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The effectiveness of platelet rich plasma therapy in chronic sinusitis patients with odor disorder undergoing endoscopic sinus surgery

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ABSTRACT

Objectives: Objectives: In this study, the objective was to compare the effectiveness of fluticasone dipropionate and platelet-rich plasma treatments added to the treatment in patients undergoing functional endoscopic sinus surgery in patients with chronic sinusitis involving odor dysfunction, different stages and types of sinusitis.

Methods: The study included a total of 60 patients between 18 and 60 years who underwent endoscopic sinus surgery due to chronic paranasal sinus infection followed by olfactory dysfunction. Group 1: paranasal sinus surgery + steroid therapy (first 30 patients) and Group 2: paranasal sinus surgery + steroid therapy + PRP therapy (second 30 patients) were grouped together without the patients' knowledge of the operating physician and of the treatment protocol. For the paranasal sinus CT evaluation, Lund-Mackey staging was used and the degree of the disease was determined using the Kennedy staging system. Modified Sniffin Stick test was applied to all patients in the preoperative 1st week and in the 3rd month postoperatively. The Modified Sniffin Stick test was conducted on all patients during the preoperative 1st week and the postoperative 3rd month. The modified Sniffin Stick test and endoscopic evaluation score were evaluated and whether or not the patients benefited from PRP treatment were compared.

Results: According to the postoperative endoscopy score, there was a difference between the experimental group and the control group in terms of postoperative endoscopy score, and it was found to be statistically significant. Besides, the postoperative endoscopy score of the experimental group was found to be lower than the control group. The average of Modified Sniffin' Stick Test scores in the postoperative period of the patients in the study was 28.27 ± 7.88 for the experimental group, while it was determined as 20.08 ± 5.75 for the control group, and this difference was statistically significant. The average anosmia times of the experimental and control group patients in the study were compared, and the mean duration of anosmia was 48.53 ± 20.40 (6-96) for the experimental group and 44.27 ± 19.45 (6.96) for the control group. The difference in the mean duration of anosmia between the experimental and control groups was not found statistically significant.

Conclusions: In this research, PRP, which is applied to functional endoscopic sinus surgery and fluticasone dipropionate treatment, has been shown to be a readily applicable, safe and highly efficient method of treatment in patients with chronic sinusitis accompanied by smell dysfunction.

Keywords: chronic sinusitis, platelet-rich plasma, functional endoscopic sinus surgery, odor

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The natural sense of smell is defined as Normosmia. Smell dysfunction, anosmia (complete loss of smell), hyposmia (reduced smell ability), hyperosmia (improved smell perception), pantosmia (improved smell perception without stimuli), parosmia (different smell stimulus perception), phantosmia (negative smell perception with no stimuli) [1, 2]. Anosmia and hyposmia are the most common feelings of odor disorders. 20 percent of the general adult population is known to be affected [3]. With the growth in the prevalence of olfactory disorder in recent years, its meaning has also been understood. In many neurodegenerative disorders such as Alzheimer's and Parkinson's disease, it is a biological marker and its physiological significance has been proved that it helps to diagnose early [4]. Also, a person's impaired eating habits have a direct effect on quality of life and vital mortality by social behavior deficits and environmental hazard exposure [5].

Many underlying diseases can trigger smell dysfunction. It can be considered similar to patients presenting with hearing loss when researching the etiology of these patients. Two major types of olfactory dysfunction may be categorized as conductive-environmental (anatomical barriers preventing odors from reaching the olfactory epithelium and receptors) or sensorineural (central; olfactory receptors, olfactory neurons, or disruption of the pathways to the olfactory centers of the central nervous system) [1, 6].

Odor loss has been associated with chronic rhinosinusitis (CRS), nasal polyposis, allergic rhinitis, inflammatory and neoplastic paranasal sinus diseases, which are obstructive nasal diseases [1, 7, 8]. The most common cause of odor dysfunction among sinonasal diseases is chronic rhinosinusitis (CRS) with or without nasal polyposis. Olfactory dysfunction is actually thought to affect 61 to 83 percent of CRS patients and 95 percent of nasal polyposis, irrespective of their subtype. It can be due to histological changes in the neuroepithelium and to cytokine-mediated dysfunction of the olfactory receptor associated with mechanical obstruction and inflammation in pathophysiology caused by polyps or edematous mucosa [9, 10].

Asthma, nasal polyposis, and smoking are described as characteristics associated with smell dysfunction in patients with CRS at the age of 65. The level of mucosal eosinophilia in these patients has been shown to predict olfactory impairment [6]. Although mechanical obstruction associated with edema and infection may cause conductive smell loss, there is significant evidence that hyposmia or anosmia is due to the effects of inflammation on olfactory neurons in some forms of chronic rhinosinusitis [11].

Diagnosis of olfactory dysfunction requires a detailed history, and a comprehensive systematic physical examination including nasal endoscopy to evaluate the olfactory bulb and sinonasal region [12]. Olfactory evaluation includes olfactory tests, which are consists of self-assessment tools (Sino-Nasal Outcome Test, Rhinosinusitis Disability Index test, Questionnaire of Olfactory Disorders, etc.), functional olfactory tests (testing true olfactory function) and physiological tests (mucociliary function, nasal airflow, or brain activity during sniffing) [9]. Psychophysical tests are performed in four groups as odor perception tests, discrimination tests, odor identification and odor identification tests. Computed Tomography is the gold standard for patients with sinus disease and is also the first study proposed to identify anatomical occlusion [2, 5].

In order to prevent exposure to smoke and natural gas, to avoid consuming spoiled foods, and to maintain nutritional health and quality of life, patients should be given a first step in the treatment of odor disorders as to the potential causes, degree and prognosis of odor loss, and patients should receive safety advice [13].

The treatment should be based on etiology and, first of all, it should be eliminated if there is an underlying pathology. For medical treatment, intranasal calcium buffers such as corticosteroids, zinc, theophylline, minocycline, vitamins, lipoic acid, phosphodiesterase inhibitors, pentoxifylline and sodium citrate are known to be effective in the treatment of olfactory dysfunction, but further studies are required [3, 11].

While odor disorders of the conductive type have a relatively good prognosis, odor disorders of the neural type have a worse prognosis and often do not improve with treatment. The patients who can benefit the most from the treatment are patients with sinonasal diseases such as septum deviation, concha bullosa, nasal stenosis, allergic rhinitis, nasal polyposis, and chronic sinusitis. In the medical treatment of the disease, systemic and intranasal steroids, antiallergic

drugs and antibiotherapy for rhinosinusitis infections are given [2].

The combined use of oral steroid sprays and topical nasal steroid sprays in the treatment of CRS patients has been shown to be more effective than nasal sprays alone. There is no consensus, however, on the duration and dosage of steroid therapy, and guidelines for treatment vary greatly. Furthermore, long-term use is discouraged in patients with CRS due to the potential side effects of oral steroids [12].

In the treatment of odor disorders that are thought to develop due to mechanical causes, surgical interventions may also be performed. By improving ventilation and probably reducing inflammation in the olfactory bulb area, functional endoscopic sinus surgery positively improves the olfactory dysfunction associated with CRS. There are studies showing that nasal polyp patients are more likely to recover after ESS from olfaction [11].

Treatment of platelet rich plasma (PRP); in recent years, it has become a favorite material for clinicians and researchers since it accelerates tissue healing, decreases bleeding, edema and pain, and has been used in many specialties and operations with increasing frequency. In orthopedic, maxillofacial, periodontic, plastic, thoracic, vascular and neurosurgery, ophthalmology and dermatology, PRP is currently being used [15-17].

Due to its advantages in wound healing, angiogenesis, use as glue material, post-operative pain and bleeding, PRP is also one of the interesting materials in otorhinolaryngology and head and neck surgery. A significant improvement in odor function was observed following platelet-rich plasma injection treatment applied in patients with anosmia [18].

PRP was first used in 2016 by Mavrogeni *et al*. [18], based on the view that platelets can accelerate the regeneration of the olfactory nerves in anosmia patients by secreting various growth factors and active metabolites, especially transforming growth factor. Following the application of PRP in the olfactory area of 5 patients with idiopathic anosmia in 4 sessions, the sense of smell returned in 4 patients and one patient stated that he could smell a little but could not smell all. In a similar study conducted in 2020, although there was no significant improvement in Sniffin Sticks score in 2 patients with anosmia, it was observed that all 5 patients with hyposmia reached normosmia after 3 months of follow-up [19]. In a study conducted by Yasak *et al*. [20] on mice, the effects of PRP on the olfactory nerve were histological. When examined, it was found that epithelial damage was significantly less in the PRP group and epithelial thickness was higher. As a result of the studies, it was concluded that the use of PRP in the treatment of odor dysfunction has curative effects.

The aim of this study was to investigate the effects of treatment with fluticasone dipropionate and platelet-rich plasma in combination with functional endoscopic sinus surgery in the treatment of cases of chronic sinusitis accompanied by odor disorder at different stages and types of sinusitis.

METHODS

This prospective study was conducted with the permission of the Local Ethics Committee with the number 3049 and 25/10/2019 date ethics document, between 16.09.2019 and 30.01.2021. The study included a total of 60 patients between the ages of 18 and 60 who underwent endoscopic sinus surgery due to chronic paranasal sinus infection followed by olfactory dysfunction. For each patient, demographic data such as age and gender, detailed history and physical examination, head and neck examination, diagnostic nasal endoscopy and computed tomography (CT) axial-coronal non-contrast scan were performed. The patients were evaluated for preoperative mean duration of anosmia, history of nasal and paranasal sinus surgery for any cause, smoking, allergic rhinitis, history of asthma, septal deviation, turbinate hypertrophy, and presence of a nasal polyp. Concomitant medical conditions, chronic systemic diseases, other potential for anosmia (tumors, Alzheimer's disease, intracranial aneurysms, brain tumors, clinical exposure to suppositories and solvents, diabetes, hormonal disorders and some drug therapies [nifedipine, terbinafine, others, Multiple sclerosis etc.]), these patients were excluded from the study if they could not be excluded. Information on the presence and severity of paranasal sinus symptoms, use of medication for the treatment of symptoms, allergy and allergy treatments were recorded. All patients were medically treated with oral antibiotics, antihistamines, nasal steroid spray and, in some cases, oral steroid combination for at least 6

months prior to the decision on operation, but the decision on surgery was taken when this medication did not improve the general clinical picture. Intranasal endoscopic exam and paranasal sinus computed tomography methods were used in the diagnosis of chronic paranasal sinus infection. In the preoperative and postoperative 3rd month, Lund-Mackey staging was used for the evaluation of paranasal sinus CT and the degree of the disease was determined by the Kennedy staging system. Modified Sniffin Stick test was applied to all patients for the odor test in the first week before the operation and in the third month after the operation to investigate their sense of smell.

All patients were informed and their consent forms were obtained about the surgery. Endoscopic sinus surgery was conducted as a surgical treatment using the Messerklinger technique. Uncinectomy, anterior ethmoidectomy, posterior ethmoidectomy, middle meatus antrostomy, frontal recess opening, sphenoidectomy, partial concha resection, polypectomy, septoplasty and concaplasty operations have been added in all cases included in our study and in cases needed according to the prevalence of infection in the paranasal sinuses.

All patients received broad-spectrum antibiotic therapy and nasal irrigation with ocean water at least twice a day for 10 days at the end of the operation. Throughout the postoperative period, all patients were administered fluticasone dipropionate, a topical steroid in the form of two sprays into each nostril once a day for three months, starting from the first postoperative week, and all patients were started on oral prednisolone at 1 mg/day/kg during the postoperative period, and the doses were gradually reduced and stopped during the 10-day treatment period.

Patients are unaware of the physician performing the operation and the treatment protocol applied to the patients; Group 1 was separated into paranasal sinus surgery + steroid therapy (first 30 patients) and Group 2: paranasal sinus surgery + steroid therapy + PRP treatment group (second 30 patients).

Thirty patients in the PRP group received a total of 3 PRP injections at the end of the operation and at the postoperative 1st month and 2 months in controls in addition to the surgical and post-medical treatments (antibiotherapy + ocean water washing + topical steroid + oral prednisone). PRP injection was applied by direct injection method to the "Regio olfactory" area. Imaging was conducted with the endovision system we used in sinus surgery operations during the application of PRP to this area in the nasal cavity, and during this process, 4 mm and 2.7 mm 0°, 30°, 45° and 70 Storz endoscopes were used as required. 3 ml of PRP obtained by soft and hard spin method with the endovision system to the olfactory mucosa covering an area of 5 cm^2 where the anatomical region called Regio olfactory is located, with a dental tip (black tipped) injector, by passing the olfactory epithelium in a thick columnar structure pseudoatrophy. It was applied to the 'Regio olfactory' area by the direct injection method by injecting approximately 0.5 ml of PRP per cm^2 to each injection by going deep under the epithelium. The Modified Sniffin Stick test was applied to all patients in the postoperative 3rd month and evaluated with an endos copic evaluation score, examining whether the patients benefited from PRP medication.

Statistical Analysis

Statistical analysis of the data used in the study was made with the SPSS 25.0 program. The distribution of information about the sociodemographic and health status of the patients was analyzed with descriptive statistics. The Shapiro- Wilk test was used to examine whether the obtained data fit the normal distribution. The mean comparisons between the two independent groups, the Independent Samples t Test if the continuous data conformed to the normal distribution, and the Mann- Whitney U test if it did not. Chi-Square Test was used for comparison of categorical data.

RESULTS

Half of the patients in the study constitute the experimental group, and the other 50% (30 patients) constitute the control group. The distribution of demographic characteristics of the patients (gender, age), Kennedy staging and Lund-Mackey staging are given in Table 1. According to the results obtained; 41.7% (25 patients) of the patients in the study were women and 58.3% (35 patients) were men. In addition, the average age of women in the study was 43.34 ± 7.24 (28-59) years, and the average age of men was 43.34 ± 6.71 (24-60) years.

Fourty percentage of the experimental group of

Table 1. Distribution of socio-demographic characteristics of experimental and control groups

Group	Gender	N	% (Group)	% (Total)	Age			
					X	SD	Min	Max
PRP Group	Female	12	40	20	43.67	7.95	28	55
	Male	18	60	30	44.06	7.21	24	60
Control Group	Female	13	43.4	21.7	42.69	6.82	34	59
	Male	17	56.6	28.3	42.59	6.28	25	51
Total	Female	25	83.4	41.7	43.16	7.24	28	59
	Male	35	116.6	58.3	43.34	6.712	24	60

PRP = platelet rich plasma, X = mean, SD = Standard deviation, Min = minimum, Max = maximum

the study (12 patients) were women and 60% (18 patients) were men. The average age of women was 43.67 ± 7.95 (28-55) years, the average age of men was 44.06 ± 7 years. Of the control group, 43.4% (13 patients) were women and 56.6% (17 patients) were men. The mean age of female patients in the control group was 42.69 ± 6.82 (34-59) years, and the mean age of male patients was 42.59 ± 6.82 (25-51) years.

The distribution of the patients included in the study regarding the operation history, smoking status, allergic rhinitis, asthma, septum deviation, concha hypertrophy, environmental allergic history, nasal discharge, nasal obstruction, congestion, headache and infection findings are given in Table 2. According to the results, 10% (3 patients) of the patients in the experimental group have a history of operation and 30% (9 patients) smoke. On the other hand, 13.4% of the control group (4 patients) had an operation history and 30% (9 patients) were smoking. In addition, 86.6% of the patients in the experimental group (26 patients) had an environmental allergic history, 36.6% (11 patients) had allergic rhinitis, 23.4% (7 patients) had asthma and 76.6% (23 patients) have a runny nose. In the control group, 83.4% (25 patients) had an environmental allergic history, 33.4% (10 patients) allergic rhinitis, 23.4% (7 patients) asthma and 33.4% (10 patients) patient) has a runny nose.

Septum deviation in 36.6% (11 patients) of the experimental group patients included in the study, concha hypertrophy in 43.4% (13 patients), nasal obstruction in 80% (24 patients) and 53.4% (16 patients) have congestion. Septum deviation in 36.6% (11 patients) of the control group patients, concha hypertrophy in 43.4% (13 patients), nasal obstruction in 80% (24 patients) and congestion in 50% (15 patients) has. In addition, 40% of the experimental group patients (12 patients) have headache and 33.4% (10 patients) have signs of infection. In the control group, 43.4% (13 patients) had headache and 30% (9 patients) had symptoms of infection.

Kennedy and Lund- Mackey staging results of the patients in the study are given in table 3. According to the Kennedy staging results of the patients; 16.7% of the patients in the experimental group (5 patients) were "stage 1", 20% (6 patients) "stage 2", 33.4% (10 patients) "stage 3" and 30% (9 patients) are in "stage 4". Of the patients in the control group, 16.7% (5 patients) were stage 1, 23.4% (7 patients) stage 2, 30% (9 patients) stage 3 and 30% (9 patients) It is found in stage 4 ($X^2 = 0.130$; $p = 0.998$).

According to Lund-Mackey staging results of the patients; While the Lund-Mackey score of 36.6% (11 patients) of the patients in the experimental group was below 11, 63.4% (19 patients) were 11 and above. The Lund-Mackey score of 40% (12 patients) of the patients in the control group was below 11, while 60% (18 patients) were 11 and above ($X^2 = 0.071$; $p = 0.791$).

The postoperative endoscopy scores of the experimental and control group patients included in the study were compared and the results obtained are given in Table 4. According to these results; The mean postoperative endoscopy score was 3.03 ± 1.71 (0-7) in the experimental group and 4.93 ± 2.38 (0-7) in the control group. This difference between the experimental group and the control group in terms of postopera-

Table 2. Distribution of the information on the health status of the experimental and control groups

Health Information		PRP Group			Control Group			Total	
		N	% (Group)	% (Total)	N	% (Group)	% (Total)	N	%
Operation Story	Yes	3	10	5	4	13.4	6.7	7	11.7
	No	27	90	45	26	86.6	43.3	53	88.3
Smoking Use	Yes	9	30	15	9	30	15	18	30
	No	21	70	35	21	70	35	42	70
Allergic Rhinits	Yes	11	36.6	18.3	10	33.4	16.7	21	35
	No	19	63.4	31.7	20	66.6	33.3	39	65
Asthma	Yes	7	23.4	11.7	7	23.4	11.7	14	23.3
	No	23	76.6	38.3	23	76.6	38.3	46	76.7
Septum Deviation	Yes	11	36.6	18.3	11	36.6	18.3	22	36.7
	No	19	63.4	31.7	19	63.4	31.7	38	63.3
Concha Hypertrophy	Yes	13	43.4	21.7	13	43.4	21.7	26	43.3
	No	17	56.6	28.3	17	56.6	28.3	34	56.7
Environmental Allergy Story	Yes	26	86.6	43.3	25	83.4	41.7	51	85
	No	4	13.4	6.7	5	16.6	8.3	9	15
Runny Nose	Yes	23	76.6	38.3	10	33.4	16.7	33	45
	No	7	23.4	11.7	20	66.6	33.3	27	55
Nasal Obstruction	Yes	24	80	40	24	80	40	48	80
	No	6	20	10	6	20	10	12	20
Congestion	Yes	16	53.4	26.7	15	50	25	31	51.7
	No	14	46.6	23.3	15	50	25	29	48.3
Headache	Yes	12	40	20	13	43.4	21.7	25	41.7
	No	18	60	30	17	56.6	28.3	35	58.3
Signs of Infection	Yes	10	33.4	16.7	9	30	15	19	31.7
	No	20	66.6	33.3	21	70	35	41	68.3

PRP = platelet rich plasma

tive endoscopy score was found to be statistically significant (t = 3.553; $p = 0.001$). The postoperative endoscopy score of the experimental group was found to be lower than the control group.

Modified Sniffin Stick Test results in the preoperative and postoperative periods of the patients in the study are given in Table 5. According to the results obtained; In the preoperative period, the mean odor threshold score was 7.69 ± 1.94 in the experimental group and 7.66 ± 1.98d in the control group, and this difference between them was not statistically significant (t = -0.059; $p = 0.953$). However, the mean odor threshold score in the postoperative period was 12.58 ± 3.03 in the experimental group and 9.53 ± 2.28 in the control group. The difference in postoperative odor threshold scores between the experimental group and the control group was found to be statistically significant (t = -4.327; $p < 0.001$). The mean odor discrimination score in the preoperative period was 6.53 ± 2.30 in the experimental group and 6.55 ± 2.32 in the

Table 3. Chi-square test of the experiment and control group Kennedy and Lund-Mackey staging

Kennedy and Lund-Mackey Staging	Stage	PRP Group		Control Group		Total		X^2	*p value*
		N	%	N	%	N	%		
Kennedy Staging	Stage 1	5	8.3	5	8.3	10	16.7	0.130	0.998
	Stage 2	6	10	7	11.7	13	21.7		
	Stage 3	10	16.7	9	15	19	31.7		
	Stage 4	9	15	9	15	18	30		
	Total	30	50	30	50	60	100		
Lund – Mackey Staging	Under 11	11	18.3	12	20	23	38.3	0.071	0.791
	11 and Above	19	31.7	18	30	37	61.7		
	Total	30	50	30	50	60	100		

PRP = platelet rich plasma

control group. In the postoperative period, themean odor discrimination score was calculated as 9.71 ± 3.14 in the experimental group and 8.02 ± 2.67 in the control group, and this difference was statistically significant (t = -2.244; p = 0.029). . The average scent recognition score for the experimental group was 2.02 ± 1.10 in the preoperative period and 5.98 ± 3.25 in the postoperative period; For the control group, it was 2.03 ± 0.89 in the preoperative period and 2.48 ± 1.28 in the postoperative period. The difference in odor recognition scores between the postoperative experimental group and the control group was found to be statistically significant (t = -5.496; p < 0.001).

The average of Modified Sniffin Stick Test scores in the postoperative period of the patients in the study was 28.27 ± 7.88 for the experimental group; It was determined as 20.08 ± 5.75 for the control group, and this difference was statistically significant (t = -4.959; p < 0.001).

The average anosmia times of the experimental and control group patients in the study were compared and the results obtained are given in Table 6. According to these results; The mean duration of anosmia was 48.53 ± 20.40 (6-96) for the experimental group and 44.27 ± 19.45 (6.96) for the control group. The difference in mean duration of anosmia between the experimental and control groups was not found statistically significant (t = -0.829; p = 0.829).

DISCUSSION

Olfaction is one of the most important basic life functions in a very large part of living things in nature, while it is relatively less important for humans. Compared to living things in nature, the human olfactory system is less developed, and it is estimated that it can distinguish about 10,000 odors 16. As a result of the stimulation of olfactory molecules by the olfactory field, cells have evolved to receive the sense of smell.

Table 4. Independent t-test used for comparison of postoperative endoscopy scores of experimental and control groups

Group	Postoperative Endoscopy Score				y	*p value*
	X	SD	Min	Max		
PRP Group	3.03	1.71	0	7	3.553	**0.001**
Control Group	4.93	2.38	1	9		
Total	3.98	2.27	0	9		

PRP = platelet rich plasma, X = mean, SD = Standard deviation, Min = minimum, Max = maximum

Table 5. Independent sample t-test performed for comparison of preoperative-postoperative modified sniffin stick test results of experimental and control group patients

Content	Period	Group	N	X	SD	t	*p value*
Odor threshold	Preoperative	PRP Group	30	7.69	1.94	-0.059	0.953
		Control Group	30	7.66	1.98		
	Postoperative	PRP Group	30	12.58	3.03	-4.327	**< 0.001**
		Control Group	30	9.58	2.28		
Discriminating smell	Preoperative	PRP Group	30	6.53	2.30	0.048	0.962
		Control Group	30	6.55	2.32		
	Postoperative	PRP Group	30	9.71	3.14	-2.244	0.029
		Control Group	30	8.02	2.67		
Smell recognition	Preoperative	PRP Group	30	2.02	1.10	0.069	0.946
		Control Group	30	2.03	0.89		
	Postoperative	PRP Group	30	5.98	3.25	-5.496	**< 0.001**
		Control Group	30	2.48	1.28		
Modified Sniffin Stick test total score	Preoperative	PRP Group	30	16.23	4.82	0.013	0.990
		Control Group	30	16.24	4.83		
	Postoperative	PRP Group	30	28.27	7.88	-4.595	**< 0.001**
		Control Group	30	20.08	5.75		

PRP = platelet rich plasma, X = mean, SD = Standard deviation, Min = minimum, Max = maximum

This specialized sense is located in the respiratory system, providing integrity of function. However, a decrease in the sense of olfaction can affect people's vital functions and quality of life. Hyposmia, defined as a decrease in smell, is observed in 16% of the general population, while the prevalence of anosmia, defined as a loss of smell, is about 5% although it varies in studies [21, 22]. Anosmia can be temporary or permanent, depending on the degree of degeneration. Although there are studies showing that systemic steroids work in the treatment of these conditions, there is no clear medical treatment option defined yet [23].

Since the 1970s, when endoscopic sinus surgery was defined, it has been the first choice within the limits of indication in the surgical procedure of diseases located in the paranasal sinus and nasal cavity. Today, its indications have exceeded the nasal and paranasal structures and have become to cover many areas, primarily the skull base, pterygopalatine and infratemporal fossa, and orbita. The main reason for this is that endoscopic surgeries are less invasive compared to open surgical procedures, and the developing endo-

Table 6. Independent t-test used for comparing the average anosmia times of the experimental and control groups

Grup	Average Anosmia Duration				t	*p value*
	X	SD	Min	Max		
PRP Group	48.53	20.40	6	96	-0.829	0.411
Control Group	44.27	19.45	6	96		
Total	46.40	19.88	6	96		

PRP = platelet rich plasma, X = mean, SD = Standard deviation, Min = minimum, Max = maximum

scope and imaging technologies are increasing this technique day by day [24, 25].

Functional Endoscopic Sinus Surgery (FESS) is applied for treatment in many diseases such as chronic rhinosinusitis, nasal polyposis, paranasal tumors, pituitary tumors, cerebrospinal fluid (CSF) rhinorrhea, and encephalocele. Epistaxis, choanal atresia, angiofibroma, Thornwaldt's cyst treatment, septoplasty, dacryocystorhinostomy, and turbinoplasty applications are among the other usage areas of FESS [26]. After FESS, properly applied postoperative care shortens the recovery time of patients and decreases the frequency of revision surgery [27]. Nasal irrigation with saline, crust debridement, systemic and local steroids, and antibiotics can be used for early postoperative care [27, 28].

There are experimental and clinical studies investigating the effects of various materials on nasal mucosal healing in the current literature. In the study conducted by Yılmaz *et al*. [29] on rats, it was shown that systemically administered N-acetylcysteine reduced goblet cell loss and inflammatory cell migration and also had positive effects on wound healing in the nasal mucosa by decreasing the subepithelial thickness index. Cassano *et al*. [30] suggested that postop hyaluronic acid nasal washing in patients who underwent endoscopic turbinoplasty (turbinate reduction) shortened mucociliary transport time and accelerated mucosal cell regeneration compared to saline irrigation, and thus had positive effects on mucosal healing. Rezaeian [31] found out that spray cryotherapy is an affordable and effective method that increases mucosal healing rates in patients undergoing FESS due to nasal polyposis.

Grzeskowiak *et al*. [32] reported that the application of soluble tampons impregnated with antibiotics and steroids in patients who underwent FESS provided a better improvement compared to saline-soaked tampons, based on the postop endoscopic examination scores, and also gave more positive results by patient satisfaction. Testa *et al*. [33] compared topical gomenol oil with topical vitamin E application in patients who underwent FESS for chronic rhinosinusitis and showed that the application of vitamin E accelerated the restoration process of the sinonasal mucosa and was more effective on healing than other treatments.

Choi *et al*. [34] reported in an experimental study performed in rabbits that applying a silastic sheath to septal perforation provided significant early closure by leading to the acceleration of healing. Chan *et al*. [35] observed in an experimental study in rabbits that the application of Spongostan impregnated with hepatocyte growth factor to the damaged area in the maxillary sinus, compared to the saline-impregnated tampon, reduced fibrosis and accelerated wound healing and ciliogenesis, especially for the first 3 days.

There are studies reporting that systemic steroids reduce symptoms due to obstruction by limiting the postoperative mucosal edema, thanks to their anti-inflammatory effects [36]. However, systemic use of systemic steroids is controversial, considering their potential for side effects [37]. Topical steroids, on the other hand, are the most common agents accepted for use in the postoperative period due to their anti-inflammatory effects and lack of systemic side effects [36].

The use of platelet-rich blood products in medicine started with their derivatives produced for hemostasis. Its effects on wound healing also began with the increase in awareness of the growth factor and cytokines of platelets. PRP is a cellular plasma component that is obtained by centrifugation of whole blood and contains a higher platelet concentration than whole blood. Normally, the cellular component of plasma consists of 93% erythrocytes, 6% platelets, and 1% leukocytes. PRP has a 3-5 times higher rate of platelets compared to normal whole blood [38]. PRP contains growth factors in hyperphysiological ratio due to its high platelet concentration. With this feature, its antibacterial, anti-inflammatory, and accelerating effect on many tissues has been proved in various animal and human studies [38].

Lund-Kennedy endoscopic scoring system is widely used in the literature for objective evaluation of functional sinus surgery. In a study conducted by Poetker *et al*. [39], who investigated the recovery after functional endoscopic sinus surgery in chronic rhinosinusitis patients with polyps, it was reported that patients significantly improved in endoscopic findings after the operation [40].

The Lund-Mackey staging was used in the evaluation of paranasal sinus CT in the preoperative and postoperative 3rd month, and Kennedy staging system was used to determine the degree of the disease in the evaluation of the patients constituting the sample of

the study. According to the Kennedy staging results of the patients, 16.7% of the patients in the experimental group (5 patients) were in "stage 1", 20% (6 patients) in "stage 2", 33.4% (10 patients) in "stage 3", and 30% (9 patients) in "stage 4". Of the patients in the control group, it was found out that 16.7% (5 patients) were in stage 1, 23.4% (7 patients) in stage 2, 30% (9 patients) in stage 3, and 30% (9 patients) in stage 4. With regards to Lund-Mackey staging results of the patients, while the Lund-Mackey score of 36.6% (11 patients) of the patients in the experimental group was below 11, 63.4% (19 patients) were 11 and above. The Lund-Mackey score of 40% (12 patients) of the patients in the control group was below 11, while 60% (18 patients) were 11 and above.

The patients who constitute the sample of the study were investigated for their preoperative sense of olfaction and at the end of the third postoperative month. According to the postoperative endoscopy score, there was a difference between the experimental group and the control group in terms of postoperative endoscopy score, and it was found to be statistically significant. Besides, the postoperative endoscopy score of the experimental group was found to be lower than the control group. Additionally, the Modified Sniffin' Stick test was applied to all patients for the smell test in the first week before surgery and in the third postoperative month. The average of Modified Sniffin' Stick Test scores in the postoperative period of the patients in the study was 28.27 ± 7.88 for the experimental group, while it was determined as 20.08 ± 5.75 for the control group, and this difference was statistically significant.

The average anosmia times of the experimental and control group patients in the study were compared, and the mean duration of anosmia was 48.53 ± 20.40 (6-96) for the experimental group and 44.27 ± 19.45 (6.96) for the control group. The difference in the mean duration of anosmia between the experimental and control groups was not found statistically significant.

A significant improvement in the loss of smell after the operation in the patient groups can be attributed to the endoscopic sinus surgery. Although there are controversial results in the literature, there are many clinical studies reporting improvement in olfaction after endoscopic sinus surgery. In a study conducted by Litvack *et al*. [41], it was reported that, especially in anosmic patients, the loss of smell significantly improved after the operation. It was also deduced that improvement in anosmia is more pronounced, especially in nasal polyposis errors. Similar results were reported in a review by Rudmik *et al*. [42] In patients with anosmic and nasal polyps, a significant improvement in anosmia was reported after endoscopic sinus surgery.

There are many studies investigating the effect of functional endoscopic sinus surgery on postoperative symptoms. In 58 studies conducted with 3 different quality of life scales, Soler *et al*. [43] reported that the most significant improvement in symptoms after sinus surgery occurred in the first 6 months, and no difference developed in symptoms after this period. In their cohort study, Smith *et al*. [44] reported that in all patients with all phenotypes of chronic rhinosinusitis, functional endoscopic sinus surgery revealed a significant increase in the postoperative quality of life in patients with both general and disease-specific quality of life. Kennedy *et al*. [45] suggested that in their study on 104 chronic rhinosinusitis patients, they found 51% improvement after functional endoscopic sinus surgery according to the results of the SNOT22 questionnaire.

Most of the studies in the literature indicated that PRP could contribute positively to wound healing. There are few studies in the literature regarding the use of PRP in different disciplines of Otorhinolaryngology. As an example of these studies that aim to benefit from the regenerative properties of PRP, Yan *et al*. [19] injected a single dose of PRP into the olfactory mucosa of seven patients who had complained of anosmia and hyposmia for more than 6 months, had no sinonasal inflammatory disease, and did not respond to topical steroid therapy in the pilot study. Although all patients reported subjective improvement in their sense of olfaction after injection, the findings stabilized later. At the 3rd month follow-up, the patient's symptoms did not change, and 5 patients with hyposmia showed 60% improvement in olfaction tests and reached the level of normosmia. The limitations of the study include being conducted in one field and the limited number of patients, and the absence of a control group. Since the primary purpose is seen as demonstrating the reliability and tolerability of PRP use, it lays the groundwork for more detailed studies.

In the study of Kütük *et al*. [46], consisting of 80

patients, the effect of topical PRP application to the tonsillar lodge after pediatric tonsillectomy on short-term postoperative pain, appetite, need for analgesia, and bleeding rates was examined. The patients were divided into two as only tonsillectomy and tonsillectomy in addition to PRP treatment groups, each consisting of 40 patients. Postoperative pain and appetite scores, analgesic requirement, and bleeding were recorded. When compared with the tonsillectomy group, the pain scores of the tonsillectomy in addition to the PRP treatment group were significantly better on days 1-10, appetite on days 1-6, and analgesic need on days 1-10. One bleeding case in the experimental group was recorded compared to the four bleeding cases in the control group. When the parameters were statistically compared, they were found to be significant [46].

In the study of Ricci *et al*. [47], which included 59 patients who underwent superficial parotidectomy due to benign parotid tumor, the effect of PRP application to the parotidectomy lodge on hospitalization, drain duration, and postoperative facial paresis rates was investigated. Superficial parotidectomy was applied to 38 patients in the control group, superficial parotidectomy was applied to the experimental group consisting of 21 patients, and PRP was applied to the surgery site. The mean drain time was three days in the control group and two days in the experimental group ($p < 0.05$). The average hospitalization time was four days in the control group and five days in the experimental group ($p < 0.05$). Postop facial paresis was observed in four (10.5%) patients in the control group and in two (9.5%) patients in the experimental group. At the end of 24 hours, facial paresis developed in 2 more patients in the control group, and the total number of patients increased to six (15.7%). Paresis was not permanent in any patient and resolved within two months. Sialocele was observed in seven (18.4%) patients in the control group and in two (9.5%) patients in the experimental group ($p < 0.05$). Frey's syndrome and keloid formation were not observed in any of the patients. Consequently, it is thought that patients benefit clinically from the application of PRP to the surgery site [47].

In 2018 the two groups allocated to the topical subjects on oil myringoplasty results PRP effect in a study conducted in Turkey on 20 rats were studied [48]. Myringotomy was performed in the left ears of the subjects randomly divided into two groups of 10 subjects each. In the control group, the fat graft taken from the inguinal region after myringotomy was shaped like an hourglass and placed in the myringotomy area. Although the same procedure was applied to the experimental group, it was kept in PRP obtained from the subject for five minutes before applying the fat graft. After 21 days of follow-up, the eardrums of the subjects who were sacrificed were extracted and examined, and the groups were compared. Adipocyte area and the number of mature vessels were higher in the experimental group compared to the control group [48].

In a study examining the effect of PRP on the healing of acute tympanic membrane perforation in 2017, 12 New Zealand rabbits were used [49]. Perforation was created on the pars tensa part of the bilateral eardrums of the subjects examined in 2 groups with the help of a needle. Then, PRP obtained from the subject itself was applied to its right ear, and the left ear was left as the control group. Ear examination was performed on the subjects on the 1st, 4th, 7th, 10th, 13th, 16th, 21st, and 35th days and the time to close the perforation was noted. The subjects were sacrificed at 2 months after the procedure, and eardrums were extracted and subjected to histopathological examination. Perforation closure time was 12 days in the experimental group and 17.7 days in the control group, and this difference was statistically significant ($p = 0.0145$) [49].

Based on the view that it may accelerate the regeneration of olfactory nerves in anosmia patients due to its inclusion of growth factors, PRP was first used in 2016 by Mavrogeni *et al*. [18] Following the application of PRP in the olfactory area of 5 patients with idiopathic anosmia in 4 sessions, the sense of smell returned in 4 patients, and one patient stated that he could smell a little but could not smell all. In a similar study conducted in 2020, although there was no significant improvement in Sniffin Sticks score in 2 patients with anosmia, it was observed that all 5 patients with hyposmia reached normosmia after 3 months of follow-up.46 In a study conducted by Yasak *et al*. [20] on mice, the effects of PRP on the olfactory nerve were examined histologically, and it was found that epithelial damage was significantly less and epithelial

thickness was higher in the PRP group. It was concluded that PRP use in anosmia patients has curative effects.

CONCLUSION

The use of blood products rich in thrombocytes, which accelerates postoperative recovery by inducing healthy epithelial healing, is gradually increasing after otorhinolaryngology surgery. Studies in this area have been increasing in recent years, and the use of these autologous products is introduced to the clinical practice of surgeons. Our research has shown that PRP has an effect on relieving the symptoms of patients with chronic sinusitis and olfactory dysfunction. We think that PRP is a material that can be used in endoscopic endonasal surgical interventions since it does not have undesirable side effects such as allergic reaction or foreign body reaction due to its preparation in autogenous blood tissue, and it is easy to prepare and cheap. Our study has shown the effectiveness of PRP and it is thought that it will shed light on future studies to become a practically usable method.

Authors' Contribution

Study Conception: SGK; Study Design: SGK; Supervision: SGK; Funding: SGK, MFT, AG, ÇA; Materials: SGK, MFT, AG, ÇA; Data Collection and/or Processing: SGK, MFT, AG, ÇA; Statistical Analysis and/or Data Interpretation: SGK, MFT, AG, ÇA; Literature Review: SGK; Manuscript Preparation: SGK and Critical Review: SGK

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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