**Approach to Headache in Patients with COVID-19**

**Abordagem da Cefaleia no Doente com COVID-19**

**Keywords**: COVID-19; Headache; Migraine; Headache Disorders, Secondary; Tension-Type Headache

**Palavras-chave**: Cefaleia; Cefaleia Tipo-tensão; COVID-19; Enxaqueca; Perturbações da Cefaleia Secundários

Dear Editor,

Headache is one of the most common neurological symptoms of COVID-19. It has an estimated prevalence of 6% to 71% with most studies reporting 6% to 21%. It often appears simultaneously with other COVID-19 symptoms, is diffuse, pressing or pulsating, and of moderate to severe intensity. Fever, physical activity, head movements and coughing are common triggers. Previous migraine history seems to correlate with earlier, longer, and more intense headaches.2

The etiology seems multifactorial: direct attack of the trigeminovascular system via transsynaptic or bloodstream dissemination, immune-mediated inflammatory responses secondary to cytokine storm, coagulopathy, and hypoxemia.1 Once hypothesized as a specific symptom of the infection, there is some consensus nowadays on the probable absence of a COVID-19 specific headache. It has been described as a very common symptom of patients with other acute respiratory illnesses, as an adequate physiological response to an acute infection.3

Most headaches in a patient with COVID-19 fit the definition of a secondary headache in the category 9.2.2 ‘Headache attributed to systemic viral infection’ (International Classification of Headache Disorders 3, ICHD3), caused by and occurring in association with other symptoms and/or clinical signs of a systemic viral infection, in the absence of meningitis or encephalitis. No further subcategorization exists in ICHD3. Nevertheless, some authors suggest to further categorize the headache in the two most common phenotypes: migraine-like, affecting around 25% of the patients (even in the absence of a previous migraine diagnosis) and tension-type-like affecting most of the remaining patients.4

This subcategorization might reflect different pathophysiological mechanisms that may correlate with different treatment responses.5

In Fig.1 we suggest a possible approach to the diagnosis

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**Figure 1** – Approach to the diagnosis and treatment of headache in an adult patient with COVID-19

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**Headache in an adult patient with COVID-19**

**Characterization** of the headache (location, associated symptoms, pain descriptors, onset, duration, intensity, alleviating and aggravating factors, impact...)

**Exclusion of red-flags** (SNOOP 4 mnemonic): systemic symptoms and secondary risk factors like cancer and HIV, neurological deficit, onset, old age (> 50), symptoms starting with P-papilledema, postural, precipitated by Valsava and progressive

**Similar to a previous diagnosed headache with no red-flags**

**Maintain usual acute and/or prophylactic treatment and healthy lifestyle habits**

**New distinctive features**

**Headache attributed to systemic viral infection**

(headache of any duration in a patient diagnosed with a systemic viral infection and no evidence of meningitic or encephalitic involvement; and at least two of: headache has developed in temporal relation to onset of the systemic viral infection; and/ or headache has significantly worsened in parallel with worsening of the systemic viral infection; and/ or headache has significantly improved or resolved in parallel with improvement or resolution of the systemic viral infection and/ or headache has either or both of the following characteristics; a) diffuse pain; b) moderate or severe intensity. Not better accounted for any other ICHD-3 diagnosis.)

**Other ICHD3 diagnosis**

(i.e., cough headache, probable external-compression headache)

**Lifestyle changes** (e.g. regular sleep patterns, regular exercise, regular meals and healthy diet, reduction of stress, avoidance of known triggers)

**Migraine-like**

(often unilateral, pulsating, moderate to severe intensity, often nausea and/ or vomiting, photo- and/ or phonophobia with avoidance of physical activity and preference for dark and quiet)

**Tension-type-like**

(often generalized, described as pressure or tightness, intensity mild to moderate, mild photo or phonophobia may occur, usually maintains activity)

**Acute treatment:**

• mild to moderate: Paracetamol 1000 mg, AAS 1000 mg, Ibuprofen 400 mg - 600 mg, Naproxen 500 mg - 550 mg, Diclofenac 50 mg - 100 mg.

• severe or refractory: triptans (zolmitriptan, sumatriptan, naratriptan, frovatriptan, almoktripran and eletriptan*)

(*) ritonavir increases its levels due to CYP3A4 metabolism

**Acute treatment:**

• if necessary: Paracetamol 1000 mg, AAS 650 mg - 1000mg, Ibuprofen 400 mg - 600 mg, Naproxen 500 mg - 550 mg, Diclofenac 50 mg - 100 mg

**Persistance of headache > 3 months, new or refractory symptoms**

**Headache consultation**

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and treatment of headache in a patient with COVID-19. A detailed clinical evaluation with emphasis on the characterization of headache and the exclusion of red flags is vital. If a secondary etiology is suspected, brain magnetic resonance imaging should be considered the imaging modality choice; there must also be a low threshold to perform a lumbar puncture. As described, after the diagnosis of headache attributed to systemic viral infection, the predominant headache phenotype should be identified, and the appropriate treatment initiated. Paracetamol, nonsteroidal anti-inflammatory medicines (no robust evidence contraindicates its use), and triptans (if a migraine-like phenotype) should be considered, after evaluation for possible contraindications.

Antiemetics may be prescribed when appropriate; the use of opioids must be cautious due to its addiction risk and the possible association with opioid-overuse headache. If the headache remains refractory or persistent, patients should be referred to a specialist headache clinic for reevaluation and to consider additional treatment options (e.g. intravenous agents, peripheral nerve blocks).

We conclude that headache is a frequent symptom of COVID-19 which may further impair our patients with respiratory symptoms. Its characteristics should be assessed, and red flags not overlooked. The possibility of refractory or chronic headache should be properly addressed.

REFERENCES