Reviewer’s report

Title: Antihistamine Effects and Safety of Fexofenadine: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Version: 1 Date: 09 Apr 2019

Reviewer: Jiraganya Bhongsatiern

Reviewer's report:

This is a systematic review and meta-analysis of 51 randomized controlled trials (RCTs) to quantitatively examine antihistamine effects and safety of fexofenadine, a selective H1 antagonist. The authors performed an electronic literature search of 841 records total and selected 51 studies of 14,551 participants (healthy subjects and patients with allergic diseases) to further conduct meta-analyses to compare fexofenadine with either other antihistamines (both the first and second generations) or placebo. The outcome measurements for antihistamine effects include inhibition rate of histamine-induced skin wheal and flare. The safety measurements were assessed by adverse event (AE) frequency, sedative effect frequency, and the change of cognitive/psychomotor function scores. Five cognitive/psychomotor function scores were used: critical flicker fusion (CFF), choice reaction time (CRT), compensatory tracking test (CTT), line analogue rating scales for sedation (LARS), and visual analogue score (VAS) for drowsiness. The risk of bias and methodological quality was also evaluated.

From my perspective, this study is good with minor edits. The study demonstrated sufficient results of positive antihistamine effects and safety profile of fexofenadine which mostly are in agreement with other published studies. There were some inconsistencies which, after sensitivity analyses, the authors suggested they were owing to differences in dose, duration and wash out periods among studies. As a consequence, two studies were excluded in the assessment of antihistamine effects. This part was acceptable.

The minor edits that I would like to suggest the authors to modify are the followings:
1) Background, Page 4, line 8: "As such, the aim of this study was to analyze…", not "analysis".
2) Background, Page 3, line 45: "Symptoms such as itching, sneezing, rhinorrhea, and rhinobyon caused by … [2]". The authors may want to double-check the word "rhinobyon". I think it does not belong here. Please check.
3) Results, Page 8, line 17: "Four studies compared with the second-generation antihistamines, as shown in Fig. 7(b), the change of CRT (WMD = 5.28…). This sentence was incomplete. Please check.
4) Table 1 "Characteristics of included studies", please double-check the total number of participants in each treatment arm.

For example, reference #57 Larbig 2006 published the randomized, double-blind, three-treatment, three-period, single-dose, cross-over study comparing levocetirizine, fexofenadine and placebo. The study also stated that thirty subjects were randomized. I think it is not accurate to report n=30 for each treatment arm.
Moreover, there was no treatment arm of levocetirizine reported for this reference (#57) and it was included in meta-analyses to only compare fexofenadine and placebo, not between fexofenadine and levocetirizine (2nd generation antihistamine). I think it is more accurate to at least discuss the reason of why the authors did not include the comparison between fexofenadine and levocetirizine in the analyses.

5) If possible, please include reference numbers in all figures for the meta-analysis results (Figures 2-10). I find it much easier to have reference numbers next to the authors' names (the same format as Table 1). If it is hard to change, the current version is fine.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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