

Letter to the Editor

In reference to *Intranasal Corticosteroid Treatment on Recovery of Long-Term Olfactory Dysfunction Due to COVID-19*

Key Words: anosmia, coronavirus, corticosteroids, COVID-19, maxillofacial surgery, olfactory dysfunction, olfactory function, SARS-CoV-2, smell.

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Dear Editor,

We have read the trial by Hosseinpoor et al.¹ analyzing the efficacy of nasal corticosteroids (NCs) in the treatment of long-lasting COVID-19 related olfactory disorders (OD). Authors concluded that NC may have a positive effect on the recovery process. Given the high social impact of COVID-19-related OD^{2–4} and regarding the lack of specific therapies for post-viral OD,^{5,6} this topic is particularly important. NCs represent a first-line therapy in the treatment of OD-related to chronic rhinosinusitis.⁷ The rationale for their use in COVID-19-related-OD arises from the detection of inflammatory olfactory neuropathy during the acute phase of SARS-CoV-2 infection.⁸ However, the anatomical damage in patients with persistent OD is probably more complex and includes a direct cytopathic effect of the virus at the level of sustentacular cells, a downregulation of the expression of olfactory receptors in olfactory sensory neurons, and a disruption of the architecture of the neuroepithelium.^{9,10}

Although it may affect the recovery time,^{11,12} the early administration of corticosteroids during the acute phase of infection does not appear to have an effect on the long-term overall recovery rate.¹³ Some preliminary studies reported promising data in the treatment of persistent OD¹⁴ that have not been supported by larger trials^{15–17} and meta-analysis.¹⁸ This is consistent with studies in post-viral olfactory loss (PVOL) prior to COVID-19,^{19,20} probably due to a failure of delivery to the OE.²¹

Hosseinpoor et al. found no significant differences in anosmia, hyposmia, and normosmia rates between the two groups, although treated patients reported a significantly higher increase in olfactory scores. However, these results must be considered with caution because the therapy group had a significantly higher parosmia rate than controls at baseline (40% vs. 14%, $p = 0.03$). Parosmia has been indicated as a favorable prognostic factor for the

recovery of OD in PVOL, and this may therefore have influenced the results.^{20–23} NCs are generally well tolerated, with a very low risk of significant adverse effects, and when using fluticasone or mometasone there is negligible systemic absorption, although this study suggests that they could accelerate recovery in the acute phases of infection, there is currently insufficient evidence to justify their prescription in patients with persistent OD or to prevent long-term dysfunction. Trials using systems that allow optimal delivery of the NCs at the level of the olfactory neuroepithelium would be highly desirable.

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BIBLIOGRAPHY

- Hosseinpoor M, Kabiri M, Haghi MR, et al. Intranasal corticosteroid treatment on recovery of long-term olfactory dysfunction due to COVID-19. *Laryngoscope*. 2022;132:2209–2216. <https://doi.org/10.1002/lary.30353>.
- Boscolo-Rizzo P, Hummel T, Hopkins C, et al. High prevalence of long-term olfactory, gustatory, and chemesthesis dysfunction in post-COVID-19 patients: a matched case-control study with one-year follow-up using a comprehensive psychophysical evaluation. *Rhinology*. 2021;59:517–527.

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3. Vaira LA, Salzano G, Le Bon S, et al. Prevalence of persistent olfactory disorders in patients with COVID-19: a psychophysical case-control study with 1-year follow-up. *Otolaryngol Head Neck Surg.* 2022;167:183-186.
4. Vaira LA, Gessa C, Deiana G, et al. The effects of persistent olfactory and gustatory dysfunctions on quality of life in long-COVID-19 patients. *Life.* 2022;12:141.
5. Javari A, Holbrook EH. Therapies for olfactory dysfunction—an update. *Curr Allergy Asthma Rep.* 2022;22:21-28.
6. Huart C, Philpott CM, Altundag A, et al. Systemic corticosteroids in coronavirus disease 2019 (COVID-19)-related smell dysfunction: an international view. *Int Forum Allergy Rhinol.* 2021;11:1041-1046.
7. Hummel T, Whitcroft KL, Andrews P, et al. Position paper on olfactory dysfunction. *Rhinol Suppl.* 2017;25:1-30.
8. Kirschenbaum D, Imbach LL, Ulrich S, et al. Inflammatory olfactory neuropathy in two patients with COVID-19. *Lancet.* 2020;396:166.
9. Vaira LA, Hopkins C, Sandison A, et al. Olfactory epithelium histopathological findings in long-term COVID-19 related anosmia. *J Laryngol Otol.* 2020;134:1123-1127.
10. Zazhytska M, Kodra A, Hoagland DA, et al. Non-cell-autonomous disruption of nuclear architecture as a potential cause of COVID-19-induced anosmia. *Cell.* 2022;185:1052-1064.e12.
11. Shigh CV, Jain S, Parveen S. The outcome of fluticasone nasal spray on anosmia and triamcinolone oral paste in dysgeusia in COVID-19 patients. *Am J Otolaryngol.* 2021;42:102892.
12. Lechien JR, Hoch CC, Vaira LA, Saussez S. The interest of fluticasone nasal spray in COVID-19 related anosmia is still not demonstrated. *Am J Otolaryngol.* 2021;42:103008.
13. Saussez S, Vaira LA, Chiesa-Estomba CM, et al. Short-term efficacy and safety of oral and nasal corticosteroids in COVID-19 patients with olfactory dysfunction: a European Multicenter Study. *Pathogens.* 2021;10:698.
14. Vaira LA, Hopkins C, Petrocelli M, et al. Efficacy of corticosteroid therapy in the treatment of long-lasting olfactory disorders in COVID-19 patients. *Rhinology.* 2021;59:21-25.
15. Abdelalim AA, Mohamady AA, Elsayed RA, Elawady MA, Ghallab AF. Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: a randomized controlled trial. *Am J Otolaryngol.* 2021;42:102884.
16. Rashid RA, Zgair A, Al-Ani RM. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: a randomized double-blind placebo-controlled study. *Am J Otolaryngol.* 2021;42:103033.
17. Genetzaki S, Tsakiropoulou E, Nikolaidis V, Markou K, Konstantinidis I. Postinfectious olfactory dysfunction: oral steroids and olfactory training versus olfactory training alone: is there any benefit from steroids? *ORL J Otorhinolaryngol Relat Spec.* 2021;83:387-394.
18. Kim DH, Kim SW, Kang M, Hwang SH. Efficacy of topical steroids for the treatment of olfactory disorders caused by COVID-19: a systematic review and meta-analysis. *Clin Otolaryngol.* 2022;47:509-515.
19. Blomqvist EH, Lundblad L, Bergstedt H, Stjerne P. Placebo-controlled, randomized, double-blind study evaluating the efficacy of fluticasone propionate nasal spray for the treatment of patients with hyposmia/anosmia. *Acta Otolaryngol.* 2003;123:862-886.
20. Yan CH, Overvest JB, Patel ZM. Therapeutic use of steroids in non-chronic rhinosinusitis olfactory dysfunction: a systematic evidence-based review with recommendations. *Int Forum Allergy Rhinol.* 2019;9:165-176.
21. Bateman ND, Whymark AD, Clifton NJ, Woolford TJ. A study of intranasal distribution of azelastine hydrochloride aqueous nasal spray with different spray techniques. *Clin Otolaryngol.* 2002;27:327-330.
22. Hummel T, Lötsch J. Prognostic factors of olfactory dysfunction. *Arch Otolaryngol Head Neck Surg.* 2010;136:347-351.
23. Liu DT, Sabha M, Damm M, et al. Parosmia is associated with relevant olfactory recovery after olfactory training. *Laryngoscope.* 2021;131:618-623.