



## The ambiguity and limit of caffeine in migraine: a literature review

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### Introduction

Migraine is a chronic disease that affects about 15% of world's population. It is the most disabling disease among men and women under 50 years. Studies indicate that the caffeine, which is the most consumed stimulating in the world and present on the daily diet, can be related to the migraine in an ambiguous way.

### Objective

Considering the epidemiologic and economic point of view, the disease pathophysiology and the accessibility to caffeine, this study aims to understand if there would be a safe minimum dosage of caffeine for patients with migraine.

### Methods

The words "migraine" and "caffeine" were searched in July 2022 at PUBMED and BVS with predetermined filters and selection of publication in qualis journals A1 and A2. 13 articles were found for this revision.

### Results

Caffeine's effects on the nervous system and its relation with headaches have been target of several studies, mainly for producing symptoms similar to the prodromic phase of migraine and for the existence of the Caffeine Abstinence Syndrome, known as a diagnostic entity by the International Migraine Classification. The sensory hypersensitivity (migraine's characteristic) does not appear at the abstinence syndrome. The lack of information about pre-existing headache at studies shows a gap in the parameter "caffeine withdrawal as a trigger per se". It is possible that premonitory symptoms such as yawns, low energy and sleepiness can lead to caffeine intake, bringing forth the wrong idea that it has initiated the migraine. Caffeine, however, induces urinary magnesium loss, reducing its reabsorption. As magnesium affects neuromuscular conduction, nerve transmission and is beneficial in chronic pain conditions and migraines, caffeine, by decreasing magnesium level, can induce headache. Additionally, caffeine contains thiaminases, enzymes that degrade thiamine, which may have protective potential in migraine. Doses between 600-1,200 mg would achieve antinociception and lower doses would have intrinsic analgesic properties. Caffeine-containing pain relievers are effective in treating primary and secondary headaches. In combination with acetaminophen or aspirin, caffeine reduced the amount of analgesic needed to achieve the same effect by approximately 40%. A retrospective study noted that dietary caffeine consumption is a modest risk factor. Regarding sleep, caffeine can disrupt sleep and disrupted sleep patterns predispose to headache. Studies show that treatment with ibuprofen and caffeine provided significantly greater analgesic effect than ibuprofen alone and revealed no association between one to two servings of caffeine and the odds of headaches that day; only three or more servings. There are studies that have not found any participants who reported caffeine as a trigger. In the Head-HUNT study, chronic headaches were more prevalent among individuals with low caffeine intakes compared to those with moderate or high intakes. Those who are regular caffeine consumers and wish to continue their consumption should keep their daily intake as consistent as possible, limiting it to 200 mg/day, at consistent times, and should not be interrupted during the weekend to avoid headache pain from caffeine withdrawal. Use of caffeine-containing pain relievers should be limited to two days a week to prevent medication overuse headache.

### Conclusion

There is evidence for the action of caffeine as an analgesic and the evidence as a trigger and on withdrawal is still uncertain. More studies are needed on the frequency and amounts that would be safe, although the literature already recommends a consumption of less than 200 mg/day. There is an attempt to describe withdrawal headache, however, as pain is a subjective experience, there is a difficulty in standardizing these classifications and in understanding the patient in relation to the pain scale.

**Keywords:** Analgesics, Caffeine, Caffeine withdrawal, Medication overuse, Migraine.