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Persistent daily headache and olfactory dysfunction after COVID-19: a case-control study

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Introduction

COVID-19 is associated with a high prevalence of olfactory disorders, with hyposmia or anosmia reported in 47–53% of individuals during the acute phase, persisting beyond six months in 10–37% of cases. Headache affects approximately 47% of patients acutely and may persist in 6–45%. Co-occurrence of olfactory dysfunction and headache in acute COVID-19 has been documented, and a shared neuroinflammatory pathophysiology involving the olfactory bulb and trigeminovascular system has been proposed. New daily persistent headache (NDPH) is a recognized post-COVID phenotype, and its association with olfactory dysfunction remains poorly understood.

Objective

To investigate whether persistent COVID-19-related daily headache is associated with olfactory dysfunction, and to examine correlations between headache severity, olfactory impairment, and depressive and anxiety symptoms.

Methods

Case-control study with participants from a cohort of COVID-19 patients with acute headache at a specialized headache outpatient clinic. Cases (n=20) had headache persisting over one year post-infection. Controls (n=40) with headache resolved after the acute phase were matched by sex, age, and time since acute COVID-19. Olfactory function was assessed using the Brazilian version of the UPSIT® scale. Headache impact was evaluated with Headache Impact Test (HIT-6), and mood symptoms with The Hospital Anxiety and Depression Scale (HADS). Headache diagnosis followed ICHD-3 criteria. Logistic regression adjusted for depression and anxiety was performed.

Results

All 20 cases were diagnosed with NDPH (18 migraine-like, 2 tension-type). No MRI abnormalities were found. Overall, 85% of participants had olfactory dysfunction: 63.3% mild hyposmia, 16.7% moderate, 5% severe; no anosmia was identified. UPSIT scores did not differ significantly between groups (31.45±3,3 vs. 32.08±2,21; p=0.534). The analysis showed no significant association between persistent headache and moderate to severe hyposmia (40% vs. 17,5%; OR=0.318; p=0.058); adjusted logistic regression also did not reach significance (adjusted OR=0.212; 95% CI: 0.034–1.19; p=0.077). No correlations were found between olfactory scores and headache intensity, frequency, or HIT-6. A significant negative correlation was observed between olfactory severity and depressive scores in the case group (rs=−0.473; p=0.035) and overall sample (rs=−0.300; p=0.02).

Conclusion

Persistent post-COVID daily headache was not independently associated with greater olfactory dysfunction after adjustment for mood symptoms. However, worse olfactory function correlated with higher depressive burden among patients with persistent headache, suggesting a shared neuroinflammatory basis. These findings indicate that post-COVID headache evaluation should routinely include olfactory screening alongside depression and anxiety scales.

Keywords:
Long COVID
Post-COVID-19 headache
New daily persistent headache
Olfactory dysfunction
Hyposmia

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