. 2020;44:511-516.
13. Karaman E, Gungor G, Alimoglu Y, *et al.* The effect of lidocaine, bupivacaine and ropivacaine in nasal packs on pain and hemorrhage after septoplasty. *European Archives of Oto-rhino-laryngology*. 2011;268:685-689.
14. Etulain J. Platelets in wound healing and regenerative medicine. *Platelets*. 2018;29:556-568.
15. Salaheldin AH, Hussein A. Effect of platelet-rich plasma on nasal mucociliary clearance after submucous diathermy of inferior turbinate. *Egyptian Journal of Ear, Nose, Throat and Allied Sciences*. 2012;13:71-75.

16. Yildirim U, Kemal O, Aksoy A, Karaca E, Terzi O, Atmaca S. Effects of submucosal PRP injection on wound healing in endonasal surgeries: an experimental study. *European Archives of Oto-Rhino-Laryngology*. 2020;277:1681-1689.
17. Tutar B, Ekincioglu E, Karaketir S, *et al*. The impact of platelet-rich fibrin (PRF) on olfactory function and pain after septoplasty operations. *European Archives of Oto-Rhino-Laryngology*. 2020;277:1115-1120.
18. Kuzucu I, Beriat GK, Ezerarslan H, Ozdemir S, Kocaturk S. Effects of the Autologous Platelet-Rich Plasma in Nasal Pack on Postoperative Quality of Life. *Journal of Craniofacial Surgery*. 2017;28.
19. Mohebbi A, Hosseinzadeh F, Mohebbi S, Dehghani A. Determining the effect of platelet-rich plasma (PRP) on improving endoscopic sinus surgery: A randomized clinical trial study (RCT). *Med J Islam Repub Iran*. 2019;33:150-150.