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Determining the Impact of Platelet-rich Plasma Therapy on Short-term Postoperative Outcomes of Pediatric Tonsillectomy Patients in Egypt

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Tonsillectomy is considered one of the most common major operations performed in pediatric population. Unfortunately, tonsillectomy is often associated with severe pain that may delay the patient discharge and influence his ability to return to the normal daily activities together with a 2–4% risk of hemorrhage. Among promising healing promoting agents is Platelet-rich plasma (PRP). It is considered as a potential adjuvant therapy improving the healing of surgical wounds and contains multiple growth and healing factors that are released upon their activation.
Methods: This was a prospective randomized controlled study carried on forty patients who underwent tonsillectomy alone or adenotonsillectomy. In each patient, PRP was used on one side " test side " and other side was used as a control. The test side was randomly allocated in all patients, so the results will be of the 40 patients, total sides 80, (test side 40; 20 right side and 20 left side).
Results: Our results revealed that mucosal healing was noted to be better in PRP treated side, particularly on 5th and 10th post-operative day, with documented less incidence of secondary post-operative hemorrhage. Pain scores were less on the PRP treated side through the post-operative period, but were statistically significant only on the 5th day postoperative.

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Conclusions: The preliminary results from this study, supported by literature, have revealed that PRP was beneficial in the amelioration of post-tonsillectomy pain, improvement of healing and bleeding risk in pediatric tonsillectomy patients.

Keywords: Platelet-rich Plasma; Tonsillectomy; Healing.

1. INTRODUCTION

Tonsillectomy is a common surgery and considered one of the most common major operations performed in pediatrics, being indicated for recurrent tonsillitis, obstructive sleep apnea and sleep disordered breathing [1]. Unfortunately, tonsillectomy is often associated with severe pain that may delay the patient discharge and influence his ability to return to the normal daily activities together with a 2–4% risk of hemorrhage [2,3].

Patients may have aversion to eat and drink due to painful dysphagia. Uncontrolled pain at home is a common reason for readmission and therefore many different techniques have been used to decrease post tonsillectomy pain and to allow a smooth recovery and a tranquil return to normal activities; these include adequate analgesic control following pediatric tonsillectomy. Other strategies include surgical technologies such as partial tonsillectomy, bipolar diathermy and plasma dissection of the field [2,4].

Also, fibrin glue had been used to decrease post tonsillectomy bleeding that may occur. Platelets play an important role not only in traditional hemostasis, but also in wound healing process and immunomodulation [5].

Platelet-rich plasma (PRP) is considered as a potential adjuvant therapy improving the healing of surgical wounds and injuries [6,7]. PRP is platelets in a concentrated volume that contain multiple growth and healing factors which are released upon their activation and assisting the body in repairing itself by stimulating other cells to regenerate new tissue. The release of these factors is triggered by activation of platelets. Initiation of this activation is occurred by a variety of substance or stimuli such as calcium chloride, thrombin, adenosine 5c-diphosphate or collagen; in addition, PRP contains fibrinogen and a number of adhesive glycoproteins that support cell migration. Different clinical situations have tested PRP in healing improvement; now it is tested whether application of autologous (PRP) on the tonsillar bed at the time of tonsillectomy would decrease postoperative pain and bleeding and allow rapid recovery and resuming the normal daily activities [8].

The aim of work was to determine whether application of autologous PRP on the tonsillar bed and pillars at the time of tonsillectomy would affect postoperative pain, bleeding and healing.

2. PATIENTS AND METHODS

This was a prospective randomized controlled study done in The Department of ORL, Tanta University Hospitals. Forty patients (23 male and 17 female) who underwent tonsillectomy alone or adenotonsillectomy, aged from 4-15 years were included in this study. In each patient, PRP was used on one side " test side " and other side was used as a control. The test side was randomly allocated in all patients, so the results will be of the 40 patients, total sides 80, (test side 40; 20 right side and 20 left side).

Each patient had a special file with code number. All pictures that taken were be only of sites of surgery and covering the face and unnamed and also for any investigations of patient privacy was assured. All results of the research were only be used for scientific purpose. The duration of the study was 6 months, started from 1st March to 1st September 2020. The study was designed to include at least 40 children who underwent tonsillectomy or adenotonsillectomy operation. The inclusion criteria: Any patient eligible for tonsillectomy, age from 4 up to 15 years and patients who underwent either tonsillectomy alone or adenotonsillectomy. The exclusion criteria: Children who expected to be unreliable in expressing pain due to behavioral pattern or disorder, developmental delay, residence outside the city or patient unable to come for follow-up, children who have cardiac and respiratory disease or congenital cleft palate.

All patients were subject to the following: Personal history: Name, age, present history: Any present complain like fever, sore throat, cough, horsy voice. Past history: bleeding diathesis or hemorrhagic dyscrasias, any co-existing disease (i.e., diabetes, epilepsy, cardiac disease) or complicated follicular tonsillitis. General examination, ENT clinical examination.

2.1 Investigations

Laboratory investigations: complete blood picture, bleeding time, clotting time, prothrombin time and activity, partial thromboplastin time, INR. Imaging: X-ray lateral view with extended head and opened mouth if adenoid is suspected. Anesthetic consultation before undergoing the surgical procedure. Our end point of this study was facing of the complications in our cases. There would be adequate provision to maintain privacy of participant and confidentiality of data by: The excised tonsils were discarded according to the conditions of ministry of health.

2.2 The Operative Procedure

The patients were hospitalized on the same day of tonsillectomy and were discharged after clinical evaluation by the operating surgeon. The anesthesia was standardized (same technique and same protocol). The classic known way of tonsillectomy with dissection ligation method was standardized for all patients with operation being done under general anesthesia with endotracheal intubation. Boyle–Davis mouth gag was introduced and opened. It was held in place by Draffin's bipods or a string over a pulley. Tonsil was grasped with tonsil-holding forceps and pulled medially.

A 25 ml of autologous blood was drawn from the patient during anesthesia induction and processed during tonsillectomy using a laboratory centrifuge. The blood was centrifuged in two sessions, the first is called a soft spin, which allowed the blood to be divided into three layers, namely the lowest layer of RBCs, the upper a cellular plasma layer which is called PPP (platelet-poor plasma) and the intermediate PRP layer which is called the Buffy coat. Then PPP and PRP and some RBCs was transferred into another tube which would now undergo a second centrifugation (hard spin) which was longer and faster than the first. This allowed the platelet to be settled at the bottom with few RBCs (Fig. 1).

The PRP was then mixed for activation with calcified thrombin, collected into syringe and then applied directly to the tonsillar pillar and bed Fig. 2.

2.3 Postoperative

All patients were discharged at the same day of surgery. They received prescriptions for home treatment with antibiotic (amoxicillin- clavulanic acid) at dose of 45mg/kg/day divided over two doses, and analgesic (paracetamol) at dose of 15mg/kg/dose bid as standard basic analgesic with (Ibuprofen) as an extra analgesic at dose of 10mg/kg/dose on demand. In addition, the patient was called after 24 hours and every 5 days to check the pain severity and surgical bed condition. Descriptive and numerical pain scale was used to measure the pain level 2 hours after surgery, day 1, day 5 and day 10 post-operative.

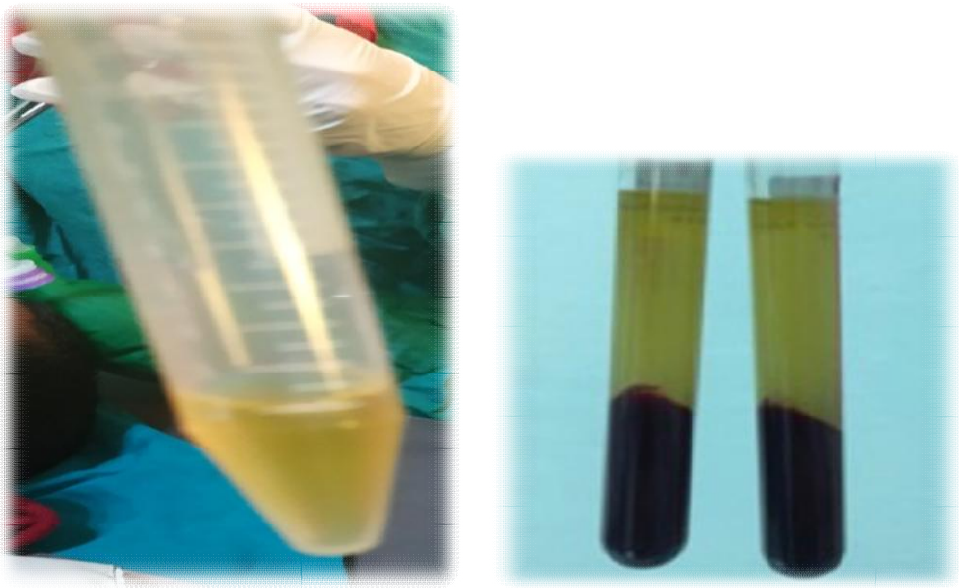

Fig. 1. layers of centrifuged blood

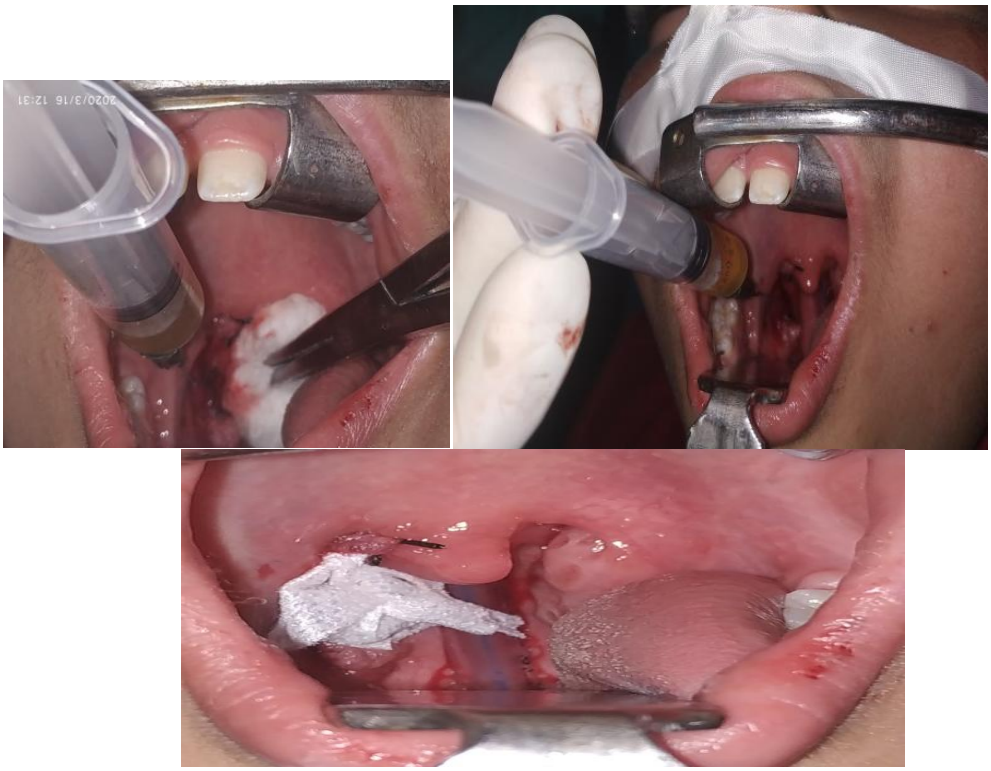

Fig. 2. Application of PRP after tonsillectomy.

2.4 Statistical Analysis

Statistical analysis was done using SPSS statistical package version 8, using fisher exact test and Man-Whitney U test to compare the differences in the medians.

3. RESULTS

Descriptive analysis of the studied cases according to age Table 1

Regarding Pain score, pain score at 2 hours post-operative was less on the PRP side than the control side in all patients but it wasn't significant. From day 1 to 10 the pain scores were less on the PRP side than on the control side but were statistically significant only on the 5th day postoperative in all patients Table 2

By doing a comparison between the two sides; we found a significant increase in pain scores from the postoperative 2nd hour to Day 1 in both sides then a decrease was noted in the pain scores of both sides starting from the 5th postoperative day Table 3.

Regarding bleeding, there was no statistically significant difference in both two groups Table 4.

Regarding the healing, mucosal recovery was noted to be better in PRP treated side compared to control side and this is documented at 5th and 10th day post-operative Table 5

4. DISCUSSION

In a study of 40 pediatric tonsillectomy patients, the effectiveness of PRP applied to the tonsillar bed (test side vs. control side in the same patient) was investigated, and PRP applied immediately after tonsillectomy on the tonsil bed and pillar was shown to accelerate the healing process and to decrease postoperative pain, together with a role in decreasing the incidence of bleeding. PRP is a fraction of whole blood that contain a concentrated growth factors and proteins. The number of basic sciences, animal, and human investigations on the PRP healing effects worldwide has risen sharply in the recent years [9].

Persistent and severe post-tonsillectomy pain has been associated with the likelihood of complications such as poor oral intake and dehydration, morbidity and delayed recovery When comparing pain by day, there was a tend toward lesser pain for the PRP treated side for

days 1 through 10.Data from the control side is consistent with the natural course of postoperative tonsillectomy pain which follows a gradual decline during the first postoperative week and a more rapid decline after this period.

The effect of PRP on pain was significant starting from day 1 through day 5. On contrary, Sidman et al. [10] found no difference on pain scale between PRP patients and control patients but they attributed this due to large dropout rate 17.1% in their study. Unfortunately, we couldn`t use need for medication as a comparing factor because the patient is served as his own control, but Sidman`s study and his group found that greater number of medications needed on day 9 and 10 on the PRP side.

Similarly, in a study of 70 pediatric patients that was done by Salah Eldin [7] PRP application was reported to have no impact on postoperative pain or recovery in terms of medication use, days to normal diet, and follow-up visits compared to the control group. Previous studies on the effectiveness of PRP on post tonsillectomy pain have revealed inconsistent findings with the amelioration of postoperative pain starting from day 1 to day 3 with the application of PRP in a study of adult patients.

Table 1. Descriptive analysis of the studied cases according to age (n=40)

	Min. – Max.	Mean ± SD.	Median (IQR)
Age (years)	4.0 – 15.0	8.48 ± 3.01	8.25 (6.0 – 11.0)

Table 1. Distribution of the studied cases according to pain in both sides (n=40)

Pain in both sides	2hours post-operative		1st Day		5th Day		10th Day	
	No.	%	No.	%	No.	%	No.	%
Test side > control side	0	0.0	0	0.0	0	0.0	0	0.0
The same	0	0.0	0	0.0	0	0.0	40	100.0
Test side < control side	40	100.0	40	100.0	40	100.0	0	0.0

Table 2. Comparison between the two side according to Pain 2h post-operative & day 1 and Pain at day 1 & day 5 post-operative

Pain 2h post-operative & day 1	Min. – Max. Mean ± SD. Median (IQR) 2hours post-operative	Min. – Max. Mean ± SD. Median (IQR) 1st Day	Z	P
Test side	1.0 – 2.0 1.40 ± 0.50 1.0 (1.0–2.0)	3.0 – 5.0 3.58 ± 0.71 3.0 (3.0–4.0)	5.563*	<0.001*
Control side	3.0 – 6.0 4.40 ± 1.01 4.0 (4.0–5.0)	4.0 – 8.0 5.75 ± 1.08 6.0 (5.0–7.0)	5.351*	<0.001*
Pain at day 1 & day 5 post-operative				
Test side	3.0 – 5.0 3.58 ± 0.71 3.0 (3.0–4.0)	1.0 – 3.0 2.05 ± 0.75 2.0 (1.50–3.0)	5.351*	**Test side**
Control side	4.0 – 8.0 5.75 ± 1.08 6.0 (5.0–7.0)	3.0 – 5.0 3.98 ± 0.66 4.0 (4.0–4.0)	5.370*	**Control side**

Table 3. Comparison between the two side according to bleeding (n=40)

Bleeding	Test side		Control side		χ^2	FEp
	No.	%	No.	%		
No	40	100.0	39	97.5	1.013	1.000
Yes	0	0.0	1	2.5		

Table 4. Distribution of the studied cases according to healing at 10th day (n=40)

Healing	No.	%
No change in both sides	10	25.0
Better in PRP side	30	75.0

Park DH et al. [11] who used fibrin glue as a sealant on one side of tonsillar bed. He found that it decreased postoperative pain on day 1,3 and 10 compared to the other non-coated control side. However, there are two major disadvantages of fibrin glue: The first is the risk of viral transmission such as hepatitis B and C. The second is that many of the growth factors are depleted from this substance. Another similar study was carried out by Ozcan et al. [12] ho used sucralfate. he found it a useful drug to decrease postoperative pain as it forms a protective layer on the tonsillar bed. However, sucralfate lacks the growth and healing factors present in the PRP and should be used several times every day for at least 5-7 days.

In another study carried by Salah Eldin et al. [7] comparing a PRP group (80 tonsillar niches) with a control group (110 tonsillar niches), a lower risk of hemorrhage (none in PRP, nine cases in control) and less severe pain was reported after local use of PRP, and thus the use of PRP in the region of the postoperative wound was stated to be effective in the prevention of hemorrhage and pharyngeal pain attenuation after tonsillectomy.

Upon review of literature, no studies were found to assess the effect of PRP application on tonsillar bed healing after tonsillectomy. However, M. stavrakas et al. [13] study documented that PRP is a material that is being used more and more frequently in many surgical specialties.

Its numerous advantages include safety (because it is an autologous material), the increased deposition of platelets and growth factors in the healing area, and a short preparation time.

PRP is now widely accepted as an effective means of promoting wound healing and tissue regeneration. Owing to its value in bio stimulation and healing acceleration, this material has various applications in many surgical specialties. New applications of PRP are also being investigated. This material is particularly interesting to the ENT surgeon because of its healing properties and as a potential packing or grafting material [14].

Besides its high platelet concentration, PRP contains a number of growth factors that are useful for wound healing such as platelet-derived growth factor (PDGF), transforming growth factor alpha (TGF-α), transforming growth factor beta (TGF-β), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor and platelet-derived angiogenesis factors, along with white blood cells, phagocytic cells, a high native fibrinogen concentration, and vasoactive and chemotactic agents. In particular, PDGF and TNF-β facilitate rapid wound healing, hemostasis and decreased scarring (Table 5) [15].

PRP is an established treatment that provides satisfactory outcomes for various clinical conditions. However, its use in ENT is not yet common and its application needs further investigation. This review describes the available evidence on the use of PRP in ENT surgery [14].

Ugur Yildirim et al. [16] study results also demonstrated positive effects of PRP on the nasal mucosa. According to their results, PRP injection to the injured nasal mucosa showed anti-inflammatory, mucus-softening, and synechia-reducing effects. Therefore, submucosal PRP injection after endonasal surgeries can be considered an effective application for maintaining nasal physiology. Therefore, these findings emphasize the potential role of PRP in the amelioration of post-tonsillectomy pain, improvement of healing and bleeding risk in pediatric tonsillectomy patients

5. CONCLUSIONS

The preliminary results from this study, supported by literature, have revealed that PRP was beneficial in the amelioration of post-tonsillectomy pain, improvement of healing and bleeding risk in pediatric tonsillectomy patients.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

An informed consent obtained from all participant in this research.

ETHICAL APPROVAL

Any unexpected risk appear during the course of the surgery was cleared to the participant and the ethical committee at time.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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