Organization's Unique Protocol ID

2025-06-010C

Brief Title

Topical Versus Injection PRP for Olfactory Dysfunction

Acronym

TOP-IN

Study Type

Interventional

Official Title

Carrier-Assisted Topical Application Versus Intranasal Injection of Autologous Platelet-Rich Plasma for Olfactory Dysfunction: A Randomized Controlled Trial

Secondary IDs

Other Grant/Funding Number: after funding being approved
Grantor or Funder Organization: Taipei Veterans General Hospital

Document Date:

July 29, 2025

Study Protocol with Statistical Analysis Plan and Informed Consent Form

Detailed Description:

Persistent olfactory dysfunction (OD) is a common sequela of viral upper respiratory tract infections, including COVID-19, and can significantly affect patients' quality of life, nutrition, and safety. Current treatment options are limited, with olfactory training being the primary evidence-based non-pharmacological therapy. Autologous platelet-rich plasma (PRP) is a concentration of platelets obtained from a patient's own blood, rich in growth factors and cytokines that promote neuronal regeneration, tissue repair, and neuroplasticity. Early clinical studies suggest PRP may improve olfactory function, but the optimal method for delivering PRP to the olfactory cleft remains unknown.

This single-blind, randomized controlled trial will include a total of 60 adult patients aged 18-80 years old with olfactory loss (hyposmia or anosmia) persisting for more than 3 months despite standardized olfactory training, confirmed by a reduced Sniffin' Sticks TDI score.

PRP will be prepared on-site immediately before application using a standardized centrifugation protocol to achieve a platelet concentration 2-3 times above baseline. efficacy and safety of two PRP delivery methods will be compared:

(1) *Intranasal Injection Group*: Autologous PRP will be injected directly into the mucosa of the olfactory cleft under endoscopic guidance. After topical anesthesia with lidocaine spray and decongestion with oxymetazoline, a 25-gauge needle will be used to deliver approximately 1 mL of PRP into multiple sites along the superior nasal cavity bilaterally.

(2) *Carrier-Assisted Topical Application Group*: Four pieces of sterile, bioabsorbable carrier (Gelfoam sponge) will be soaked with approximately 5 mL of autologous PRP. Under endoscopic guidance, two pieces of PRP-soaked carrier will be placed gently into each side of olfactory cleft, ensuring contact with the olfactory mucosa. Carriers will remain in place for a short duration to allow diffusion of PRP before dissolving naturally or being removed.

Primary Outcome:

(1) Sniffin' Sticks Olfactory Test: Change in TDI score from baseline to 1 and 3 months post-intervention (with possible follow-up at 6 and 12 months).

Secondary Outcomes:

(2) Procedure evaluation: Record procedure time; assess pain via visual analogue scale (0–10) immediately post-procedure; document adverse events (e.g., persistent bleeding, infection) during procedure and within 2 weeks post-intervention.

(3) Sniffin' Sticks Parosmia Test: Assesses qualitative olfactory function in parosmia at baseline and 3-month follow-up.

(4) Montreal Cognitive Assessment (MoCA): Widely used to screen for mild cognitive impairment; olfactory loss may reduce sensory input to the brain, potentially impacting neural processing and cognitive function at baseline and 3-month follow-up.

(5) Visual Analogus Scale and Olfactory-Related Questionnaires: QOD, SNOT-22, PQ, subjective improvement ratings, 20-item retronasal olfactory test, SSParoT, procedure tolerability, and adverse event rates assessed pre-intervention and at 1 and 3 months (with possible follow-up at 6 and 12 months) post-intervention.

(6) Retronasal Olfactory Test: Uses standardized odorized powders/capsules in the oral cavity; participants exhale through the nose and rate the perceived odor; evaluates olfactory function via the retronasal route at pre-intervention and at 3 months post-intervention.

(7) Beck Depression Inventory (BDI): Standardized self-report tool assessing depressive symptom severity; olfactory loss from viral or other causes has been linked to mood disturbances and reduced emotional well-being.

Post-intervention care: All participants will continue standardized daily olfactory training for 12 weeks after PRP administration. Follow-up visits at 1 week, 1 month, and 3 months will assess smell function, symptom changes, and safety.

This study aims to determine whether carrier-assisted topical PRP application is as effective or superior to intranasal PRP injection for improving olfactory function, while potentially offering a less invasive and more tolerable treatment approach. Results will help define optimal PRP delivery strategies for olfactory rehabilitation in clinical practice.

Reference

Yan, C. H., et al. (2020). The use of platelet-rich plasma in treatment of olfactory dysfunction: A pilot study. *Laryngoscope Investigative Otolaryngology, 5*(2), 187–193.

Lechien, J. R., et al. (2022). Platelet-rich plasma injection in the olfactory clefts of COVID-19 patients with long-term olfactory dysfunction. *European Archives of Oto-Rhino-Laryngology, 280*(1), 2351–2358.

Moffa, A., et al. (2024). Platelet-rich plasma for patients with olfactory dysfunction: Myth or reality? A systematic review. *Journal of Clinical Medicine, 13*(3), 782.

Duffy, A., et al. (2024). Topical platelet-rich plasma as a possible treatment for olfactory dysfunction: A randomized controlled trial. *International Forum of Allergy & Rhinology, 14*(9), 1455–1464.

Abo El Naga, et al. (2022). The potential therapeutic effect of platelet-rich plasma in the treatment of post-COVID-19 parosmia. *The Egyptian Journal of Otolaryngology, 38*(1), 130.

Sekine, R., et al. (2022). Assessment of postviral qualitative olfactory dysfunction using the short SSParoT in patients with and without parosmia. *European Archives of Oto-Rhino-Laryngology*.

Heilmann, S., et al. (2002). Clinical assessment of retronasal olfactory function. *Archives of Otolaryngology–Head & Neck Surgery, 128*(4), 414–418.

Landis, B. N., et al (2010). Evaluating the clinical usefulness of structured questions in parosmia assessment. *The Laryngoscope, 120*(8), 1707–1713.

Yuan, B.-C., et al (2010). Investigation of the Sniffin' Sticks olfactory test in Taiwan and comparison with different continents. *Journal of the Chinese Medical Association, 73*(9), 483–486.

Nasreddine, Z. S., et al (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*(4), 695–699.

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同 意 執 行 證 明 書

日期：114 年 7 月 29 日

IRB 編號：2025-06-010C

部門/計畫主持人：耳鼻喉頭頸醫學部 / 趙勻廷醫師

計畫名稱：自體血小板濃厚液以載體輔助局部置入與經鼻注射治療嗅覺功能障礙之隨機對照研究

本案經本院人體試驗委員會（三）審查通過，由本院人體試驗委員會（三）自行列管，由臨床研究受試者保護中心複核相關文件，代表機構正式同意本案執行。

臺北榮民總醫院
臨床研究受試者保護中心主任
曾令民副院長

臺北榮民總醫院 臨床研究受試者保護中心 Human Research Protection Center Taipei Veterans General Hospital

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Implementation Letter

Date: Jul 29, 2025

TPEVGH IRB No.: 2025-06-010C

Department/Principal Investigator: Department of Otolaryngology-Head and Neck Surgery / Yun-Ting Chao, M.D.

Protocol Title: Carrier-Assisted Topical Application Versus Intranasal Injection of Autologous Platelet-Rich Plasma for Olfactory Dysfunction: A Randomized Controlled Trial.

The protocol has been approved by the Institutional Review Board (3) of Taipei Veterans General Hospital and supervised by 「the Institutional Review Board (3) of Taipei Veterans General Hospital」. After the review by Human Research Protection Center, the implementation of the protocol is approved.

臺北榮民總醫院 臨床研究受試者保護中心 Human Research Protection Center Taipei Veterans General Hospital

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