Author’s response to reviews

Title: Fatigue and disturbances of sleep in patients with Osteogenesis imperfecta - a cross-sectional questionnaire study

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Cover letter
Editor-in-Chief
BMC Musculoskeletal Disorders

Dear Dr Mockridge

Thank you for your kind response, and the detailed and constructive comments from the referees. Please find enclosed our revised manuscript entitled “Fatigue and disturbances of sleep in patients with Osteogenesis imperfecta – a cross-sectional questionnaire study”.

We have made the revisions as suggested, and our responses are given point by point on the attached pages.

Sincerely yours,

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Fatigue and disturbances of sleep in patients with Osteogenesis imperfecta - a cross-sectional questionnaire study

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Remzi Cevik Reviewer 1: This is the cross-sectional study analyzed experienced fatigue and sleep disturbances in patients with Osteogenesis imperfecta.

- The aim of the study and hypothesis are good but there are some methodological deficiencies. These deficiencies causing poor quality study.

- The fatigue and sleep disturbances evaluated only by VAS or dichotomous (yes/no) manner. No any other generic or disease specific scales used that better assessing the disease co-morbid problems. Using generic or disease specific quality of life scale may increase study quality. By this stiutaions it is not suitible for publishing by this way.

RESPONSE: We agree that disease-specific scales would be ideal in quantifying fatigue and other evaluated co-morbidities of Osteogenesis imperfecta (OI). To date, disease-specific scales for assessing fatigue and sleep disturbances do not exist however. Our study is the first report on the prevalence of sleep apnea co-morbidities in OI population. By publishing the present findings, we hope to increase knowledge so that future research on the subject can be designed in a way that takes into consideration the specific features of this patient group, such as poor applicability of BMI.

John Gjevre (Reviewer 2): This is an interesting report that helps to further the knowledge of fatigue and sleep in a rare disease population. Other authors have noted that OI is associated with pain & fatigue and interventions such as physiotherapy (Van Brussel, 2008) or bisphosphonates (Salehpour, 2010) may help the pain and/or fatigue. However, there is very little in the literature about OI and sleep and thus I welcome this large cross-sectional study which adds to our knowledge.

RESPONSE: Thank you for this encouraging statement. Thank you also for drawing our attention to the paper by Salehpour and Tavakkoli from 2010. We now refer to this paper [39] when discussing the eventual positive effects of bisphosphonates.
There are some minor issues with the study. Fatigue is a broad term and there are multiple factors contributing to fatigue. While the VAS fatigue scale is reasonable, the paper would have been much stronger by using an additional assessment for sleep such as the Epworth scale. Also, other sleep questionnaires would have been beneficial such as the Pittsburgh sleep quality questionnaire and the simple and short STOP-BANG questionnaire. Perhaps those could be included in any future research in this group.

Clearly, there is a higher incidence of sleep symptoms in the OI group as per Table 1. It may be useful to break out the 8 OI subjects who are diagnosed with sleep apnea (and on positive pressure ventilation) and see how their Table 1 scores compare to the the non-diagnosed group (presumably better on therapy).

RESPONSE: Thank you for your helpful suggestion. We have now separately analyzed the results of those study subjects with sleep apnea diagnosis, and compared them with the results of the non-diagnosed group. We found surprisingly that the results did not notably differ from each other. This information has been added to the manuscript (Results section, third paragraph, last sentence).

Finally, it is unfortunate that the authors did not have access to the subjects medication list. Certainly part of the issue with poor sleep & fatigue is due to chronic pain and knowledge of pharmaceutical therapy would have been useful. Also, it would be useful in any future study to measure neck circumference since BMI in this population may be less accurate given height loss.

RESPONSE: Based on the findings of this study further research is needed on this topic. We will most definitely look more precisely into all of the mentioned factors. We thank you for your constructive comments.

Overall, this is an interesting study that contributes to the knowledge of fatigue and sleep in this rare population.

Afitap Içagasioglu (Reviewer 3): No additional comments