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Platelet-Rich Plasma for Posttraumatic Olfactory Dysfunction: Preliminary Report of 33 Patients

Jerome R. Lechien, MD, PhD, FACS[1,2,3,4]

Abstract

The platelet-rich plasma (PRP) injection into the olfactory clefts has been suggested as an effective treatment for long-lasting post-viral olfactory dysfunction (OD). Currently, no prospective clinical studies have been conducted in other OD etiologies. In this preliminary study, the PRP injection outcomes were investigated in 33 posttraumatic OD patients (19 females; mean duration: 55.6 ± 45.1 months), and olfactory outcomes were compared with those of patients adhering to an olfactory training (OT). Following PRP injection, 66.7% of posttraumatic patients reported subjective improvement. Threshold, discrimination, and identification (TDI) scores significantly increased in both groups, achieving a minimal clinically important difference only in posttraumatic injected patients. In the posttraumatic group, the baseline TDI (8.4 ± 8.1) significantly increased at the 3-month posttreatment (16.5 ± 9.6; $P = .003$). The 3-month TDI score was significantly higher in posttraumatic injected patients versus OT patients (16.5 ± 9.6 vs 13.3 ± 8.5; $P = .038$). PRP injection can be an option for posttraumatic OD patients to improve olfactory recovery.

Keywords

anosmia, COVID-19, hyposmia, olfactory, otolaryngology, otorhinolaryngology, parosmia, platelet-rich plasma, posttraumatic, recovery, rhinology, SARS-CoV-2, smell, trauma

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The injection of platelet-rich plasma (PRP) into the olfactory clefts is a new rhinological procedure for accelerating the olfaction recovery of patients with long-lasting post-viral olfactory dysfunction (OD).[1-4] Most studies evaluated PRP on post-COVID-19 or post-viral OD, with randomized controlled trials demonstrating the superiority of PRP injection over the placebo.[2] To date, the largest cohort studies have demonstrated that PRP injection into the olfactory clefts is associated with significantly greater threshold, discrimination, and identification (TDI) increases and olfactory disorder questionnaire (ODQ) reductions at 4 months postinjection in patients with post-COVID-19-related OD compared to individuals following only olfactory training (OT) protocols.[3] In post-viral OD, PRP injections have shown significant TDI increases, sometimes occurring several decades after the initial infections.[4] PRP stimulates cell regeneration and accelerates the recovery process. Currently, no studies have investigated the benefits of PRP for posttraumatic patients with OD.

The present preliminary controlled study investigated the effectiveness of PRP injections into the olfactory clefts of patients with posttraumatic OD.

Methods

Setting and Patients

Patients with self-reported persistent posttraumatic OD (>6 months) were consecutively recruited from March 2021 to October 2024 in the ENT-Dour Medical Center (Belgium). Patients were included if the OD was clearly related to a head trauma. Patients with chronic rhinosinusitis with/without nasal polyposis, active rhinitis, neurological degenerative disease, nasal chemo/radiation, or functional endoscopic sinus surgery were excluded. Patients with a history of post-viral/COVID-19 OD after the trauma were excluded from the trauma group. The study protocol was approved by the ethics committee (CHU Saint-Pierre Hospital-2102028). Electronic informed consent was obtained.

Demographics and Clinical Outcomes

Age, gender, comorbidities, allergies, tobacco consumption, and past treatment/OT outcomes were collected.

[1]Department of Otolaryngology, Polyclinic of Poitiers, Elsan, Poitiers, France
[2]Department of Surgery, UMONS Research Institute for Health Sciences and Technology, Faculty of Medicine, University of Mons (UMons), Mons, Belgium
[3]Department of Otolaryngology–Head & Neck Surgery, Foch Hospital, School of Medicine, UFR Simone Veil, Université Versailles Saint-Quentin-en-Yvelines (Paris Saclay University), Paris, France
[4]Department of Otorhinolaryngology and Head and Neck Surgery, CHU Saint-Pierre, Brussels, Belgium

Corresponding Author:
Jerome R. Lechien, MD, PhD, FACS, Department of Surgery, UMONS Research Institute for Health Sciences and Technology, Faculty of Medicine, University of Mons (UMons), Mons, Belgium.
Email: Jerome.Lechien@umons.ac.be

Psychophysical evaluation was performed with the TDI (Medisense)[5] using the validated normative data (anosmia: TDI ≤ 16 points; hyposmia TDI ≤ 30.75 points). OD impact on quality of life (QoL) was evaluated with the French version of the ODQ,[6] a validated patient-reported outcome questionnaire measuring parosmia (0-12 points), QoL (0-57 points), and sincerity (0-18 points) subscores.[6]

Procedure and Control Groups

Posttraumatic patients were compared with a TDI-, age-, and gender-matched control group composed of non-injected patients with post-viral or posttraumatic OD (declined PRP because cost, fear, or too long distance between home and medical office). The PRP injection procedure was described in previous papers.[3,4] All posttraumatic and control individuals were instructed to adhere to an OT protocol[7] for 3 months despite a potential history of unsuccessful OT before injection. Olfaction was assessed before injection and at 3 to 4 months postinjection.

Statistical Analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS, v30.0; IBM Corp). Between-group comparisons (demographics, comorbidities, and olfactory outcomes at baseline and 3 months) used analysis of variance, Student's *t* test, and chi-square tests. Within-group olfactory changes were analyzed using paired Student's *t* tests. Associations between epidemiological, clinical, olfactory, and procedural outcomes were assessed using Spearman correlations.

Results

Thirty-three posttraumatic patients met the inclusion criteria (19 females). The mean age of posttraumatic patients was 46.5 ± 11.1 years. The control group included 40 OT-matched patients for age, gender ratio, and baseline TDI (**Table 1**). OT patients had post-viral (n = 37) or posttraumatic (n = 3; **Figure 1**). The mean OD duration of posttraumatic patients and controls was 55.6 ± 45.1 and 11.5 ± 2.0 months, respectively ($P = .001$; **Table 1**). Initial TDI scores were comparable across groups, while OT group showed significantly higher parosmia and sincerity statement scores (**Table 1**). All patients had adhered to the OT protocol.

Table 1. Demographics, Epidemiological, and Clinical Features

	Posttraumatic	Controls	
Outcomes	(n = 33)	OT (n = 40)	*P*-value
Age (mean, range)	46.5 ± 11.1	49.9 ± 15.9	NS
Sex			
Male	14 (42.4)	18 (45.0)	NS
Female	19 (57.6)	22 (55.0)	
Comorbidities			
Reflux	6 (18.2)	2 (5.0)	NS
Thyroid disorder	1 (3.0)	1 (2.5)	NS
Hypertension	1 (3.0)	2 (5.0)	NS
Depression	2 (6.1)	2 (5.0)	NS
Asthma	2 (6.1)	1 (2.5)	NS
Mellitus diabetes	0 (0)	1 (2.5)	NS
Cardiologic affections	0 (0)	0 (0)	NS
Respiratory insufficiency	1 (3.0)	0 (0)	NS
Renal insufficiency	0 (0)	1 (2.5)	NS
Hepatic insufficiency	1 (3.0)	0 (0)	NS
Allergy	3 (9.1)	1 (2.5)	NS
Tobacco consumption	4 (12.1)	2 (5.0)	NS
Duration of OD, mo	53.1 ± 39.0	11.5 ± 2.0	.001
Intervention preinjection			
Alpha lipoic acid	2 (6.1)	1 (2.5)	NS
Nasal corticosteroids	4 (12.1)	7 (17.5)	NS
Oral corticosteroids	1 (3.0)	2 (5.0)	NS
Vitamin B12	8 (24.2)	3 (7.5)	NS
Vitamin A	3 (9.1)	2 (5.0)	NS
Zinc	6 (18.2)	10 (25.0)	NS
Parosmia	3.9 ± 2.8	6.9 ± 3.9	.002
Life quality statement	27.4 ± 10.7	23.4 ± 7.8	NS
Sincerity statement	5.2 ± 2.9	7.0 ± 2.9	.016
ODQ total score	36.5 ± 14.0	37.2 ± 8.1	NS
Threshold	2.1 ± 2.1	1.8 ± 1.7	NS
Discrimination	3.5 ± 3.9	3.9 ± 2.7	NS
Identification	3.1 ± 3.6	3.6 ± 2.9	NS
TDI total score	8.4 ± 8.1	9.3 ± 5.0	NS

Abbreviations: NS, nonsignificant; OD, olfactory dysfunction; ODQ, olfactory disorder questions; OT, olfactory training; TDI, threshold, discrimination, and identification.

Preinjection to Postinjection Olfaction Changes

Following intervention, binary subjective olfactory improvement (yes/no) was reported by 66.7% (n = 22/33) of posttraumatic patients and 30.5% (n = 15/40) of OT patients. The mean time for detecting the first recovered odors was 5.4 ± 6.0 weeks in the posttraumatic group.

The ODQ and TDI changes over time are described in **Table 2**. In the posttraumatic group, the baseline TDI (8.4 ± 8.1) significantly increased at the 3-month posttreatment (16.5 ± 9.6; $P = .003$), reaching the minimal clinically important difference (MCID) of TDI (5.5).[8] In control group, the baseline TDI (9.3 ± 5.0) significantly increased after 3-month OT (13.3 ± 8.5; $P = .001$) without reaching the MCID. Note that the 3-month TDI was significantly higher in posttraumatic injected patients versus OT patients ($P = .038$). Threshold score improvements (Z) were significantly greater in the PRP group. No group achieved the MCID (5.2)[9] of ODQ.

Associations in Posttraumatic Group

Pearson correlation study reported that females had significantly higher postinjection threshold scores compared

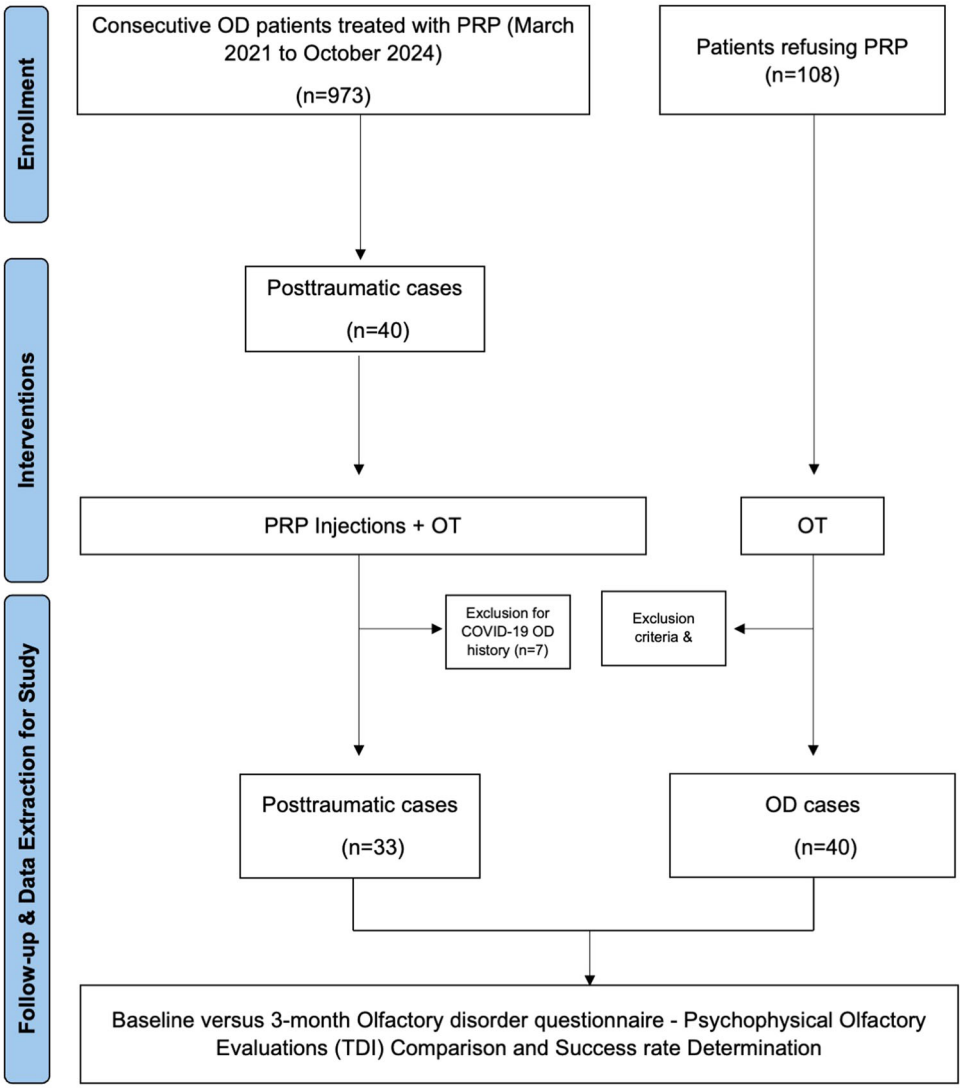

Figure 1. Chart flow. Matched control groups were composed from the database of platelet-rich plasma (PRP) injection of the first author. Only patients with full pre- to post-intervention threshold, discrimination, and identification (TDI) and olfactory disorder questionnaire (ODQ) data were included. OD, olfactory dysfunction; OT, olfactory training.

to males ($P = .036$). However, the female gender was associated with a higher postinjection parosmia score compared to males ($P = .037$). The baseline ODQ was positively correlated with the postinjection ODQ ($r_s = 0.653$; $P = .006$). The baseline TDI was positively correlated with the 3-month TDI ($r_s = 0.738$; $P = .001$). The duration of OD was not correlated with the post-PRP TDI and ODQ scores.

Discussion

To the best of our knowledge, this investigation is the first report of PRP effectiveness in posttraumatic OD patients. Currently, it has been reported that approximately 16.8% to 27% of posttraumatic OD patients may experience some degree of spontaneous recovery, which is attributed to the high degree of neuroplasticity of the olfactory system.[10-12] Despite distinct pathophysiological mechanisms between post-viral and posttraumatic OD,[13] PRP injection effectiveness into the olfactory cleft supports potential neural regeneration through growth factors and anti-inflammatory mediators. The patient's subjective recovery after PRP injection was 66.7% in the posttraumatic group, which was lower than post-COVID-19 patients (80.3%) regarding the literature.[8] Compared to post-COVID-19 OD, the mean duration before detecting the first recovered odors was substantially longer in posttraumatic cases (5.4 vs 3.4 weeks),[8] which may be attributed to the greater extent of cellular injury. Since the incidence of total anosmia is higher in posttraumatic patients than in those with post-viral conditions,[14] it is reasonable to assume that posttraumatic anosmia results from damage to the majority of nerve fibers, whereas in post-viral OD, some cells are likely preserved due to immune system activity. This hypothesis requires confirmation in future studies.

Despite promising results, the low number of posttraumatic patients, the lack of long-term follow-up, and

Table 2. Olfactory Dysfunction Features of Patients and Controls

					mo 0 versus mo 3	mo 3
Outcomes	Patients	Baseline	3 mo	*Z*	*P*-value	Intergroup
Parosmia	Posttraumatic	3.9 ± 2.8	3.9 ± 2.6	0.0	NS	0.007
	OT	6.9 ± 3.9	6.1 ± 2.9	−0.7	NS	
Life quality statement	Posttraumatic	27.4 ± 10.7	24.6 ± 10.4	−2.8	NS	NS
	OT	23.4 ± 7.8	23.7 ± 8.6	0.1	NS	
Sincerity statement	Posttraumatic	5.2 ± 2.9	4.6 ± 3.0	−0.7	NS	0.001
	OT	7.0 ± 2.9	8.3 ± 3.4	1.5	NS	
ODQ total score	Posttraumatic	36.5 ± 14.0	33.0 ± 13.3	−3.5	NS	NS
	OT	37.2 ± 8.1	38.1 ± 11.6	0.2	NS	
Threshold	Posttraumatic	2.1 ± 2.1	3.1 ± 3.1	1.0	.001	NS
	OT	1.8 ± 1.7	2.3 ± 2.3	0.5	.001	
Discrimination	Posttraumatic	3.5 ± 3.9	7.2 ± 4.7	3.7	.013	NS
	OT	3.9 ± 2.7	5.4 ± 4.0	1.5	.025	
Identification	Posttraumatic	3.1 ± 3.6	6.1 ± 3.7	3.0	.010	NS
	OT	3.6 ± 2.9	6.0 ± 4.0	2.4	.001	
TDI	Posttraumatic	8.4 ± 8.1	16.5 ± 9.6	8.1	.003	0.038
	OT	9.3 ± 5.0	13.3 ± 8.5	4.0	.001	

Abbreviations: mo, month; NS, nonsignificant; ODQ, olfactory dysfunction questionnaire; OT, olfactory training; TDI, threshold, discrimination, and identification.

neurophysiological evaluations are the primary limitations of the paper. The OT control group, consisting mainly of post-viral OD patients, represents a potential sample bias due to distinct clinical profiles, pathophysiological mechanisms, and recovery patterns. However, since posttraumatic OD is commonly more severe than post-viral OD and associated with poorer prognosis,[12,15] our intergroup comparison might have reached even more significant differences had we used a control group consisting solely of posttraumatic OD patients undergoing OT. Future prospective controlled studies should consider both posttraumatic groups with similar demographic and clinical outcomes. Moreover, the shorter duration of OD in controls could bias the results of the study, with potentially better natural recovery in controls compared to posttraumatic subjects. Thus, the differences across groups should be greater.

Conclusion

The injection of PRP into the olfactory cleft is an option for posttraumatic OD patients, reporting better recovery outcomes compared to those adhering to an OT protocol. Future randomized controlled trials are needed to evaluate the PRP effectiveness in posttraumatic OD patients.

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Author Contributions

Jerome R. Lechien, Design, acquisition of data, data analysis and interpretation, drafting, final approval, accountability for the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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