Reviewer's report

Title: Zolpidem reduces pain intensity postoperatively. A systematic review and meta-analysis of the effect of hypnotic medicines on post-operative pain intensity.

Version: 0 Date: 17 Jul 2020

Reviewer: Santhani Selveindran

Reviewer's report:

This is an interesting article exploring whether (or not) sedative-hypnotics have a role to play in the reduction of pain intensity in the post-operative period. Overall, it is a well written article. I do have some suggestions:

Title: It might be useful to highlight the element of 'pain intensity' in the title. This is because there is another recent systematic review by Bjurstrom et al. that looks at this topic (although they are studying post-operative pain control and sleep promotion).

Introduction: Perhaps explore a bit more the bi-directional relationship between sleep and pain, particularly the implications i.e. post-operative morbidity, and through this explanation introduce the concept of sedatives as pharmacological agents that could potentially reduce pain intensity. I am not sure if the sentence 'It is possible that pain intensity may be reduced by the administration of hypnotic medicines' and the bit on the 'low quality evidence that hypnotic medicines may have a role in postoperative pain management' (lines 27-28) have been deliberately repeated. I feel these should follow the explanation of the relationship between sleep and pain. I would also suggest being clear that the pain intensity being described in the sentence 'Pain intensity strongly predicts persistent postoperative pain' is 'immediate post-operative', as there are phases in post-operative recovery. It would be good to define the postoperative periods since this study appears to include all phases. Not sure what is meant by 'duration of follow up'.

Methods:
Intervention-Perhaps indicate that all post-operative periods were included

Data items- It is good that extracted data items were included, but perhaps indicate the fields that relate to the topic of study i.e. drug being studied, measure of pain intensity etc.

Appendix 2: Would it be possible to give a more thorough description of the secondary outcomes? I.e, how were sleep and other measured parameters assessed?

Results: Figure 4 is not very clear (dotted lines vs firm lines-what do these mean?)

Discussion: I am not sure it is fair to make this statement 'it is difficult to know the exact mechanisms of hypnotic medicines' without some kind of reference to back it up. Is there any literature that can explain/back up the opioid-sparing effects of sedative hypnotics? As both are CNS depressant drugs, would there be any proposed mechanism that leads to this, which may not
necessarily be analgesic? Are there other factors in play? Were the paragraphs with the headings erroneously put under 'Strengths and Weaknesses'?

Are there other areas of research that could be explored/carried out given the findings of this study? i.e. Does the type of surgery really matter? Are there any other factors that could have influenced these results?

Would it be possible to display how your findings relate to the current literature in this area?

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