

Gastroesophageal Reflux Disease (GERD) and obstructive sleep apnea

Kalina Grivcheva Stardelova¹, Popova Jovanova R. ¹, Deriban Gj. ¹, Zdravkovska M.²

¹Univ. Clinic of Gastroenterohepatology, Medical Faculty Skopje, Univ St Cyril and Methodius, Skopje

² Faculty of medical sciences, University "Goce Delcev" , Stip

ABSTRACT:

Introduction: There is some data supporting close association between nocturnal GERD and sleep disturbances. Sleep disturbances in patients with GERD are poorly recognized. Both are common chronic diseases and share several similar risk factors. Since obesity is a key risk factor to both OSA and GORD, it is not surprising that simple coincidence might explain this association and indeed there is evidence to support the lack of a causal link between the two, as follows:

Aim: the purpose of this review is to understand the association between obstructive sleep apnea (OSA) and extra esophageal reflux disease (EER) in the adult population.

What is clear from this and other studies reported above is that nocturnal GERD, whether or not it is implicated in the genesis of OSA episodes, contributes to nocturnal arousals in OSA and therefore to daytime somnolence. Clearly, ant reflux therapy has a potential role in reducing this burden for patients with sleep apnea.

Results: A total of patients were included in the study: physician questionnaires were available for all of them. Nocturnal gastro-esophageal reflux disease symptoms were reported by patients (63.9%) and regular (at least once weekly) gastro-esophageal reflux disease-related sleep disturbances by (41.7%). Multivariate analysis showed that nocturnal gastro-esophageal reflux disease symptoms, obesity, use of hypnotic drugs, and age over 50 years were significant independent predictors of sleep disturbances. The proportion of patients reporting at least one nocturnal gastro-esophageal reflux disease symptom during the previous week decreased following treatment, from 98.8% to 39.3% ($P < 0.001$).

Conclusions: Nocturnal gastro-esophageal reflux disease symptoms are common in the Macedonian population and are associated with sleep disturbances. Effective treatment can significantly improve sleep duration and quality.

Key words: Gastro esophageal Reflux Disease, Nocturnal GERD, Obstructive sleep apnea (OSA),

Introduction:

Obstructive sleep apnea (OSA) is characterized by repeated episodes of apnea and hypopnea during sleep occurring despite normal respiratory drive. These episodes are related to upper airway collapse during negative pressure inspiration, and they result in repeated asphyxia with oxyhemoglobin desaturation and arousals from sleep.

Obstructive sleep apnea provokes fluctuations in autonomic nervous system activity, heart rate, and systemic and pulmonary vascular resistance

Sleep is essential for good health. Evidence has shown that sleep disorders might contribute to respiratory, hormonal, gastrointestinal, cardiovascular, and emotional impairment, while the chronic dependence on hypnotics is a substantial economic burden.(1–4) Gastroesophageal reflux disease (GERD) may play a pathogenic role in sleep disturbance.(5–7) Nocturnal acid reflux can induce sensory stimuli and esophageal clearance, and interrupt sleep stage progression, even in the absence of cognitive awakening.(8) In addition, reflux events during sleep are characterized by longer acid-mucosal contact that stems from lower saliva production, lower frequency of swallowing, and slower gastric emptying, all of which increase the risk of mucosal damage, intensity of noxious stimuli, and disruption of normal sleep (8-10);

There is some data supporting close association between nocturnal GERD and sleep disturbances. Sleep disturbances in patients with GERD are poorly recognized and rarely elicited during clinic visits. Despite the significant impact of these disturbances on patients' quality of life and, probably, on their perception of the severity of their disease. Sleep disturbance is not usually asked about in the routine history taken from patients with reflux disease

Several trials have assessed the therapeutic effect of acid suppressants on sleep but the results were inconclusive. Johnson et al(11) found that proton-pump inhibitors (PPIs) can reduce nighttime heartburn, improve sleep quality, and thus increase work efficacy. Dimarino et al(12) found that decreasing reflux-related arousal with acid suppressant agents increases total sleep time and rapid-eye movement sleep. However, using actigraphy to record sleep efficiency and percentage immobility time, Chand et al(13) found that PPIs improve subjective but not objective measures of sleep quality. In addition, these studies were mainly on patients with reflux symptoms and a favorable response could have been expected.

Reflux is a heterogeneous condition and can be categorized as erosive and non-erosive reflux disease (NERD), as well as symptomatic and asymptomatic. Among the general population, some patients with erosive disease have no reflux symptoms, which may lower their awareness of the disease and incentive for treatment.(14–16) Therefore, our aim was to assess the association between GERD and sleep in subjects who were categorized on the basis of their reflux symptoms and endoscopic findings.

Definition of Nocturnal GERD

Presently, we are still devoid of an accepted definition for nocturnal GERD.

Interestingly, studies that assessed either prevalence or therapeutic response of patients with nighttime heartburn, lacked clear definition of nocturnal GERD (1,2,10). Farup et al. offered the following definition of nighttime GERD: nocturnal awakening by GERD symptoms; nocturnal awakening caused by coughing or choking, regurgitation or fluid or food, and acidic/bitter taste; GERD symptoms while in the supine position; and morning awakening secondary to GERD symptoms (3). This is an inclusive definition that may include patients that experience GERD-related symptoms in the supine position while still awake. In contrast, Fass et al. suggested that nighttime heartburn should be defined as heartburn that awakens patients from sleep during the night [Fass, NIH study,

DDW2003(4) . While this is a much more restrictive definition, it underscores the importance of having GERD-related symptoms during sleep physiology(17)

Aim of the study:

The purpose of this review is to understand the association between obstructive sleep apnea (OSA) and extra esophageal reflux disease (EER) in the adult population. We will attempt to answer two main questions:

1. What is the association between OSA and EER, and is there any evidence for a cause and effect relationship?
2. Does the treatment of EER by acid inhibition improve OSA symptoms?

Patients and methods:

This three years prospective study clinical trial was conducted on Univ. Clinic for Gastroenterohepatology and gathered data from 642 patients with GERD symptoms. Demographics included age and gender. Clinical characteristics included physical comorbidity, psychiatric comorbidity, body mass index (BMI), currently smoke cigarettes, use of spice food, prescription GERD treatment, and over-the counter GERD treatment. Patients between 18 and 75 years old, with average age $37,5 \pm 8,2$ were included (we restricted older people to decrease the risk of malignancy) with clinical history of heartburn, acid regurgitation, or both during the previous 3 months, all the participants were asked to respond to the questionnaire, along with another detailed questionnaire consisting of 6 original questions. Additional 20 questions include enquiries about symptoms related to the upper gastrointestinal tract, medical history, lifestyle factors and so on. Upper endoscopy was done to all patients.

Sleep difficulties were defined independently of GERD symptoms, because previous research has shown that most disruption of sleep in this population occurs without the presence of GERD symptoms. Respondents who experienced insomnia or sleep difficulty during the past 12 months were further asked to report on the frequency with which they experienced sleep difficulties. Response options included once or twice a year, every other month, once a month, a few times each month, once a week, 2–3 times per week, 4 or more times per week. Those who reported experiencing sleep difficulties at least once a month were categorized as experiencing sleep difficulties. Respondents who did not experience sleep difficulties during the past 12 months were classified as not experiencing sleep difficulties. Respondents who experienced sleep difficulties less than once per month were excluded from the analyses.

All subjects were interviewed by the physician, and their weight (with minimal clothing) and standing height were recorded at the clinic.

Statistics:

Univariate statistics were used to examine means, standard deviations and shapes of distribution for continuous variables and frequencies were identified and corrected as necessary; no data were imputed. Study participant test scores were eliminated if all

question on a test were answered with the same answer choice. For bivariate analysis, outcome measures were examined using t- tests for variables with two categories. Multiple linear regression was used to determine the relationship between GERD manifestation and quality of life outcomes while controlling for potential factors (age, gender, BMI, current alcohol use, smoking current use of spicy food, current use of ant reflux medication and comorbidity) and patient perception of GERD severity. Subjects with missing data on relevant variables were excluded from the multivariable analysis

Results:

During the study 642 patients who had complete data were included in the analysis. Of these, 58,73% females. The average age was 37,5 ±8,2 years, no gender difference BMI for females were higher than in males 26,8±4,1vs. 24,9±3,8, p<0,001. With positive endoscopic finding, and Erosive Repllux disease were 522 (81,7%), and with negative and EER, were 120 (18,3%) patients.

.Table 1. Characteristics of GERD Respondents With and Without sleep disturbance

Characteristic	With	Without	P value
Demographics			
Age, mean (y) (SD)	37,5	39,0	0,113
Female	228	30	<0,001
Clinical characteristics			
No. of physical comorbidities	3,07	1,79	<0,001
Have psychiatric comorbidity	187		<0,001
BMI, mean (SD)	28,8	26,8	<0,001
Currently smoke		300	64<0,05
Use of alcohol	312	43	<0,05
Use spice food	289	73	<0,05
Use prescription medication for GERD	400	122	
Use over-the-counter product for GERD	130	27	
Sleep difficulties			
Experience sleep difficulties, n (%)	123 (68.3)	28 (37.9)	001
Experience induction symptoms with or without maintenance symptoms, n (%)	473 (49.1)	49 (25.5)	001
Experience maintenance symptoms with or without induction symptoms, n (%)	450 (58.3)	72 (31.0)	001
Experience both induction and maintenance symptoms, n (%)	456 (41.9)	66 (20.5)	..001

Table 2 . Characteristics of EER Respondents With and Without sleep disturbance

Characteristic	With (n . 11,685)	Without(n . 29,634)	P value
Demographic			
Age, mean (y) (SD)	38,2	47.93	0,113
Female	27	3	001
Clinical characteristics			
No. of physical comorbidities	3,07	1,79	001
Have psychiatric comorbidity	6	9	001
BMI, mean (SD)	30.13	28.24	024
Currently smoke		26	38
Use of alcohol	28	36	
Use spice food	422	200	001
Use prescription medication for GERD	54	18	
Use over-the-counter product for GERD	16	3	
Sleep difficulties			
Experience sleep difficulties, n (%)	43 (68.3)	28 (37.9)	001
Experience induction symptoms with or without maintenance symptoms, n (%)	83 (49.1)	39 (25.5)	001
Experience maintenance symptoms with or without induction symptoms, n (%)	76 (58.3)	46(31.0)	001
Experience both induction and maintenance symptoms, n (%)	78 (41.9)	34 (20.5)	..001

Results showed that there is significance between GERD and EER and OSA. It was showed that significance was found between life style factors as a risk fascots for GERD and EER and as factors for increasing of OSA episodes.

Anti reflux therapy shoves in this group of patients as good to decrease OSA episodes. Conclusion: Despite these shortfalls in the design of the study, the authors have produced interesting and novel data: there is little information in this area of treatment of GOR in OSA patients. The evidence that GERD treatment improves OSA severity is much less convincing than vice versa (18-22). The three studies all show improvement in the number of arousals during sleep, but only one showed a significant difference in apnea. (23) Perhaps, the most promising result is that in the Senior et al. study, 3 of 10 patients (30%) had OSA treatment response to GERD therapy alone. All of these preliminary studies illustrate the significant role that GERD plays in sleep symptoms and sleep pathology. They also show the promising role that GERD therapy could play in OSA treatment (24). What is not clear is if GERD therapy has long lasting effects on OSA, the quantitative impact of treatment on OSA, and whether these measured parameters will reduce OSA-related morbidity. The results highlight the need for a controlled clinical trial with objective monitoring to detect an effect on apneic episodes. At present the role of GERD in OSA remains contentious and unclear; it seems to us just as likely that reflux and OSA are both linked independently to obesity.

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