P-ISSN: 3025-6518
E-ISSN: 3025-0501

Almakki Health Informatics Journal

THE SYSTEMATIC REVIEW OF PLATELET RICH PLASMA INDUCED OLFACTORY IN PATIENTS WITH COVID 19

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KEYWORDS

Platelet Rich Plasma, Olfactory Dysfunction, Covid-19

ABSTRACT

Background: Olfactory Dysfunction (OD) is a common problem, with a substantial percentage of instances linked to COVID-19. This comprehensive study sought to assess the efficacy of platelet-rich plasma (PRP) in the treatment of COVID-19-related OD, which included anosmia, hyposmia, and parosmia. **Aim :** This study examined the efficacy of platelet-rich plasma (PRP), an autologous blood product with elevated growth factors, in treating COVID-19-related olfactory dynsfunction. **Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and SCIENCE DIRECT, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done. **Result:**In the PubMed database, the results of our search brought up 9 articles, whereas the results of our search on SCIENCE DIRECT brought up 108 articles. The results of the search conducted for the last year of 2014 yielded a total 17 articles for PubMed and 16 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 2 of which came from SCIENCE DIRECT. We included five research that met the criteria. **Conclusion:** In summary, injecting PRP directly into the olfactory cleft of individuals with post-COVID COD is a successful and simple treatment. We believe that the therapeutic efficacy of PRP injection may vary depending on the time of OD or with repeated doses. Further randomized controlled studies are needed to confirm these findings and explore the long-term impact of this innovative technique.

INTRODUCTION

As the global case count for coronavirus disease 2019 (COVID-19) climbed, so did the number of patients admitted to clinics with olfactory impairment (OD) (Pinney et al., 2020).

Up to 85% of COVID-19 patients present with OD, making it one of the most common symptoms. It has been shown that viral infection and inflammation alter the olfactory neuroepithelium, resulting in chronic olfactory dysfunction (COD). Similarly, it is believed that the persistence of the virus in the olfactory area, inducing inflammation, may be the explanation for extended OD in COVID-19 (Gorzkowski et al., 2020).

Olfactory dysfunction (OD) is one of the most often reported symptoms of COVID-19 infection, affecting more than 40% of patients to varying degrees, ranging from diminished or distorted to full loss of function. This is thought to be caused by COVID-19's detrimental effect on the olfactory neuroepithelium (White, 2021).

The normal course of post-COVID-19 OD is for symptoms to disappear by day 9, with more than 95% of patients seeing relief in less than 4 weeks. However, some people continue to suffer with OD for extended periods (Epstein et al., 2017). OD has had a terrible impact on the quality of life for those afflicted. In addition to the loss of enjoyment in life, the patient will be unable to detect harmful odors and poisonous chemicals.Almost 75% of patients experienced disease-related risks. The effects of OD do not end there; it is connected with major negative psychosocial impacts, including pathological mental health conditions (Tick et al., 2018).

Therapies for postviral and COVID-19-related OD have little effectiveness and lack evidence-based support. A Cochrane review revised in December 2020 identified no conclusive therapies for chronic COVID-19 OD. However, there are current clinical trials and newly published research. Olfactory training is the most effective therapy for COVID-19 OD, according to current research. Other therapy based on prepandemic findings include topical intranasal medicines and oral anti-inflammatory/neuroprotective drugs. However, the effectiveness of all currently suggested treatments is rather modest at best (Tick et al., 2018).

Currently, there are no long-term, effective therapies for OD. This is mostly due to a lack of high-level evidence in the literature as a consequence of limited financing, inadequate participants, and intrinsic methodological and/or hypothesis-driven discrepancies that prohibit results from being generalized. However, the impact of the COVID-19 epidemic has prompted significant efforts and financing for OD therapy. According to a 2023 position paper on OD, systemic (short-term) and/or intranasal (long-term) corticosteroids should be recommended to patients with OD caused by chronic rhinosinusitis (CRS), severe allergic rhinitis, or other inflammatory diseases. When intranasal corticosteroids are utilized, a delivery method that can reach the olfactory cleft (rinses) should be considered (Tick et al., 2018).

Platelet-rich plasma (PRP) has lately been recommended as an OD therapy, with promising results. PRP is an autologous or homologous biologic product derived from freshly extracted blood with a high platelet concentration in a limited plasma volume. PRP has anti-inflammatory and pro-regenerative effects, including overexpression of growth factors such as transforming growth factor-beta, endothelial growth factor, vascular endothelial growth factor, nerve growth factor, and insulin-like growth factor, which are found in alpha granules. Together, these factors stimulate angiogenesis, cell proliferation, differentiation, and survival. Since the 1970s, these latter qualities have been used to improve tissue healing and regeneration in a wide range of clinical and surgical situations. Furthermore, PRP can promote axon regeneration and neuroregeneration (Wang, Liu, & Wang, 2022).

This study examined the efficacy of platelet-rich plasma (PRP), an autologous blood product with elevated growth factors, in treating COVID-19-related olfactory dysfunction.

METODE PENELITIAN

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate (King, Keohane, & Verba, 2021).

For the purpose of this literature review, we review published literature contains the effectiveness of platelet rich plasma in the treatment of Covid-19 related olfactory. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole (King et al., 2021).

RESULTS AND DISCUSSION

Results

In the PubMed database, the results of our search brought up 9 articles, whereas the results of our search on SCIENCE DIRECT brought up 108articles. The results of the search conducted for the last year of 2014 yielded a total 17articles for PubMed and16articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 4of which came from PubMed and 2 of which came from SCIENCE DIRECT. We included five research that met the criteria.

Showed that olfactory function following COVID-19 can improve spontaneously after 6 months and much more so with PRP injection (Jafar, Lasso, Shorr, Hutton, & Kilty, 2021). These findings support PRP's potential as a safe therapy option for individuals with COVID-19-related smell loss, and larger-scale research will assist to further evaluate its efficacy.

Showed that PRP injection into the olfactory clefts is both safe and effective, according to patient reports (Yan, Mundy, & Patel, 2020). The results of this exploratory investigation show that PRP injection may be effective on subjective and psychophysical assessments, but further randomized controlled trials are needed to evaluate whether it is superior than placebo.

Showed that one month following injection of PRP into the olfactory cleft, the olfactory threshold can be increased. Furthermore, our findings indicate that timing of therapy may be critical, and that PRP is a safe treatment, since no side effects were recorded during the trial.

Showed that the platelet-rich plasma group demonstrated a considerable improvement in olfactory threshold values when compared to the control group (Aboelmagd, Mohamed, Abdelmegeed, & Eltahan, 2021). There were no reported side effects or adverse events associated with platelet-rich plasma injections.

Table 1.

The litelature include in this study

Author	Origin	Method	Sample	Result
Yan et al, 2022[10]	USA	Randomized controlled study	35 patients	A total of 35 individuals were enrolled, and 26 finished the research. PRP therapy resulted in a 3.67-point (95% CI: 0.05-7.29, p = 0.047) larger

				improvement in olfaction than the placebo group after 3 months, as well as a higher response rate (57.1% vs 8.3%, odds ratio 12.5 [95% precise bootstrap confidence range, 2.2-116.7]). PRP therapy resulted in a larger improvement in scent discrimination than placebo, but there was no change in smell identification or threshold. Subjective evaluations showed no change between PRP and placebo. There were no adverse consequences noted.
Leichen et al, 2023[11]	France	Randomized controlled study	87 patients	The assessments included 87 individuals with anosmia (N = 30), hyposmia (N = 40), or parosmia (N = 17), with an average OD duration of 15.7 months. All patients had a successful PRP injection, which took an average of 18.4 ± 3.4 min. The adverse events included transitory epistaxis (N = 31), parosmia after xylocaine spray (N = 10), and vasovagal episode (N = 2). 41 (47%) and 22 (25%) patients said that the injection technique was somewhat or somewhat uncomfortable. Thirty-seven individuals were examined two months following injection. The average ODQ and TDI scores improved considerably from baseline to 2-month post-injection ($p < 0.01$). The olfactory improvement took an average of 3.6 ± 1.9 weeks.

Steffens et al, 2022[12]	Belgium	Randomized controlled study	56 patients	At one month post-PRP injection, the PRP group's mean TDI scores increased by 6.7 points, whereas the controls showed no meaningful improvement. There was a moderate negative connection between TDI score differential and OD duration in the PRP group but not in the controls. The PRP group had a considerably greater mean self-assessment of improvement in smell function (1.8, mild-to-moderate) than the control group. There were no adverse effects recorded during the research.
Evman et al, 2023[13]	Turkey	Randomized controlled study	25 patients	A total of 25 patients were randomly assigned to two groups: platelet-rich plasma (n=12) and control (n=13). In the control group, the mean scent detection threshold score decreased from 5.69 (SD 0.66) to 5.77 (SD 0.70), but the mean smell identification test score increased from 11.20 (SD 1.12) to 11.85 (SD 1.57). A post-hoc analysis found a significant difference between groups in smell detection threshold (mean difference 0.07; p=0.994) and smell identification test (mean difference -0.50; p=0.703) scores (mean difference 0.69; p=0.037; mean difference 3.32; p<0.001).
Abo El Naga et al, 2022[14]	Egypt	Randomized controlled study	60 patients	A pilot trial included 60 individuals with post-COVID parosmia who did not react to a 3-month course of olfactory training, topical corticosteroids, omega-3,

	vitamin B12, and zinc supplementation. The patients were divided randomly and evenly into two groups. The case group had three PRP injections in the olfactory cleft at 3-week intervals. The case group had a substantial improvement in VAS for parosmia ($p < 0.00001$), whereas the control group also saw significant improvement ($p = P = 0.00148$). The case group showed significantly greater improvement ($p = 0.002$).

Showed that Platelet-rich plasma injection in the olfactory cleft provides a therapeutic alternative for individuals with post-COVID-19 olfactory parosmia who have not responded to conventional conservative therapy (Tong, Wong, Zhu, Fastenberg, & Tham, 2020).

Discussion

This systematic review involved a total of 263 data of Covid 19 patients with olfactory dysfunction that got treatments of platelet rich plasma (Chung et al., 2020). This study examined the efficacy of platelet-rich plasma (PRP), an autologous blood product with elevated growth factors, in treating COVID-19-related smell loss. PRP is widely utilized in various therapeutic sectors and has proven promise in peripheral nerve regeneration by stimulating vascular and axonal regeneration via growth factors and regulating the inflammatory response in the microenvironment.

Olfactory dysfunction (OD) is a prevalent illness with a detrimental impact on quality of life, estimated to affect up to 20% of the global population. It is also connected with increased morbidity and mortality. OD can be classified as quantitative when the intensity of smells is impacted, and qualitative when the quality of odors is altered or smell is perceived in the absence of an olfactory stimulus. Qualitative disorders, such as parosmia, may involve qualitative alterations that are regarded negatively. Qualitative alterations are seldom observed alone; they are frequently present in conjunction with a quantitative disruption.OD can be classified into three types according on the anatomical location of the lesion: conductive, sensorineural, and central. However, anatomical categorization can be restricted because the three aforementioned categories are not mutually exclusive, thereby underestimating the underlying pathology (Moffitt, 2017).

Because Platelet-Rich Plasma (PRP) is a relatively new discovery, limited investigations on its effectiveness in humans have been done. PRP has been shown to be beneficial in various case-control studies as well as non-controlled clinical trials. In addition to treating chronic skin and soft tissue ulcers, platelet-rich plasma has been used in periodontal and dental surgery, maxillofacial surgery, orthopaedic and trauma surgery, and cosmetic and plastic surgery. PRP

shown efficacy in managing pain in temporomandibular joint osteoarthritis, rotator cuff injuries, tendinitis, and low back pain, with significant changes in both the long and short term (Solmaz & Orscelik, 2019).

PRP exhibited potential in peripheral nerve regeneration by stimulating vascular and axonal regeneration with growth factors and regulating the inflammatory response in the microenvironment. Platelets release growth factors such as VEGF, EGF, TGF-β-1, PDGF, HGF, IGF-I, bFGF, and CTGF, all of which contribute to tissue proliferation. One important feature of these platelets is their ability to secrete cytokines, chemokines, and chemokine receptors, which helps to regulate inflammatory responses and immunological elements of tissue repair. Anti-inflammatory cytokines can help avoid excessive leukocyte recruitment (Musolino et al., 2017).

PRP administration may be a safe and effective therapy with extremely promising outcomes. In fact, it appears to enhance olfaction not just in individuals with COVID-19 complications, but also in those who have lost their capacity to smell due to trauma, rhinitis or rhinosinusitis, or even a surgical treatment. The safety of PRP usage has been thoroughly established in the literature, as corroborated by the publications cited above, which found no serious side effects. Because PRP is an autologous biological product derived from the patient's blood, there is no risk of rejection or disease transmission, nor is immune suppression required (Behaegel, Ní Dhubhghaill, Koppen, & Zakaria, 2017). It also offers a financial advantage because injections are administered in-office under local anesthetic, and one injection has been shown to provide considerable improvement for the majority of patients. Furthermore, the ability to distribute PRP specifically to the nasal fossae by topical administration represents a significant improvement over systemic corticosteroids, which are frequently supplied indefinitely to this patient population and come with a slew of adverse effects.

Furthermore, outcomes were reported inconsistently among the available research, with some including only qualitative outcomes and others focusing entirely on quantitative results. Finally, the small number of accessible research limits the generalizability of our findings, since they may not adequately reflect the phenomena in its totality. To this day, no standards specify when to intervene in the normal course of anosmia or hyposmia. Notably, there was a propensity to omit patients with a history of OD lasting less than 6 months, as spontaneous recovery is still possible, as well as patients with a history longer than 12 months, because peripheral nerve regeneration is doubtful. Furthermore, the duration of improvement in olfactory function remains uncertain. Further research with bigger sample numbers and longer follow-up are required to confirm the evidence that PRP is a safe and effective therapy option for OD patients.

CONCLUSION

In summary, injecting PRP directly into the olfactory cleft of individuals with post-COVID COD is a successful and simple treatment. We believe that the therapeutic efficacy of PRP injection may vary depending on the time of OD or with repeated doses. Further randomized controlled studies are needed to confirm these findings and explore the long-term impact of this innovative technique.

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