

# Post-COVID-19 Syndrome? New daily persistent headache in the aftermath of COVID-19

Síndrome Pós-COVID-19? Nova cefaleia diária persistente após COVID-19

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Dear Editor,

We read with great interest the systematic review article entitled “Neurological complications in patients with SARS-CoV-2 infection: a systematic review” by Munhoz et al<sup>1</sup>, published in this journal in May 2020. We want to congratulate the authors for this successful article and add our own contributions.

Recently, we noticed frequent clinical visits (General Neurology Outpatient Clinic and a Radiology Clinic) with complaints suggestive of New Daily Persistent Headache (NDPH) following recovery from SARS-CoV2 infection, which is characterized by a clear and distinct onset, persistent headache. It is known that extracranial viral infections are the main triggering factor of NDPH, in addition to stressful life events and invasive procedures such as intubation<sup>2</sup>.

Headache is a frequent symptom associated with ongoing SARS-CoV2 infection, as reported by Munhoz et al. (up to 34%); however, headache persistence has been observed even weeks after recovery<sup>3</sup>, and as described in case reports and in the authors' experience, enough to fulfill International Classification of Headache Disorders, 3rd edition (ICHD-3), diagnostic criteria for NDPH. To our knowledge, there is still no comprehensive review of remote morbidities following recovery.

In our experience, the following patterns were agreed upon: they had mild or moderate respiratory symptoms,

treated on an outpatient basis, mainly without a diagnosis of pre-existing primary headache, had characteristics of holocranial, pressure-like pain starting within 2 weeks after recovery of respiratory symptoms, no pathological causal findings have been observed in contrasted imaging studies (excluding cerebral venous thrombosis, a known neurological complication of SARS-COV2 infection).

The pathophysiology of NDPH is largely unknown, some studies believe that the pain may be due to the production of cytokines and persistent glial activation that arise in response to precipitating events<sup>4</sup>, which is also one of the hypotheses for CNS involvement by COVID-19, thus occurring synergy between pathophysiological mechanisms.

In clinical practice, most headache specialists treat NDPH based on the main headache phenotype, whether it is migraine or tension-type. No medication has shown to be advantageous in the studies conducted to date. As such, prophylactic treatment was used mostly with a tricyclic antidepressant or anticonvulsant (namely, amitriptyline and topiramate), with varying success<sup>4,5</sup>.





In our opinion, as we follow an increasing number of patients recovered after SARS-CoV-2 infection, a better understanding of the pathophysiology and course of the disease (and therefore the best treatment approach) is certainly warranted.

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