DERMATOLOGICA SINICA xxx (2017) 1–7

Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

ORIGINAL ARTICLE

# Sleep quality and disturbances in patients with dystrophic epidermolysis bullosa

Giulio Fortuna [a, b, c, *], Massimo Aria [d], Sarah Whitmire [e], Rodrigo Cepeda-Valdes [b], Maria Guadalupe Moreno Trevino [f], Julio Cesar Salas-Alanís [b, f]

[a] Department of Diagnostic Science, Louisiana State University School of Dentistry, 1100 Florida Ave, New Orleans, LA 70119, USA
[b] D.eb.RA. Mexico Foundation, Otomí #211, casi esq. P. Elías Calles Colonia Azteca, Guadalupe N.L., 67150 Monterrey, Nuevo Leon, Mexico
[c] Federico Navarro Institute – School of Orgonomy "Piero Borrelli", Corso Umberto I, 35, 80138 Naples, Italy
[d] Department of Economics and Statistics, Federico II University of Naples, via Cinthia, Monte Sant'Angelo, 80126 Naples, Italy
[e] Department of Bioinformatics and Genomics, University of North Carolina, 9201 University City Blvd, Charlotte, NC 28223, USA
[f] Department of Basic Science, Universidad de Monterrey, Av. Ignacio Morones Prieto 4500 Pte., 66238 San Pedro Garza García, N.L., Mexico

ARTICLE INFO

*Article history:*
Received: Mar 2, 2017
Revised: Jun 3, 2017
Accepted: Jul 26, 2017

*Keywords:*
EB
Sleep quality
Sleep disturbances
Epidermolysis bullosa
Anxiety
Depression

ABSTRACT

*Background:* Sleep disturbances in patients with dystrophic epidermolysis bullosa (DEB) have never been investigated and still remain an open question. We sought to examine sleep quality and its relationship with pain and mood disorders in DEB patients.
*Methods:* Twenty-eight DEB patients and 26 healthy individuals completed the following battery of scales: the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Medical Outcomes Study (MOS) Sleep Scale, the Visual Analogue Scale (VAS), the Hamilton Rating Scale for Anxiety (HAM-A) and Depression (HAM-D). Linear correlations and hierarchical regression analyses were performed.
*Results:* Patients with DEB have significantly lower scores in daytime sleepiness ($p = 0.003$) and higher level of pain ($p = 0.009$) in comparison to controls. The analysis of all PSQI and MOS items failed to demonstrate any statistically significant differences between DEB patients and controls, except for a sub component of PSQI measuring sleep disturbances ($p = 0.003$). In the study group, a positive correlation was found between PSQI and depressive symptoms ($r = 0.56$; $p = 0.002$), anxiety symptoms ($r = 0.46$; $p = 0.015$), and pain ($r = 0.44$; $p = 0.020$). These results were consistent with the hierarchical regression analysis showing a significant contribution of depression ($\Delta R^2 = 21.8$; $p = 0.008$), anxiety ($\Delta R^2 = 14.5$; $p = 0.027$), and pain ($\Delta R^2 = 13.5$; $p = 0.032$) to poor quality of sleep.
*Conclusions:* DEB patients showed a greater degree of sleep disturbances that can be influenced by depressive symptoms, anxiety symptoms, and pain compared with controls. Therefore, they should be screened for sleep issues that can be possibly impacted by pain and mood disorders.



## Introduction

Human beings cannot survive without sleep. Not only can chronic sleep impairment lead to mood disturbances or altered pain severity perception, but also to a negative general health and quality of life.[1,2] Sleep disturbances (SD) have been observed in a variety of diseases, including autoimmune/immuno-mediated[3,4] and inherited ones.[5,6]

Epidermolysis bullosa (EB) is an inherited muco-cutaneous disorder, characterized by an extreme fragility of skin and mucous membranes to mild trauma[7] and, in some subtypes, by severe internal organ involvement.[8] Four major types of EB have been described based on the ultra-structural site of epithelial-connective tissue cleavage (Simplex, Junctional, Dystrophic, and Kindler syndrome). This has been broken down into 30 subtypes caused by hundreds of different mutations involving more than 18 genes.[9]

Dystrophic EB (DEB) has been the subject of much research. Psychosocially, DEB patients failed to demonstrate more

* Corresponding author. Department of Diagnostic Sciences, Louisiana State University School of Dentistry, 1100 Florida Ave, New Orleans, LA 70119, USA. Fax: +1 504 941 8336.
*E-mail address:* giulio.fortuna@gmail.com (G. Fortuna).

http://dx.doi.org/10.1016/j.dsi.2017.07.003

statistically significant mood disturbances than healthy individuals,[10] but tend to experience a higher level of generalized pain.[11] Physical, mental, and social aspects of patient health and quality of life,[12] as well as oral-health related quality of life have been previously described.[13] However, these measures do not take insomnia or other sleep abnormalities into account.

Several studies have described a relationship between SD and mood disturbances such as anxiety and depression, but not in EB.[14,15] Furthermore, insomnia can be a useful marker of onset of major depression[16] and anxiety disorder.[17]

Similarly, the association between SD and pain has been widely studied, concluding that their relationship is close and bidirectional, with pain possibly disrupting sleep quality, and poor sleep quality possibly exacerbating pain.[18] However, several micro-longitudinal studies have been able to demonstrate that SD can be a stronger risk factor for pain than the reverse.[2]

While the research investigating the mood disorders in DEB patients is limited,[10] no study regarding sleep quality and disturbances in DEB patients has been reported thus far.

Therefore, the objectives of this study are: i) to characterize SD using the three different sleep scales in DEB patients and healthy controls, and ii) to determine the role of SD on mood disorders, specifically anxiety and depressive symptoms, and pain.

## Materials and methods

### *Study design and patients*

We designed a cross-sectional study performed at the EB Clinic at D.eb.RA. Mexico, Monterrey (Mexico). Twenty-eight DEB patients and 26 healthy individuals were screened to participate between June and November 2011. The control group consisted of individuals who work at D.eb.RA. Mexico as volunteers or caregivers.

All patients received printed information and provided their written informed consent for the management of personal data before participating into the study. This study was approved by the local Ethical Committee of the Universidad de Monterrey (Mexico).

All DEB and control patients were matched for age and gender and were included in the study in accordance with specific inclusion criteria as previously published.[10]

The exclusion criteria for both groups encompassed: 1) patients with unstable medical conditions or debilitating pathologies, that may potentially affect the quality of sleep, such as cancer, diabetes, asthma, cardiovascular diseases, musculo-skeletal diseases, GERD, thyroid diseases, obesity; 2) patients with psychiatric illness, organic brain syndrome, neurological disease; 3) patients in treatment with psychoneuropharmacological medications, such as anxiolytic, antidepressants, anticonvulsants, or psychotropic drugs; 4) patients in treatment with systemic medications that may potentially affect the quality of sleep, such as corticosteroids, antiarrhythmics, beta blockers, diuretics, antihistamines, thyroid hormone; 5) patients with social habits of smoking, drinking, or using recreational drugs.

### *Socio-demographic and clinical information*

Two dermatologists were responsible for selecting DEB patients and healthy individuals as controls, in addition to collecting the following data: sociodemographic (age, gender), type of DEB (dominant versus recessive), and data from the aforementioned sleep, psychometric and pain scales. At admission, each patient underwent a medical anamnesis (including history, clinical features and treatment), a general medical examination, and an intra and extra-oral examination.

### *Study variables*

Upon admission, DEB and healthy patients were administered the following evaluation scales: the Epworth Sleepiness Scale (ESS), The Pittsburgh Sleep Quality Index (PSQI), the Sleep Scale from the Medical Outcomes Study (MOS), the Hamilton Rating Scale for Depression (HAM-D), the Hamilton Rating Scale for Anxiety (HAM-A) and Visual Analogue Scale (VAS).

All these scales were reviewed for completeness before collection and were administrated in validated Spanish versions.[19–21]

### *Sleep scales*

*The Epworth sleepiness scale*

The Epworth Sleepiness Scale (ESS) is a simple, self-administered questionnaire, which is shown to provide a measurement of the subject's general level of daytime sleepiness. It is based on questions referring to eight everyday situations, some known to be very soporific, others less so (e.g. watching television, talking with someone). Patients are asked to rate their likelihood of dozing off or falling asleep in each situation on a scale of 0 (never doze) to 3 (high chance of dozing), based on their current way of life.[22] The ESS total score is the sum of the eight items that can range between 0 and 24 with a cutoff score of 10, which indicates excessive daytime sleepiness.[23]

*The Pittsburgh sleep quality index*

The Pittsburgh Sleep Quality Index (PSQI) is a self-reported questionnaire assessing sleep quality and disturbances over a 1-month time interval.[24] This instrument comprises 19 self-rated questions, which are grouped into the following 7 components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Each component has a score ranging from 0 to 3, which when summed, generates a global PSQI score ranging from 0 to 21. A cutoff value of >5 is a sensitive and specific measure of poor sleep quality.[24]

*The sleep scale from the medical outcomes study*

The MOS-Sleep includes 12 items grouped into 7 dimensions: sleep disturbances, sleep adequacy, daytime somnolence, snoring, awakening short of breath or with headache, quantity of sleep, and optimal sleep.[25]

For item 1, patients were given the following five possible responses in terms of minutes: 0–15, 16–30, 31–45, 45–60 or >60 min. For item 2, patients were required to report the average number of hours slept over the past 4 weeks. Items 3–12 are reported using a 6- item Likert scale (1 = All of the time, 2 = most of the time, 3 = a good bit of the time, 4 = some of the time, 5 = a little bit of the time, 6 = None of the time).

Additionally, two indices can be generated: sleep problem index (SPI) I and II. In this study, we generated SPI II, containing nine (1, 3, 4, 5, 6, 7, 8, 9, 12) of the 12 items of the scale to better assess overall sleep problems.[26] The first five dimensions and SPI II are transformed to a 0–100 scale. Higher scores indicate that the attribute being measured is more impaired (e.g. greater amount sleep disturbance or greater adequacy of sleep.[25] No formal cutoff scores are provided.[26] Additionally, the “quantity of sleep” dimension is a measure of the average amount of sleep (in hours) reported by the patient, and the “optimal sleep” dimension is a dichotomous variable marked “1” if the patient reported an average of 7 or 8 h of sleep per night.

Please cite this article in press as: Fortuna G, et al., Sleep quality and disturbances in patients with dystrophic epidermolysis bullosa, Dermatologica Sinica (2017), http://dx.doi.org/10.1016/j.dsi.2017.07.003