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DOI

[10.1016/j.smr.2020.101286](https://doi.org/10.1016/j.smr.2020.101286)

Publication date

2020

Document Version

Final published version

Published in

Sleep Medicine Reviews

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[Link to publication](#)

Citation for published version (APA):

Lancee, J., Yücel, D. E., Souama, C., & van Emmerik, A. A. P. (2020). Reply to Zhang et al.: Downgrading recommendation level of prazosin for treating trauma-related nightmares: Should decision be based on a single study? *Sleep Medicine Reviews*, 51, Article 101286. <https://doi.org/10.1016/j.smr.2020.101286>

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REPLY

Reply to Zhang et al.: Downgrading recommendation level of prazosin for treating trauma-related nightmares: Should decision be based on a single study?



We would like to thank Zhang and colleagues [1] for their response to our article in *Sleep Medicine Reviews* [2]. We started with the current project because the American Academy of Sleep Medicine (AASM) taskforce downgraded the recommendation for prazosin [3]. In our group we focus on Imagery Rehearsal Therapy (IRT) for nightmares because we think it has the most potential in treating this trauma-related complaint [4]. Even though the study that informed the AASM's decision was of very high quality [5], the highest level of evidence is obtained via meta-analytic procedures, as noted by Zhang et al. [1]. For this reason we decided to carry out a meta-analysis that included this new study. We expected that the results would be in line with the new guidelines and IRT would be superior to prazosin.

The results did come out different than expected. In the meta-analysis [2], both the random effects model and the fixed effects model showed no difference in effect between IRT and prazosin. These results are even more striking since the prazosin studies seem to be carried out in a more rigorous manner (e.g., double-blind). These results are thus very much in contrast with the decision of the AASM taskforce to downgrade prazosin [2,3].

We were therefore glad to read that Zhang and colleagues [6] carried out a similar meta-analysis that pooled all prazosin studies (not IRT). While using slightly different in- and exclusion criteria they still reached the same conclusion that prazosin appears an effective treatment for posttraumatic nightmares. In their letter, Zhang and colleagues [1] rightly point out the following issues that need to be addressed because they could influence the effects of prazosin: 1) the role of apnea; 2) the influence of psychiatric comorbidity; 3) the role of REM sleep; 4) the use of self-report measurements. However, as noted by Zhang and colleagues themselves [1], primary studies as yet provide insufficient data to investigate the role of these factors in a meta-analytic review and they are important factors that need to be addressed in future studies.

Overall we do agree with the conclusion of Zhang and colleagues [1] that we now have two meta-analytic reviews that showed the efficacy of prazosin for posttraumatic nightmares [2,6] and that downgrading of the recommendation of prazosin [3] is premature. On the other hand, the study by Raskind and colleagues [5] illustrates the need for new high quality studies investigating prazosin. If more null-results are reported then this may support the downgrading of prazosin after all. Another critical issue is that the IRT studies could be of higher standard. New high-quality IRT studies with placebo control groups are therefore just as important.

As a research group, we still think that IRT for posttraumatic nightmares has more potential than prazosin. There are several options that can be explored to further enhance IRT: 1) We have been working on identifying the working mechanisms of IRT. It appears that mastery is an important mechanism [7]; this knowledge can be used to develop treatment modules that more explicitly target mastery. 2) Another interesting option is the combination of IRT with cognitive behavioral treatment for insomnia, for which the first results are promising [8,9]. 3) The combination of IRT with prazosin may also be interesting to explore.

To conclude, we think that the research literature as a whole still shows equal effects for IRT and prazosin in treating posttraumatic nightmares and that as long this is the case, the AASM's and other guidelines should advocate this. As noted in our original article: this is essentially good news for patients and practitioners, who have a choice between two effective but very different treatment formats for posttraumatic nightmares.

Acknowledgements

All authors declare that they have no competing interests and did not receive financial support.

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10 January 2020

Available online 13 February 2020