

Research Brief



Project:	Fatigue and Sleep Disturbances In OI – Prevalence, Characteristics, and Impact on the Quality Of Life
Category:	Medical Research
Principal Researcher:	Heidi Arponen DDS, PhD (1)
Research Group:	Outi Mäkitie professor, Children’s Hospital (2) Helena Valta MD PhD, Children’s Hospital (2) Janna Waltimo-Sirén DDS PhD (1) Leif Bäck MD PhD, Head and neck Center(2) Adel Bachour MD PhD, Sleep Research Clinic (2)
Institutions:	(1) University of Helsinki (2) Helsinki University Central Hospital, Finland
Duration:	2016- 2019

Why the research

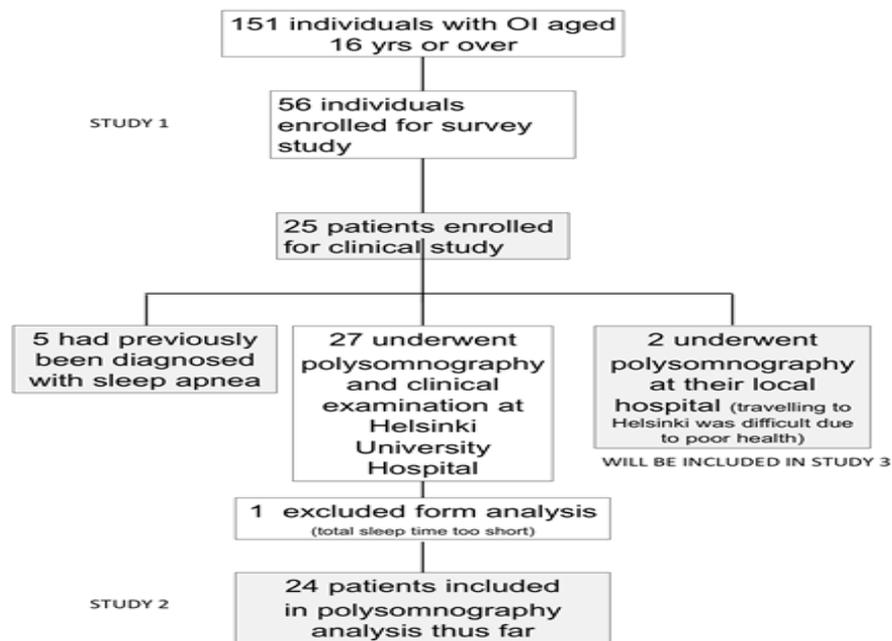
Fatigue is a common problem in people with OI and can have multiple physical and mental consequences. They can be too tired to engage in mental or physical activity leading to fewer social interactions, underperforming at school or work and may even have higher risk of accidents.

Different researches have tried to pin down the cause of fatigue in OI. Some of these findings indicated, muscle functions, level of physical activity and compromised lung function as causes of fatigue. But no research has yet specifically tried to relate fatigue with sleep disturbance.

This project hence tries to answer this important question by investigating the relationship between fatigue and sleep apnea (which a potentially serious sleep disorder) in people with OI. The findings will contribute to improve the quality of life of people with OI by finding a medically treatable cause for fatigue which hopefully will lead to design of targeted diagnostic and therapeutic approaches.

How was the research carried out?

The project has different phases. The first part constituted a questionnaire study on self-reported pain, fatigue and sleep disorder-related symptoms. And the second part compose a clinical examination of upper respiratory tract and a sleep study (polysomnography). The third part of the project combines all the data gathered during the previous studies and medical records of those individuals that have already been diagnosed with sleep apnea. the following Figure presents a flow chart of the three studies and the participant inclusion in the projects.



What were the findings?

The findings are very interesting and have already been published in two international scientific peer-review journals*.

The results show that fatigue was reported by 96%, and daily pain by 87% of individuals with OI. Notably, the level of daily fatigue reported was similar between OI population and healthy control group. However, various sleep disturbances are significantly high among individuals with OI than the control group. Eight OI- respondents of the survey study had a diagnosis of sleep apnea whereas 96% of those without sleep apnea diagnosis reported one or more sleep disturbance related symptoms. The following table show the summary:

Table 1: Prevalence of self-reported symptoms related to sleep-disturbances and sleep apnea among the respondents in the Osteogenesis imperfecta patient cohort and controls

	number of patients with symptoms (%) n = 56	number of controls with symptoms (%) n = 56	significance of difference between the study groups (chi-square test)
snoring	32/52 (62)	15/54 (28)	11.1 p = 0.001
Pauses of breathing during sleep	13/42 (31)	3/54 (6)	9.9 p = 0.002
Restless sleep	43/55 (78)	23/54 (43)	12.9 p < 0.001
Grinding of teeth during sleep	22/52(42)	23/55 (42)	non-significant
Recurrent nightmares	16/50 (32)	2/55 (4)	13.3 p < 0.001
Daytime sleepiness	43/53 (81)	34/56 (61)	5.6 p = 0.018
Likelihood of dozing	14/52 (27)	5/56 (9)	6.3 p = 0.012
Dysphagia (swallowing disorder)	17/51 (33)	1/55(2)	20.0 p < 0.001
Difficulties of concentration	24/50 (48)	6/54 (11)	16.6 p < 0.001
Nocturia(multiple waking up to urinate)	15/51 (29)	5/54 (9)	5.8 p = 0.016
Restless legs	19/51 (37)	8/54 (15)	10.0 p = 0.002
Diagnosed sleep apnea	8/54 (15)	1/55 (2)	5.4 p = 0.020

Moreover, the experienced bodily pain was significantly more severe among respondents with OI and is correlated with the reported fatigue. One can anticipate that suffering from chronic pain makes you exhausted.

The clinical sleep study shows obstructive sleep apnea in as many as half of the individuals with OI. Unexpectedly, however, no correlation was present between sleep apnea and daytime sleepiness, experienced bodily pain, severity of OI, Mallampati score (the distance from the tongue base to the roof of the mouth) or neck circumference, which are the usual clinical predictors physicians are looking for.

Implications and way forward

The results will help to understand fatigue and its relationship with sleep disorders and also its prevalence in the OI population. In addition to the findings being relevant to the whole OI community; all individuals in the study with newly discovered sleep apnea have now received treatment for it, so the study has directly improved their well-being and quality of life. The researchers also recommend to the physicians to be alert on the possibility of sleep apnea with OI patients. The third stage of this study-project (study 3) will look into the associated factors of sleep apnea and fatigue, such as lung function and depression, in a more comprehensive scale. The study is anticipated to be finalized this year.

What else is needed?

Experiencing fatigue and persisting daytime tiredness can limit what people can do and achieve. Fatigue and tiredness affect significantly individual's day-to-day life, social relationships, as well as ability to participate and work. This innovative project is the first of its kind and focuses on a well-recognized yet very poorly studied topic. Unraveling undiagnosed sleep apnea as underlying cause of tiredness and receiving appropriate treatment for it can make a huge positive long-term difference in an individual's life.

Innovative researches like this with new focuses and new questions can shade light into the various issues around OI. More findings and informed treatments can address the challenges people with OI face every day.

*Arponen H, Waltimo-Sirén J, Valta H, Mäkitie O. Fatigue and disturbances of sleep in patients with osteogenesis imperfecta - a cross-sectional questionnaire study. *BMC Musculoskelet Disord.* 2018;19(1):3.

*Arponen H, Bachour A, Bäck L, Valta H, Mäkitie A, Waltimo-Sirén J, Mäkitie O. Is sleep apnea underdiagnosed in adult patients with Osteogenesis imperfecta? –A single-center cross-sectional study. *Orphanet Journal of Rare Diseases* 2018 (epub ahead of print).