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Understanding the Process Involved in Post-COVID Headache Development and What the Literature Suggests as Therapeutic Approach: A Literature Review

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Introduction

After the emergence of SARS-CoV-2, numerous individuals were affected and continue to experience lingering effects, prompting extensive research. Headache, being a common worldwide condition, was observed in the post-COVID-19 context, leading to the identification of a phenomenon known as "long COVID," a wide range of symptoms that arise after recovery from acute SARS-CoV-2 infection, persisting for more than 12 weeks after the onset of the disease.

Significant research in the literature indicates prevalent neurological manifestations in post-COVID- 19 syndrome, whether due to neuroinvasion or systemic infection. Post-infection headache, well- documented and recognized by the International Classification of Headache Disorders, 3rd edition (ICHD-3), gains attention as a complication in this context, due to its potential for moderate to severe intensity and its persistence, which contribute to the resulting disability associated with headache. In this study, we will review what the literature says about this phenomenon and the most recommended therapeutic approaches for these patients. **Objective**

This study was conducted through a systematic literature review, addressing the topic of headache and COVID-19, in the PubMed, Scielo, and UpToDate databases. The parameters used for evaluation include English and Portuguese languages, with publication dates ranging from 2019 to 2023.

Methods

The purpose of this work is to understand the inflammatory process responsible for post- COVID headache, aiming to establish a line of reasoning that facilitates decision-making in the therapeutic approach to these patients by non-specialist physicians. **Results**

Post-COVID condition is not directly related to active viral infection and infectivity but rather to a prolonged pro-inflammatory res-ponse (cytokine storm), which can lead to mast cell hyper-responses, neuroinflammation through IL-6, and overactivation of ACE2 receptors, the same mechanisms associated with tension headaches and migraines. Therefore, SARS-CoV-2 infection shares common mechanisms with the pathophysiology of headaches, supporting the idea that patients with no previous history of headaches may subsequently develop a persistent headache of post-infectious origin. This manifestation may meet the criteria for New Daily Persistent Headache (NDPH), characterized by severe and continuous pain from its onset, following a systemic trigger, and with a phenotype resembling migraine or tension-type headache. In light of this, it has been observed that the therapy for these individuals is based on the inflammatory characteristic of the headache, suggesting the use of common analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief, lifestyle changes to reduce stress, and physiotherapy to reduce muscle tension. Furthermore, it is recommended that patients previously diagnosed with headache continue with specific treatment, and for patients diagnosed with post-COVID headache, therapy should be tailored to the subtype that best fits their presentation.

Conclusion

Post-COVID headache is a relatively new condition, and although there are already studies on the subject, they are still very recent, making it challenging to establish defined protocols and treatments for this condition. However, in light of the pathophysiology better established by the data collected to date, it can be understood that this condition originates from an inflammatory process similar to tension headaches and migraines. Therefore, an individualized therapeutic approach for each patient is recommended. Additionally, the use of pain relief medications and the management of precipitating or aggravating factors are also advised. It is further emphasized the importance of research in this area to develop new therapeutic options and personalize treatment for these individuals, aiming to better understand this condition and improve the approach to these patients.

Keywords: SARS-CoV-2; COVID-19; headaches; Migraine Disorders.