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ORIGINAL ARTICLE

The Effect of Using Perioperative Platelet-Rich Plasma on Wound Healing Rate and Prevention of Salivary Fistula Formation in Patients Undergoing Partial Parotidectomy

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ABSTRACT

Objectives: This study aims to examine the effects of autologous platelet-rich plasma (PRP), which increases new connective tissue synthesis and revascularisation, on healing in parotid surgery wounds, prevention of salivary fistula formation, drain removal time and hospitalisation in the postoperative period.

Materials and Methods: Fifty-four patients who had an operation on partial parotidectomy were randomised, and then two groups were created. PRP was obtained by centrifuging the blood taken from the patients in the study group at the end of the surgery. This obtained PRP was injected into the surgical site, and then the wound flap was closed by suturing. Patients were evaluated for parameters such as the development of salivary fistula, duration of drain removal, discharge time and all other complications during the postoperative 4 weeks.

Results: Drain removal and discharge times of the PRP group cases were statistically shorter than those in the control group. The rate of development of a salivary fistula was remarkably high in the control group, but it was not statistically significant. A statistically significant correlation was found between the location of the compared tumour, the volume of material removed and the incidence of all complications.

Conclusions: PRP reduced the duration of drain removal and discharge times for those who had an operation on partial parotidectomy. Thus, the decreased discharge time provides both reduced health costs and reduced risk of developing nosocomial infections. Although it was not statistically significant, a significant difference was observed in the rates of salivary fistula development.

1 | Introduction

Parotidectomy is a frequently performed surgical procedure in the head and neck region. Many surgical techniques have been described for the parotid gland. Superficial parotidectomy, partial superficial parotidectomy, extracapsular dissection, conservative total and radical total parotidectomy are frequently performed procedures today [1].

Complications that may occur in patients reduce the success of treatment. The data obtained as a result of the studies, by providing the development of treatment protocols,

Summary

- Head and neck surgeons need treatments to help minimise the risk of complications during and after parotid gland surgeries.
- Salivary fistula is a complication that can be encountered frequently in the late period after parotid gland surgery and forms the basis of our study.
- PRP, which increases new connective tissue synthesis and revascularisation use was evaluated in terms of wound healing and complications after parotid gland surgery.
- Fistula development did not show any statistically significant difference across the groups. The current results showed that PRP reduced drain removal time and discharge time from the hospital in patients who underwent partial parotidectomy.
- We believe that the effects of PRP will be understood much better with larger study populations.

help physicians avoid undesirable results after surgery [2]. Complications like fistula, sialocele, wound infection, Frey's syndrome and skin flap necrosis can also result from issues with wound healing and the continued production of saliva by the glandular residue [3].

Platelet-rich plasma (PRP) is the processed fluid fraction of autologous peripheral blood with a platelet concentration above the baseline. PRP treatments have been used for over 30 years for various indications, resulting in significant interest in the potential of autologous PRP in regenerative medicine [4]. The purpose of using PRP is to activate the body's healing mechanisms. Therefore, unlike traditional treatments, it is the basic principle to trigger inflammation instead of suppressing it. PRP is an autologous graft, so the risk of allergic reactions and infectious diseases is minimal [5].

The scientific rationale underlying PRP therapy is that concentrated platelet injection at the wound site can initiate tissue repair through the release of many biologically active molecules (growth factors, cytokines, lysosomes) and adhesion proteins responsible for initiating the haemostatic cascade, stimulating new connective tissue synthesis and revascularisation [6].

It was thought that PRP applied in different areas could help to avoid complications in parotid gland surgery. In this study, we aimed to evaluate the effect of PRP on wound healing and preventing salivary fistula development in patients who underwent partial parotidectomy.

2 | Material and Methods

Institutional review board approval was obtained from the Haydarpasa Numune Training and Research Hospital Ethics Committee (HNEAH-KAEK 2020/16) with the decision number. This study included patients who applied to Haydarpasa Numune Training and Research Hospital Ear Nose Throat and Head and Neck Surgery policlinic between January 2020 and January 2022 and were given partial parotidectomy indications.

Patients aged between 18 and 80 years who were operated on with partial parotidectomy and who volunteered to participate in the study were included in the study. Patients younger than 18 or older than 80 and having impaired wound healing; chronic diseases such as heart failure, anaemia, immunodeficiency, diabetes and hypertension; and conditions that negatively affect wound healing, such as smoking history, were excluded from the study.

Patients participating in our randomised controlled prospective study were randomised according to whether the order of surgery was odd or even. Fifty-four patients were included in the study, including the study group ($n = 27$) in which PRP was applied with even numbers during the operation and the control group ($n = 27$) with odd numbers during the operation, where PRP was not applied. The numbers required for a significant outcome were obtained using a power calculation.

After the patients were informed about the study, the informed consent form was read, and their written consent was obtained. Participants were included in the study on a voluntary basis.

2.1 | Surgical Technique

The operations were performed under general anaesthesia. With the modified Blair incision, the skin and subcutaneous incision are made, and the subcutaneous tissues and platysma muscle are retracted anteriorly. The preauricular area was also opened with blunt dissection and the tragal cartilage, which served as a landmark for the facial nerve, was exposed. Haemostasis was achieved with bipolar electrocautery throughout the operation. After the facial nerve was identified, the parotid gland on the surface of the facial nerve was carefully dissected, preserving the nerve's integrity. The superficial part of the gland was dissected from the facial nerve branches, the sample was removed and the partial parotidectomy procedure was completed.

2.2 | Preparation and Application of PRP

Close to the end of the surgery, 8 cc of blood was taken from the patient's vascular access and centrifuged at 3000 rpm for 12 min (Nüve NF 2000). Care was taken to use a wide needle, such as an 18 gauge, to ensure that the platelets were less traumatised and inactive before the application while drawing blood. After centrifugation, whole blood is separated by gravity into three layers: plasma (upper layer), platelets and leukocytes (middle layer called “buffy coat”) and erythrocytes (bottom layer). First, platelet-poor plasma was withdrawn from the tube with an injector and was not used. The remaining middle layer was removed from the tube, and approximately 2 cc of PRP was obtained. When we injected the prepared PRP into the surgery area at 1-cm intervals, we found that approximately 2 cc of PRP was sufficient. Then, PRP was injected into the surgical wound bed and under the skin, paying attention to sterility conditions.

2.3 | Patient Evaluation

For participants who gave consent to participate in the study, a form was filled out regarding their sociodemographic characteristics and clinical background. In addition, information such as postoperative drain withdrawal time; discharge time; development of complications such as salivary fistula, sialocele, Frey's syndrome, skin flap necrosis and wound infection; the volume of material removed; and localisation of the mass was added to the form. During the daily dressing of the patients, the 24-h fluid accumulation in the drain, the condition of the wound site and the patient's additional complaints were noted.

Drains were removed from patients whose 24-h fluid accumulation was below 20 cc. The drain removal time, discharge times and adhesion time of the wound flap evaluated by palpation were evaluated hourly. The salivary fistula was evaluated by inspecting and palpating the wound site at the postoperative four-week follow-up. The wounds were checked twice a day before the patients were discharged. After discharge, all wounds were checked daily. Since one of the parameters we used in our study was recovery time, we checked it frequently. Wound healing was evaluated by the same researcher for all patients.

2.4 | Statistical Analysis

The Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum and maximum) were used while evaluating the study data. The conformity of the quantitative data to the normal distribution was tested with the Shapiro-Wilk test and graphical examinations. Independent groups *t*-test was used to compare normally distributed quantitative variables between two groups, and the Mann–Whitney *U* test was used for comparisons between two groups of non-normally distributed quantitative variables. Pearson's chi-squared test, Fisher's exact test, and Fisher-Freeman-Halton exact tests were used to compare qualitative data. Statistical significance was accepted as $p < 0.05$.

3 | Results

The study was conducted with 54 cases, 50% ($n = 27$) female and 50% ($n = 27$) male. The patients ranged from 21 to 77 years, with a mean age of 52.63 ± 13.48 years. The demographic information of the patients, drain duration, hospital discharge time, biopsy-pathology compatibility and complication rates are shown in Table 1.

The gender and age of the cases did not differ statistically significantly across the groups ($p > 0.05$). The drain removal time of the subjects in the control group was found to be statistically significantly higher than those in the PRP group ($p = 0.001$; $p < 0.01$) (Table 2). The hospital discharge time of the subjects in the control group was found to be statistically significantly higher than those in the PRP group ($p = 0.001$; $p < 0.01$) (Table 2). Fistula development, complications, tumour location, compliance with biopsy and pathology diagnoses and volume of material removed did not show any statistically significant difference across the groups ($p > 0.05$).

Pleomorphic adenoma and Warthin tumours were seen at the highest rate in both groups. In patients diagnosed with lymphadenopathy and lipoma preoperatively, we removed the entire superficial lobe to clarify the diagnosis. In patients with lipoma, extensive dissection was performed and superficial parotidectomy was performed because the mass was large and spread to the deep lobe.

4 | Discussion

Head and neck surgeons need treatments to help minimise the risk of complications during and after parotid gland surgeries. In this study, PRP use was evaluated in terms of wound healing and complications after parotid gland surgery. The current results showed that PRP reduced drain removal time and discharge time from the hospital in patients who underwent partial parotidectomy. Consequently, this provides reduced health costs and decreased risks of nosocomial infections.

TABLE 1 | Demographic information and follow-up information of the patients.

Gender	Female	27 (50.0)
	Male	27 (50.0)
Age	Mean ± Sd	52.63 ± 13.48
	Median (min–max)	53.5 (21–77)
Drain duration (hour)	Mean ± Sd	60.00 ± 13.79
	Median (min–max)	48 (48–96)
Discharge time (hour)	Mean ± Sd	84.00 ± 13.79
	Median (min–max)	72 (72–120)
Development of salivary fistula	No, *n* (%)	49 (90.7)
	Yes, *n* (%)	5 (9.3)
Complications	No, *n* (%)	23 (42.6)
	Yes, *n* (%)	31 (57.4)
	Skin flap necrosis	2 (3.7)
	Facial paresis	8 (14.8)
	Frey's Syndrome	4 (7.4)
	Hypoesthesia	20 (37)
	Sialocele	2 (3.7)
	Wound infection	3 (5.6)
Location of the tumour	Anterior, *n* (%)	12 (22.2)
	Deep, *n* (%)	9 (16.7)
	Inferior, *n* (%)	32 (59.3)
	Superior, *n* (%)	1 (1.9)
Biopsy-pathology compatibility	No, *n* (%)	7 (13.0)
	Yes, *n* (%)	47 (87.0)
Material volume (cm^3)	Mean ± Sd	31.67 ± 25.30
	Median (min–max)	24.15 (4–126.9)

TABLE 2 | Comparison of follow-up parameters by groups.

		Groups		
		PRP ($n=27$)	**Control ($n=27$)**	***p***
Drain duration (hour)	Mean ± Sd	53.33 ± 10.17	66.67 ± 13.86	[a]**0.001****
	Median (min–max)	48 (48–72)	72 (48–96)	
Discharge time (hour)	Mean ± Sd	77.33 ± 10.17	90.67 ± 13.86	[a]**0.001****
	Median (min–max)	72 (72–96)	96 (72–120)	
Development of salivary fistula	No	26 (96.3)	23 (85.2)	[b]**0.351**
	Yes	1 (3.7)	4 (14.8)	
Complications	No	15 (55.6)	11 (40.7)	[c]**0.276**
	Yes	12 (44.4)	16 (59.3)	
Location of the tumour	Anterior	6 (22.2)	6 (22.2)	[d]**1.000**
	Deep	5 (18.5)	4 (14.8)	
	Inferior	16 (59.3)	16 (59.3)	
	Superior	0 (0.0)	1 (3.7)	
Biopsy-pathology compatibility	No	3 (11.1)	4 (14.8)	[b]**1.000**
	Yes	24 (88.9)	23 (85.2)	
Material volume (cm^3)	Mean ± Sd	28.3 ± 16.37	35.06 ± 31.84	[a]**0.910**
	Median (min–max)	26.9 (4–67.3)	22.5 (5.5–126.9)	

**$p < 0.01$.
[a]Mann–Whitney *U* Test.
[b]Fisher Exact Test.
[c]Pearson chi-squared Test.
[d]Fisher Freeman Halton Test.

Treatment of benign masses in the parotid gland is partial parotidectomy, which preserves the facial nerve and removes the tumour with a clear margin. Removal of the superficial lobe provides a low incidence of tumour recurrence but can cause a range of major and minor complications due to dissection of the facial nerve and loss of volume in the parotid gland [7]. The most important complication is facial nerve dysfunction, which may manifest as paralysis or paresis [8]. Other complications after partial parotidectomy include infection, salivary fistula, bleeding, haematoma, sialocele/seroma, aesthetic deformity, numbness around the earlobe and Frey's syndrome [9]. Factors associated with complications after partial parotidectomy remain unclear, and the incidence varies considerably. In general, most of these studies are retrospective and lack standardised methods for assessing postoperative complications.

Salivary fistula is a complication that can be encountered frequently in the late period after parotid gland surgery and forms the basis of our study. It is thought that salivary fistula is caused by the continuation of saliva secretion by the gland tissue that was not resectioned in the postoperative period [7]. During a meal, especially while chewing, the flow from the fistula increases, and the fistula may become permanent. At the same time, saliva is one of the critical factors that impair wound healing [10]. The secretion from the wound site may not be evaluated clearly in some cases. In doubtful cases, analysis of the fluid can confirm parotid gland secretion due to its high amylase content. Most fistulas develop within 1 month after surgery, classically occur during eating and may persist long after wound healing [11]. Although it usually disappears spontaneously within 6 weeks, it may be a source of anxiety in the patient during this period and may predispose them to the risk of secondary infection.

Paradoxically, salivary fistula appears to occur more frequently in patients who have had less extensive parotid surgery. The factors that may affect the formation of salivary fistula after parotidectomy have not yet been fully understood, and there are studies in which there are disagreements about this. One study concluded that the larger the resection, the less likely fistula formation is, as less tissue is left to generate saliva [12]. In 66 parotidectomy patients, Tuckett et al. reported that fistula development was more common in patients with less gland resection, but facial nerve dysfunction was less common [13].

A salivary fistula can also cause visible scarring and wound infections. Continuous pressure dressing of the parotid region is necessary to prevent these complications, but this may lead to cosmetic problems, prolonged hospitalisation, increased costs and psychological problems in patients. Therefore, it is important to identify new treatments that reduce the occurrence of salivary fistulas. The basis of our study was the prevention of salivary fistula complications and PRP application, which we believe may contribute to wound healing.

Many methods used to prevent complications have been seen in the literature, and the effects of most of them have been observed to be limited. The lack of a complete preventive treatment or method also causes most surgeons to develop an idea to avoid parotidectomy complications. It was observed that fibrin sealant application following parotidectomy did not significantly affect the development of postoperative wound complications [14].

The rate of Frey's syndrome following parotidectomy is heterogeneous in the literature (reported in 10%–40% of cases) and reflects discrepancies in reporting and diagnosis. This variability may also be related to the surgical technique used, diagnostic method and length of follow-up. However, up to 90% of patients have been reported to have a positive starch iodine test (Minor's test) [15]. In our study, Frey's syndrome was detected in four (8%) patients. Longer-term follow-up of participants may be necessary for results more consistent with the literature. Lipofilling has been shown to reduce the incidence of Frey's syndrome and consistently improve postoperative cosmetic outcomes in the absence of significant morbidities [15]. Dermofat grafting has been suggested as one of the alternative techniques after partial parotidectomy to prevent deformities and Frey's syndrome, but fat resorption has been shown as a limitation in this technique [16].

Autologous PRP is the processed fluid fraction of autologous peripheral blood with a platelet concentration above the baseline level, and these treatments have been used for various indications for over 30 years. The scientific rationale underlying PRP therapy is that concentrated platelet injection at the wound site can initiate tissue repair through the release of many biologically active molecules (growth factors, cytokines, lysosomes) and adhesion proteins responsible for initiating the haemostatic cascade, stimulating new connective tissue synthesis and revascularisation [6].

PRP's biggest advantage is that it is an autologous product with no known side effects, unlike commonly used corticosteroids [17]. PRP has been used in many studies requiring rapid healing and tissue regeneration. In the study conducted by Yuksel et al., PRP was applied to the facial skin three times with an interval of 2 weeks in 10 healthy volunteers, and a significant difference was observed in the PRP group in terms of general appearance, skin tightness and wrinkle status [18]. In a comprehensive analysis of studies on the efficacy of PRP therapy on postoperative wound healing, patients treated with PRP showed better vascularisation [19] and less pain [20] via angiogenesis. A difference of 15.9 days was shown in terms of recovery time between the control group and the group treated with PRP [21]. Sönmez et al. proved that the use of PRP in postoperative skin flaps stimulated angiogenesis through the activity of growth factors (especially VEGF) in the composition of PRP, thus further accelerating flap healing [22].

There are also various studies on PRP in otolaryngology. In 2001, Navarrete Alvaro et al. reported a satisfactory result in PRP-supported type I tympanoplasty for central tympanic membrane perforations [23]. In some studies investigating PRP use in vocal cord damage in the field of laryngology, better-organised collagen tissue was observed, and it was shown that the damaged vocal cord preserves its natural structure [24, 25]. PRP was also used in paediatric tonsillectomy patients, but no significant difference was found in postoperative pain and wound healing [26].

Our study is a prospective study, and the complications of all patients were followed long-term. However, although the data for all patients were fully recorded, we cannot exclude the possibility that some complications may have been overlooked. Another limitation is that, as far as we know, there is no pioneering study on this subject, and the number of patients is low. This number was probably insufficient to detect any reduction in the incidence of complications with PRP. We believe that the effects of PRP will be understood much better with larger study populations.

5 | Conclusion

This study was preliminary, and PRP use was evaluated in terms of wound healing and complications after parotid gland surgery. Results showed that PRP reduced drain removal time and hospital discharge times in patients who underwent partial parotidectomy.

Author Contributions

Selim Kul: conceptualisation, data collection and curation, funding acquisition, methodology, validation, visualisation and writing – original draft. **Sema Zer Toros:** conceptualisation, data collection and curation, funding acquisition; investigation, methodology, project administration, resources, supervision and writing – review and editing. **Çağrı Becerik:** conceptualisation, data curation, methodology and supervision and visualisation. **Lütfü Şeneldir:** conceptualisation, data curation, methodology and visualisation. **Sebahat Aksaray:** project administration, supervision and writing – review and editing.

Ethics Statement

The ethics approval was given by Haydarpaşa Numune Training and Research Hospital Clinical Ethics Committee for the study (Approval number: 2020/16).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/coa.14265.

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