The combination of ibuprofen plus caffeine was effective in a single dose for the treatment of moderate to severe postoperative pain, giving some of the lowest values of analgesics in pain models (number needed to treat (NNT) 2.1 for the ibuprofen 200 mg+caffeine 100 mg group; NNT 2.4 for the ibuprofen 100 mg+caffeine 100 mg group) and a low percentage of re-medication. It was also shown that the combination of these two drugs was more beneficial than when administered separately.

Commentary
The authors acknowledge certain limitations of the review, the most important one being the small number of studies they presented, as well as the small number of participants. Even though this paper focused on ibuprofen plus caffeine versus placebo, a study by Diamond and colleagues have also made comparison of its combination, or each one use separately and placebo for tension headaches. The combination of ibuprofen plus caffeine provided a greater pain relief than ibuprofen alone, caffeine alone or placebo.  
Just as explained by the authors, several studies for postoperative oral surgery pain compared the combination of ibuprofen and caffeine at different doses versus placebo in molar procedures, the combination of both analgesics showed an earlier onset of analgesic effect, 2.4–2.8 times as potent as ibuprofen alone. Even though other studies were not taken into consideration in this analysis, Mehlisch et al.234 also showed the efficacy of ibuprofen alone, when used to treat pain compared to other NSAIDs. However, a very small study conducted by Raisian et al (N=80) reported no difference in pain relief (p=0.073) with ibuprofen alone when compared to a combination of ibuprofen, acetaminophen and caffeine.6

Implications for practice
Even though there have been very few national and international studies comparing the efficacy of the combination of ibuprofen plus caffeine, there have not been major trials that show their superiority over ibuprofen alone. This needs to be taken into consideration especially in countries where this combination is not approved, thus the implementation of this combination remains a challenge.

Contributors
SB and KC-L had substantial contributions to the conception and interpretation of the data. KC-L drafted the work and revised critically for important intellectual content. SB approved the final version of the manuscript.

Competing interests
None declared.

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