

Peer Review File

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Reviewer A

Just some suggestions

- I prefer the terms "acute" or "symptomatic", instead of "abortive" treatment

Reply 1: We have modified our text as advised (see Page 4, line 87 and page 13, line 266).

- Though the authors cite IHS in first paragraph of discussion, I think that two last papers of recommendations should be referred and considered all along the discussion (Cephalalgia 2018 Apr;38(5):815-832, and Cephalalgia 2020 Sep;40(10):1026-1044)

Reply 2: The recommendations have been added and discussed in the study as advised (see Page 11-12, line 239-248).

Reviewer B

Regarding this study, I have some suggestions which can be verified below:

1. RESULTS (line 187)

In the following sentences, please verify the numbers of statistical analysis. They are not in accordance to those in the fig 7.

“The percentage of withdrawals was significantly higher in the topiramate (MD=2.18, n=531, 95% CI 1.07 to .44, Z=2.14, P = 0.03) and DVPX ER (MD=1.87, n=450, 95% CI 1.02 to 3.43, Z=2.03, P = 0.04) groups than the placebo group (Fig 7).”

Reply 1: The figure 7 was checked and modified (see Fig 7).

2. DISCUSSION (line 325)

Please, write the doses of topiramate and DVPX ER that the conclusion is about.

Topiramate (2-3 mg/kg/d and 100 mg/d)

DVPX ER (250 mg/d, 500 mg/d and 1000 mg/d)

Reply 2: The doses of topiramate and DVPX ER have been added in the conclusion (see Page 17, line 355-357)

Reviewer C

There are recent practice guidelines from the American Academy of Neurology and the American Headache Society that reviewed all the preventive medications that have been tested in youth with migraine. These need to be discussed in the introduction and the discussion.

The study by Lakshmi et al. needs to be excluded and the rigor assessment needs to be adjusted. This trial did not include a baseline without medication use prior to

randomization to med or placebo. This is not consistent with the International Headache Society guidelines for prevention clinical trials in adults or the most recent trial guideline for pediatrics (which also should be discussed in the paper). This is from the Lakshmi paper:

The total duration of the study was a period of 4 months, which included a baseline period of 4 weeks during which topiramate was titrated weekly in 25-mg increments over 4 weeks to 100 mg/d in 2 divided doses or to the maximum tolerated dose.

Without a true baseline, this trial would not meet typical criteria. This trial had a big clinical effect and without it, the analyses would be more consistent with recent guidelines that did not find support for this class of medications.

A more accurate paper would only include 4 trials.

Making inferences from such a small number of trials is also a weakness of this analysis.

I would encourage inclusion of up to date guidelines for trial design and practice guidelines, and would refocus the discussion of limitations taking into account these current guidelines and the notable flaw in the Lakshmi trial.

Reply:

1. The practice guidelines from the American Academy of Neurology and the American Headache Society have been cited and discussed as advised (see Page 5, line 93-99 and page 13, line 271-274).
2. As the reviewer advised, the study by Lakshmi et al is excluded in our analysis and finally 4 studies including 7 trials are identified. A more accurate assessment has been adjusted and the major results and conclusions are not changed, which also imply our results are stable and reliable (see Fig1-7 and the results section).
3. The latest guidelines for preventive treatment of migraine in children and adolescents in 2019 have been added and discussed in the study as advised (see Page 11-12, line 239-248). The flaw in the Lakshmi trial was also added (see Page 12, line 244-246 and page 13, line 273-274).