



Caffeine as adjuvant therapy for Tension-Type Headache: A systematic review

Pedro Lucas Grangeiro de Sá Barreto Lima; Júlia Viana de Castro; Luciana Alencar Fialho Bringel Aquino; Pedro Helder de Oliveira Junior; Lívio Leite Barros; Fernando Antonio Guimaraes Junior; David Augusto Batista Sá Araújo; Sophia Costa Vasconcelos; Leonardo José Rodrigues de Araújo Melo; Paulo Ribeiro Nóbrega

Universidade Federal do Ceará, Fortaleza - CE - Brazil

Categoria: Cefaleia do Tipo-Tensão

Introduction

Tension-type headache (TTH) is a very prevalent headache disorder, characterized by mild or moderate non-pulsatile pain, often described as pressure. The use of caffeine as an adjuvant to other common analgesics, such as acetaminophen, dipyron, and ibuprofen, has shown significantly improved efficacy in terms of time and pain relief in the treatment of headaches. However, little literature has assessed the use of caffeine specifically in TTH.

Objectives

To review the effects of caffeine as an adjuvant therapy for TTH.

Methods

Systematic search in PubMed/Medline, Scopus and Web of Science databases was conducted from inception to August 19, 2023. Description terms "Caffeine" and "Tension-Type Headache" were used to conduct the search. Articles were included according to the following criteria: (1) Articles involving patients with TTH; (2) Only Randomized Controlled Trials selection; (3) The study must have data comparing the use of caffeine combination and isolated analgesic in TTH; (4) Were published from 2000 to August 2023; (3) Involved only human subjects and (4) Were written in English. Review articles, Articles written in languages but English, and articles involving animal subjects were excluded. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines. Rayyan app was utilized to organize and label the articles for peer analysis. Results were expressed as descriptive data.

Results

The search yielded a total of 529 articles for evaluation. 87 duplicates were excluded, and 442 entries proceeded for the screening. After inclusion and exclusion criteria, 2 articles were considered suitable for review. These 2 articles enrolled a total of 451 TTH patients. In study 1, a multicenter, double-blind trial was conducted with 385 adult Americans to evaluate the use of combination of ibuprofen and caffeine for TTH treatment. Results in pain-intensity difference (PID), peak PID, summed PID (SPID), pain relief scores (PRS), peak relief, and total pain relief (TOTPAR) all significantly favored the combination therapy in comparison to ibuprofen alone. Overall, subjects individual evaluation of therapy was higher for combination therapy. Adverse effects were more common in caffeine-ibuprofen group (34% compared to 14% in ibuprofen alone), with nausea, nervousness and dizziness being the most frequent. Study 2 was a multicenter single-blind crossover study that evaluated the use of paracetamol-sodium bicarbonate-caffeine combination for TTH treatment compared to paracetamol alone in 66 patients. Results showed no clinically significant difference between the combination and paracetamol alone for time to perceptible pain relief. However, favorable results for combinations were registered in PID, PRS, SPID and TOTPAR results. The proportion of subjects that took combination therapy reporting complete resolution of headache (PRS 4 + pain-intensity rating 0) was significantly higher than paracetamol group. Treatment-emergent adverse events were more common in the paracetamol-sodium bicarbonate-caffeine group (4.3%, compared with 0% in paracetamol alone), with asthma exacerbation and upper respiratory tract infection being the main reported events.

Conclusion

This review analyzed the use of caffeine combined with different analgesics in the treatment of tension-type headaches. Combination formulations with caffeine have shown to be more effective than analgesics alone in most aspects studied. This study has some limitations, only a few trials in the literature studied specifically caffeine adjuvant therapy and most of them did not compare the combination group to isolated treatment in TTH group. Therefore, there is a clear need for more careful and in-depth studies on the subject to clarify the adjuvant effect of caffeine, thus providing better possibilities for the treatment of Tension Time Headache.

Keywords: Caffeine; Tensio-Type Headache; Treatment; Adjuvant; Therapy; Pain relief.