

Role of Platelet-rich Plasma on Nasal Mucociliary Clearance after Septoplasty - A Randomized Clinical Study

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Abstract

Background: Intranasal surgeries include septoplasty, endoscopic sinonasal surgeries, and endonasal dacryocystorhinostomy for different indications. During the post-operative period, the patients frequently encounter problems due to the absence of nasal mucociliary clearance (NMC) such as dryness of the nasal mucosa, crusting, bleeding from the nose, and halitosis. The present study is conducted to find the efficacy of using platelet-rich plasma (PRP) on NMC at the end of septoplasty surgery.

Aim of the Study: The aim is to study the efficacy of douching the nasal cavity with PRP following septoplasty in terms of recovery of normal mucociliary function and prevention of crusting.

Materials and Methods: A single-blinded, randomized, prospective study involving 74 patients divided into two groups. Group A consisted of 37 septoplasty patients in whom plasma rich with platelets was instilled in the nasal cavity and Group B 37 subjects used as control group in whom normal saline was used. Patients followed up at the 7th post-operative day and after 2 weeks. NMC was assessed pre-operatively and post-operatively. The incidence of crust formation was also observed in both the groups.

Observations and Results: NMC was improved in both the groups, but there was a statistical significant early restoration of NMC in Group A. Crust formation was lower in Group A (PRP group).

Conclusions: Application of PRP was an effective method of recuperating nasal mucociliary function in patients undergoing septoplasty decreasing the time taken to return to normal nasal function. PRP also reduced the incidence of crust formation.

Key words: Dysfunction, Endoscopic sinus, Mucociliary, Plasma, Platelets, Saccharin clearance

INTRODUCTION

Indications for the various intranasal surgeries include inflammatory and allergic sinonasal diseases, benign and malignant tumors of the nose, and paranasal sinuses. They are being performed extensively after the introduction of sinus endoscopes. Apart from these various approaches through nasal cavities such as to lacrimal system, pituitary fossa is being carried out in every part of the world. At the end of the surgery, large cavities are left to heal which depends on the pre-operative mucosal status and NMC

of that particular patient. All age groups are subjected to these surgeries. NMC mechanism helps as nature's best air conditioner and protects the upper as well as lower respiratory tracts and the delicate alveoli. The mucous film, with its immunological active ingredients, its adsorbent power, and its water content, makes the inhaled air almost sterile, sufficiently humid and at par with the body temperature. This mucociliary mechanism can be easily impaired by structural abnormalities of the nose and paranasal sinuses.^[1] Andersen *et al.*^[2] used a method of depositing a small particle of saccharine on the nasal mucosa and noting the time that it took the subject to report a sweet taste to calculate and assess the NMC. The values for mucociliary clearance have been reported in different parts of the world with wide variations depending on various geographical, physiological, and pathological conditions.^[3-6] The reliability and validity of the saccharin test were previously confirmed by Puchelle *et al.*^[7] Platelet-rich plasma (PRP) was first used in cardiothoracic surgery

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by M. Ferariwho used PRP in 1987 after an open heart surgery; now, it is widely used in various fields such as dentistry, orthopedics, otorhinolaryngology, maxillofacial surgery, dermatology, plastic and cosmetic surgery, urology, and wound healing.^[8] Platelets isolated from the blood form a rich autologous source of growth factors. When PRP is applied to the surgical site, more predictable outcome can be expected. A blood clot is the important factor in soft tissue healing in all natural wounds. PRP behaves in a similar strategy initiating a more rapid and complete healing process. A natural blood clot usually contains 95% red blood cells (RBC's), 5% platelets, and <1% of white blood cells (WBCs) and numerous amount of fibrin strands. A PRP blood clot contains 95% of platelet, 4% of RBC's and 1% of WBC's.^[9] Autologous PRP also has a potential for use as a hemostatic agent because it binds tissues and locally activates the coagulation cascade. When the coagulation cascade is activated, high concentrations of platelets adhere to the wound surface. Platelet activation and degranulation release a number of hemostatic substances.^[10] Post-operative treatment consisted of the standard protocol of systemic cephalosporin antibiotic, nonsteroidal anti-inflammatory drugs, and multivitamins for 1 week. In the present study, post-operative NMC was assessed by the saccharin test preoperatively as well as 3 months after surgery (functional endoscopic sinus surgery [FESS]) under the same climatic conditions (room temperature 23°C and relative humidity 60%).

Aim of the Study

The aim is to study the efficacy of applying topically PRP following intranasal surgeries in terms of recovery of normal mucociliary function and preventing crusting.

Study Period

The study period was from April 2014 to March 2016.

Institute of Study

The study was conducted at Kurnool General Hospital Attached to Kurnool Medical College, Kurnool, A. P.

MATERIALS AND METHODS

In the present study, 74 patients undergoing septoplasty were randomly selected using online services for random selection (andrew.hedges.name/experiments/random). They were divided into 2 groups. Group A consisted of 37 patients in whom PRP was instilled at the end of the surgery. Group B consisted of 37 patients in whom normal saline was instilled at the end of the septoplasty. Inclusion criteria: (1) Patients aged above 18 years and below 47 years were included. (2) Patients undergoing septoplasty for the time were included. (3) Patients with

primary disease without complications were included. (4) Patients with congenital anomalies of the choanae were included. Exclusion criteria: (1) Patients aged below 18 years and above 47 years were excluded. (2) Patients with diabetes mellitus and endocrine disorders were excluded. (3) Patients on mucoregulatory drugs 2 weeks before surgery were excluded. The platelet rich with plasma was prepared by the following method:^[10]

Preparation of Autologous PRP

1. 50 mL of blood was drawn from the patient and placed in a five 10 mL test tubes with 1.4 mL anticoagulant citrate phosphate dextrose adenine (cpda-1) solution in each one aseptically. Fluid replacement may be needed for sensitive patient after drawing of blood.
2. This was centrifuged with a soft spin at 2500 rpm in 5 min.
3. The centrifuged was stopped to allow a 60-s count-down to help loosen platelets. The concentrated platelet was collected with the buffy-coat, and the RBCs are discarded.
4. After the 60-s countdown, a hard spin was allowed at 3500 rpm in 10 min and the PRP was collected which is in the bottom of the test tube, and buffy coat was drawn up using a pipette and discarded. The test tube was then transported in the surgical field. Note: The remaining 1–2 cc of plasma was used to resuspend the concentration of platelets and white cells.

The test tube was labeled PRP. It was instructed to continuously shake the test tubes while on transport or waiting douching. Pre-operative nasal mucociliary clearance time (NMCT) was calculated with saccharin test by the following method:^[11] NMC was assessed using the saccharin transit time (ST) test on the 1st day of the study as a baseline before severe mucosal damage (SMD) (patients with ST >30 min were excluded) and was done after 2 weeks and 2 months postoperatively. The patients were seated comfortably in the test room with constant humidity and room temperature of 20–22°C for at least 20 min to keep them in a stable physiological and environmental state while instructions were given before testing. A 5 mg of saccharin particle was applied on the inferior turbinate 1.5 cm from the nares under direct visualization. After placement of saccharin, the patient was asked to refrain from sneezing, sniffing, or bending. The transit time was recorded from the placement of the saccharin on the inferior turbinate until the patient reported a sweet taste to the nearest minute. 30 min was set as the upper limit of the normal. All the patients undergoing surgery were thoroughly investigated and surgical profile was done. After surgery, PRP was instilled/douched into the nasal cavity taking care that the entire operation sites were in contact with PRP. Nasal cavities were packed to avoid oozing of

blood wherever necessary. Patients were followed up on 3rd, 7th post-operative day, and after 2 weeks. NMCT with saccharin test was calculated postoperatively after 7th post-operative day after 2 weeks (2 values were recorded). All the data collected were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

Of 74 patients in Group A, there were 23 males and 14 females with a male-to-female sex ratio of 1.64:1. These patients were in the age groups of 18–47 years with a mean age of 26.35 ± 2.60 (95% confidence interval). In Group B, there were 22 males and 15 females with a male-to-female sex ratio of 1.46:1. These patients were in the age groups of 18–47 years with a mean age of 28.20 ± 1.90 [Tables 1 and 2].

Pre-operative NMCT measured in both the groups is shown in Table 3, and there was no statistical significant difference between Groups A and B before septoplasty and the $P = 0.014$. Apart from NMCT, there were no post-operative incidences in either group. Post-operative pain was complained in 5/37 in Group A and 7/37 (18.91%) of Group B. Crusting was reported in 3/37 (8.105) of the Group A and 11/37 (29.72%) of the Group B which was statistically significant difference.

Table 1: The age and gender incidence of the Group A patients (n=37)

Age groups	Male	Female	Percentage
18–24 (10)	05	05	27.02
25–31 (13)	07	08	35.13
32–39 (09)	05	04	24.32
40–47 (05)	03	02	13.51

Table 2: The age and gender incidence of the Group B patients (n=37)

Age groups	Male	Female	Total percentage
18–24 (11)	06	05	29.72
25–31 (12)	07	05	32.43
32–39 (08)	05	03	21.62
40–47 (06)	03	03	16.21

Table 3: The difference in NMCT values pre-operatively (n=74)

Group and number	Mean and SD	Mean difference	T	P
A-37	14.99±4.20	1.02	4.45	0.014
B-37	16.01±4.10			-

NMCT: Nasal mucociliary clearance time, SD: Standard deviation

In Group A, NMC mean was 14.99 ± 4.20 before the operation and on 7th day and after 2 weeks postoperatively, NMC mean was 13.38 ± 3.80 and 11.25 ± 3.20 , respectively, the P value in this group was highly significant 0.008 [Table 4]. In Group B, pre-operative NMC mean was 16.01 ± 4.10 , and on 7th day and 2 weeks later after operation, was 15.73 ± 4.65 and 13.87 ± 4.46 , respectively, and the P value was less significant (0.038) than in Group A [Table 5]. Comparison between pre-operative and post-operative NMCT values in each group at biweekly intervals showed a statistical significance in the values of Group A [Table 4].

DISCUSSION

Nasal obstruction is a common presenting symptom in otolaryngology. Most patients having septal deviation will have hypertrophied inferior turbinate on the opposite side due to nature’s compensation mechanism. In the extensive study of neonatal septal deviation by Gray,^[12] the incidence of deviated nasal septum was found to be 48–60%. However, Jeppensen and Windfield,^[13] Jazbi,^[14] and Alpini *et al.*^[15] found an incidence of <4%. Septal deviation is corrected by septoplasty but the treatment of hypertrophied inferior turbinate by a wide range of surgical methods. Intranasal surgeries are fraught with early complications including bleeding, adhesion, and persistent nasal obstruction (due to edema and crust formation) remain as problems which lead to the search for minimal invasive surgeries.^[16] There is certain controversy remaining in the appropriate surgical treatment of the inferior turbinate hypertrophy because the hypertrophy tends to recur after most treatments.^[17] Early recovery of NMC would avoid the early complications mentioned above. The PRP contains multiple growth and healing factors such as platelet-derived growth factor, transforming growth factor, and vascular endothelial growth factor. The

Table 4: The mean with SD and P values of Group A NMCT values, (n=74)

Time of NMCT	Mean with SD	P
Pre-operative	16.01±4.10	-
7 th day	15.73±4.65	-
After 2 weeks	13.87±4.46	0.008

NMCT: Nasal mucociliary clearance time, SD: Standard deviation

Table 5: The mean with SD and P values of Group B NMCT values, (n=74)

Time of NMCT	Mean with SD	P
Pre-operative	14.99±4.20	-
7 th day	13.38±3.80	-
After 2 weeks	11.25±3.20	0.038

NMCT: Nasal mucociliary clearance time, SD: Standard deviation

release of these factors is triggered by the activation of platelets which can be initiated by a variety of substance or stimuli such as thrombin, calcium chloride, collagen, or adenosine 5c-diphosphate; in addition to these growth factors, PRP contains fibrinogen and a number of adhesive glycoproteins that support cell migration.^[18] In this study, there was no statistical difference in mucociliary clearance between Group A and Group B before the operation as $P = 0.014$ [Table 1]. It means that both groups were randomly selected and there was no statistical bias which allows comparing mucociliary clearance postoperatively in both groups. Post-operative pain was complained in 5/37 of Group A and 7/37 (18.91%) of Group B. Crusting was reported in 3/37 (8.105) of the Group A and 11/37 (29.72%) of the Group B which was statistically significant difference. Even though the study is based on small data and shorter duration, the raised the importance of PRP in decreasing crust formation and bleeding after septoplasty cannot be ignored. In the present study, NMC in Group A patients was improved postoperatively and this improvement increased at 2 weekly post-operative NMCT calculated with P value at 0.008 (P was considered statistically significant at 0.05), [Table 4]. On the other hand, the NMC clearance improvement in Group B patients was more at 2 weeks ($P = 0.038$), [Table 5]. The improvement of mucociliary clearance in Group A ($P = 0.008$) was more compared to Group B ($P = 0.38$). The improvement in NMC was more at 2 weeks postoperatively because of less crust formation and more healing of mucosa at that time. The present study concludes that using PRP has shown early recovery of NMC and lesser crust formation in the post-operative period.

On the contrary, Rice^[19] was not happy about the use of PRP as the studies conducted by him and showed no benefits in the application of PRP after endoscopic sinus surgery, and the study was terminated early after 13 operations. In a similar study by Jakse *et al.*^[20] on the effects of PRP on bone regeneration after sinus lifting, they found a 3–4% increase in bone generation with PRP, the difference was not statistically significant, and the regenerative capacity of PRP was described as being of “quite low potency.” These previous research studies implied no significant effect in the application of PRP after surgery, this may be because the surface area needed for healing is large and cannot be covered all with PRP; this is because with current harvesting techniques, 20 ml of a patient’s blood yields only 2–3 ml of PRP. In the present study, the topical application of PRP was significant in the improvement of NMC because the surface area needed for healing is not so large, and also, there is a less mucosal injury with SMD. Erkilet *et al.* suggested that PRP is effective in accelerating tympanic membrane perforation healing in rats and that it may be effective in human subjects, particularly

as it is an autologous material.^[21] The idea in Erkilet *et al.* study is similar to the present study in terms of the small surface area needed for healing. Furthermore, Man *et al.* described the benefits of the use of PRP in cosmetic surgery.^[22] Adler and Kent reported the advantage of using PRP in face-lifts.^[23] Finally, Abuzeni and Alexander reported the benefits of PRP in autologous fat transfer in cosmetic surgery.^[24] As this study is only with 74 subjects, further studies are needed on larger numbers of patients with a longer period of follow-up to evaluate the effect of adding PRP on nasal ciliary functions and healing of nasal mucosa after various nasal surgeries.

CONCLUSIONS

Using PRP in septoplasty gives a chance for the nasal mucosa to recover NMC, especially within 2 weeks. Adding PRP is added at the end of intranasal surgeries which leave a large aw surfaces especially after FESS, there will be a greater improvement of NMC with less bleeding and crust formation. PRP is simple and easy to be prepared with no reported side effects.

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