Sleep Medicine 22 (2016) 33–38

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Association between respiratory events and nocturnal gastroesophageal reflux events in patients with coexisting obstructive sleep apnea and gastroesophageal reflux disease

Nattapong Jaimchariyatam [a,b,*], Warangkana Tantipornsinchai [a], Tayard Desudchit [b,c], Sutep Gonlachanvit [d]

[a] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[b] Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
[c] Division of Neurology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[d] Division of Gastroenterology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand

ARTICLE INFO

Article history:
Received 27 January 2016
Received in revised form 16 April 2016
Accepted 19 April 2016
Available online 8 June 2016

Keywords:
Obstructive sleep apnea
Gastroesophageal reflux disease
Arousal
Esophageal pH monitoring
Esophageal impedance monitoring

ABSTRACT

Background: Literature has addressed the increased prevalence of gastroesophageal reflux disease (GERD) in obstructive sleep apnea (OSA). Significant improvement of GERD has been found after OSA treatment. However, precise mechanisms underlying this correlation remain unclear. We examined the association between nocturnal gastroesophageal reflux (GER) and sleep events in patients with coexisting OSA and GERD.

Methods: A case-crossover study among 12 patients with coexisting moderate–severe OSA and GERD was conducted. Participants underwent simultaneous polysomnography and esophageal impedance and pH monitoring. GER subtypes (ie, acid reflux, non-acid reflux) were defined as outcomes. Respective control time points were selected in all eligible control periods. Each sleep event was assessed individually. Estimated odds ratios (ORs) and 95% confidence intervals (CIs) were analyzed. A p-value of < 0.05 was considered significant.

Results: Patients were determined as moderate to severe OSA (respiratory disturbance index of 42.66 [±22.09]). There were a total of 50 GER episodes, 22 acid reflux and 28 non-acid reflux. Arousals and awakenings were significantly associated with subsequent GER events. The OR for GER following an arousal was 2.31 (95% CI 1.39–3.68; $p < 0.001$) and following an awakening was 3.71 (95% CI 1.81–7.63; $p < 0.001$). GER events were significantly less likely to occur after other respiratory events (OR 0.38 [95% CI 0.18–0.82]; $p = 0.01$). No sleep events followed GER events ($p > 0.05$).

Conclusions: Both awakening and arousal appear to precipitate any subtype of GER events in patients with coexisting GERD and moderate to severe OSA. However, GER events were significantly less likely to occur after other respiratory events and did not appear to cause sleep-related events.

1. Introduction

Gastroesophageal reflux disease (GERD) is a common chronic disorder presenting with a broad spectrum of symptoms, including esophageal and extraesophageal symptoms. Normal sleep physiology results in many changes of gastroesophageal function that contribute to the pathogenesis of GERD. Sleep may alter physiological mechanisms responsible for normal esophageal clearance, resulting in impairment of esophageal acid clearance. The rate of swallowing is reduced during sleep, leading to a decrease in primary peristalsis, a pivotal defense mechanism that is responsible for volume clearance of refluxate from the esophagus. Diminished salivary production during sleep, as well as reduced delivery of saliva to the distal esophagus due to decreased primary peristalsis delay alkalization and thus, normalization of esophageal pH after acid reflux occurs. The upper-esophageal sphincter basal pressure is significantly reduced, resulting in an increased risk of aspiration. In addition, gastric acid secretion is increased and gastric emptying is delayed during nighttime [1]. Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repeated episodes of upper-airway occlusion that result in brief periods (at least 10 s) of breathing cessation (apnea) or a marked reduction in tidal

* Corresponding author. Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Road, Phathumwan, Bangkok 10330, Thailand. Tel.: +66 2256 4252; fax: +66 2256 4252.
E-mail address: drboy48@yahoo.com (N. Jaimchariyatam).

http://dx.doi.org/10.1016/j.sleep.2016.04.013
1389-9457/

volume (hypopnea). GERD and OSA frequently occur together. GERD has been shown to be prevalent in patients with OSA on the basis of studies recording symptoms and esophageal pH [2–5], but data on non-acid reflux have been rarely reported. Patients with OSA are at a significant risk for nocturnal gastroesophageal reflux (GER). Favorable effects of continuous positive airway pressure (CPAP) in patients with GERD and OSA have been reported [4,6–8]. Despite the apparent epidemiologic link between these two conditions, the exact association remains a controversy [9,10]. Apneic episodes may be associated with increased transdiaphragmatic pressure and decreased intrathoracic pressure, favoring gastroesophageal reflux [4,10,11]. On the other hand, arousals and awakenings rather than apneas or hypopnea may play important roles in the development of acid reflux [9]. Likewise, the association between non-acid reflux and sleep apnea remains uncertain. The aim of the study was to further explore the association between respiratory events and all types of nocturnal gastroesophageal reflux in patients with coexisting OSA and GERD.

2. Methods

2.1. Study population

Consecutive patients between the ages of 18 and 75 years with comorbid OSA and GERD in King Chulalongkorn Memorial Hospital were recruited. The diagnosis of GERD was performed using 24-h pH monitoring. Standard was utilized to diagnose OSA. Patients were excluded if they had any unstable medical conditions, previous history of acid-reducing surgery, or other surgeries of the esophagus or upper-gastrointestinal tract. Other exclusion criteria were patients with pyloric stenosis, gastroparesis, or any other gastrointestinal conditions that might affect pH measurement for GERD.

2.2. Study procedures

The study protocol was approved by the Institutional Review Board and Ethics Committee of the Faculty of Medicine, Chulalongkorn University (IRB: 059/57). All individuals provided informed consent to participate in the study. Prior to the study initiation, individuals were asked to discontinue CPAP and/or any GERD-related medications, if any, for at least seven days. These medications included proton pump inhibitors, H2 receptor antagonists, metoclopramide, antacids, or any other medication affecting acid-producing and/or gastrointestinal motility.

Individuals were also asked to fill out a questionnaire in order to assess the basic demographic information, sleep history, as well as the Epworth Sleepiness Scale (ESS), and body mass index (BMI). All individuals underwent an 8-h standard polysomnography with simultaneously combined pH-metry and esophageal impedance monitoring. To avoid potentially reflux-provoking stimuli, diet was restricted and individuals were asked to avoid eating for 2 h before starting the test.

2.3. Polysomnography

Overnight sleep testing was conducted under standard polysomnographic protocols [12], using Polysmith® to acquire and analyze the collected sleep data. Polysomnographic evaluation included the following parameters: nasal and oral airflow and nasal pressure transducer, respiratory and abdominal efforts, oxyhemoglobin saturation by pulse oximetry, end tidal CO_2, electrocardiograms (ECGs), submental and leg electromyelograms (EMGs), electrooculograms (EOGs), body position, snoring (nasal pressure transducer and microphone), and electroencephalograms (EEGs: international 10–20 system). The EEG was the primary variable to document wakefulness, arousals, and sleep stages during the sleep study. The EEG consisted of six channels: two central channels referenced to an ear mastoid site (C4-M1, C3-M2), two frontal channels referenced to an ear mastoid site (F4-M1, F3-M2), and two occipital channels referenced to an ear mastoid site (O2-M1, O1-M2). Sleep parameters including sleep apnea events were identified and scored using the American Academy of Sleep Medicine manual for the scoring of sleep and associated events: rules, terminology, and technical specification, Version 2.1 [12]. All scoring was performed by only one sleep technician and one sleep physician for consistency.

Awakening (stage W) is scored when there is an alpha rhythm in greater than 50% of the epoch and may still be scored if one of the three following markers of alertness are detected: eye blinks with the eyes open or closed (with a frequency of 0.5–2 Hz); reading eye movements (consisting of a slow phase followed by a rapid movement in the opposite direction); or the presence of irregular conjugate eye movements with normal or high chin muscle tone suggesting that the subject is awake and looking around. An apnea was defined as cessation (at least 90% reduction) in airflow for at least 10 s during sleep and a hypopnea defined by an abnormal respiratory event lasting for at least 10 s with ≥30% reduction in airflow accompanied by ≥3% oxygen desaturation from pre-event baseline and/or the event was associated with an arousal. We scored a respiratory event as a respiratory-effort related arousal (RERA) if there was a sequence of breaths lasting ≥10 s characterized by increasing respiratory effort or by flattening of the inspiratory portion of the nasal pressure leading to arousal from sleep when the sequence of breaths does not meet the criteria for an apnea or hypopnea. The apnea–hypopnea index (AHI) was defined as the number of respiratory events (apneas and hypopneas) per hour of sleep time. The respiratory disturbance index (RDI) was defined as the number of respiratory events (apneas, hypopneas, and RERA) per hour of sleep time. OSA was defined as an RDI of at least 5/h (mild OSA: 5/h ≤ RDI < 15/h, moderate OSA: 15/h ≤ RDI < 30/h, severe OSA: RDI ≥ 30/h). Arousals were defined as an abrupt change in EEG frequency lasting ≥3 but <15 s that was preceded by 10 s of sleep. All sleep data were acquired and scored by a registered polysomnographic technologist and a board-certified sleep physician without knowledge of the results of the questionnaire or esophageal pH/impedance.

2.4. Combined pH-metry and esophageal impedance

Distal esophagus pH and esophageal impedance were continuously monitored and recorded for the duration of the polysomnography study with an antimony single-use multichannel esophageal impedance pH monitoring catheter (VersaFlex®, Sierra Scientific Instruments, USA). The catheters were calibrated in polyelectrolyte buffer solutions of pH 7 and 1 before use. Placement of the catheter was performed transnasally using the standard esophageal manometry to identify the lower esophageal sphincter (LES). The catheter was placed at 5 cm above the upper border of the LES. The catheter was connected and calibrated to the sleep-monitoring computer so that all sleep and GER data could be recorded simultaneously.

The multichannel capability of the recording catheter captures the direction of this esophageal liquid and enables a clearly defined retrograde bolus transit as a marker of reflux. The reflux patterns were detected by impedance-pH monitoring. Reflux is defined as either pure liquid or a mixture of liquid and gas detected by impedance. Liquid-only reflux is defined as a retrograde 50% decrease in impedance from the baseline in the two distal impedance sites. Gas reflux was defined as a simultaneous increase in impedance >3000 Ω in any two consecutive impedance sites with one site having an absolute value >7000 Ω. Mixed liquid and gas reflux is defined as gas reflux occurring during or immediately before liquid reflux. According to the pH monitored simultaneously, the information ob-