Reviewer’s report

Title: Antipsychotic drug use and risk of stroke and myocardial infarction: a systematic review and meta-analysis

Version: 3 Date: 17 May 2019

Reviewer: C Lee

Reviewer's report:

Comments

Abstract

Background
The effect of antipsychotic (AP) drugs on risk of stroke and myocardial infarction (MI) remains unclear, due to methodological limitations of, and inconsistencies across, existing studies.

We aimed to systematically review studies reporting on the associations between AP drug use and stroke or MI risk, and to investigate whether associations differed among different sub-populations.

Methods
We searched Medline, EMBASE, PsychINFO and Cochrane Library (from inception to May 28, 2017) for observational or experimental studies reporting on AP drug use and MI or stroke occurrence.

Since this study only included observational studies, "or experimental" may need to be deleted here.

Results

, albeit with substantial heterogeneity (pooled HR 2.31, 95% CI 1.13, 4.74).
Please put I-squared here.

with no heterogeneity (pooled HR 1.16, 95% CI 1.00, 1.33)

I assumed I-squared (I2 would be zero to state that there is no heterogeneity. Please report the I-squared here.
Introduction
Line 11-16: The authors also reported that among those with dementia in particular, use of any AP was associated with a very low risk of cerebrovascular disease [19].

In ref 19, Hsu et al (2017) found that use of antipsychotic use in patients with dementia was associated with a low risk of cerebrovascular accident (OR 1.17; 95% CI 1.08 e 1.26).
OR = 1.17 means 17% increase in the odds comparing to non-use. I would not interpret that 17%, which is higher than 10% or even 15%, is a "very low" risk.
Please delete "very" in this sentence.

Line 33-35: Interestingly, a subsequent additional review (which was performed concurrent to our review)
Ref. 23 Huang KL et al (2017) searched databases from their inception to the end of June 2016, but Zivkovic et al. searched Embase, MEDLINE, PsychINFO (via OVID) and the Cochrane Library from their origin to May 28, 2017. Please delete "(which was performed concurrent to our review)"

Results
Page 12
For what it's worth, there was no clear evidence that AP drug use was associated with increased risk of MI (Figure 3).
"For what it's worth," is not formal in medical publications. You may need to change to "Moreover", or "In addition."

Discussion
Page 13
We found that AP drug use was associated with a 16% increased risk of stroke in those with dementia, which was similar to the 17% (OR 1.17, 95% CI 1.08 to 1.26) reported by Hsu and colleagues [19]

Since odds is not the same as risk, it would be better if the authors can change the sentence to "with a 16% increased 'odds' of stroke in those with dementia."

Page 15
APs may also increase risk of thrombosis. A recent meta-analysis [63] found that AP drug use is associated with a 50% increased risk of venous thromboembolisms…
Ref 63 Barbui et al. (2014) indeed reported ORs and stated that
"Antipsychotic exposure was associated with a significant increase in risk of developing VTE [odds ratio (OR) 1.54, 95% confidence interval (CI) 1.28-1.86, 11 studies]."
The authors may need to change "risk" to "odds" here.

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?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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