Esophageal Acid Clearance during Sleep in Patients with Barrett’s Esophagus

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Sleep-related gastroesophageal reflux and esophageal acid clearance have been shown to be important components in the pathogenesis of reflux esophageal disease. Previous studies have suggested that patients with more severe esophagitis are distinguished by an accumulation of acid mucosal contact time during sleep. These data would suggest that patients with Barrett’s esophagus should have particularly severe impairment of acid clearance, most notable during sleep. To address this issue, 16 asymptomatic healthy volunteers and 13 patients with Barrett’s esophagus were studied. Acid clearance was assessed by timing the reestablishment of an esophageal pH of 4 following the infusion of 15 ml 0.1 N HCl. Sleep was polygraphically monitored in order to objectively determine sleep and waking. The results indicated that while patients with Barrett’s esophagus had a marked increase in the frequency of spontaneous gastroesophageal reflux during sleep, they unexpectedly demonstrated faster acid clearance times during both waking and sleep. A greater percentage of arousal responses to acid infusion during sleep was noted in the Barrett’s group. It is concluded from these results that patients with Barrett’s esophagus can adequately clear acid from the distal esophagus but experience considerable acid mucosal contact through repeated episodes of spontaneous reflux during sleep.

KEY WORDS: gastroesophageal reflux; sleep; Barrett’s esophagus; acid clearance.

Previous work has demonstrated the importance of sleep-related gastroesophageal reflux and compromised esophageal acid clearance in the pathogenesis of gastroesophageal reflux disease (1, 2). Studies from our laboratory have documented prolonged acid clearance during sleep in normals with a negative acid perfusion test as well as in patients with reflux disease and a positive acid perfusion test. These studies have emphasized the importance of an arousal from sleep in facilitating clearance of acid from the distal esophagus (3, 4).

Barrett’s esophagus is generally recognized as a complication of chronic gastroesophageal reflux (5, 6). Several abnormalities of esophageal physiology have been described in Barrett’s esophagus including decreased lower esophageal sphincter pressure, disordered esophageal peristalsis, and prolonged acid clearance (7, 8). These physiologic abnormalities, along with our sleep data on normal subjects and patients with esophagitis, might be extrapolated...
to suggest that patients with Barrett's esophagus should have particularly severe impairment of acid clearance during sleep (3, 4). Using our established protocol of acid infusion during sleep and waking, the present study was designed to test the hypothesis that patients with Barrett's esophagus might exhibit unusually prolonged acid clearance during sleep.

MATERIALS AND METHODS

Study Population. Sixteen asymptomatic healthy normals (10 men, six women; mean age 25.6 years, range 23–34 years) who either denied or rarely had heartburn participated as normal volunteers. All subjects had normal esophageal manometry, and none had any evidence of esophageal mucosal sensitivity during an acid perfusion test. Thirteen patients with Barrett's esophagus were studied (five women, eight men; mean age 56 years, range 30–73 years). The diagnosis of Barrett's esophagus was established by the presence of metaplastic columnar mucosa noted on biopsy more than 2 cm above the endoscopically determined esophagogastric junction. The average length of columnar mucosa in the esophagus as determined by biopsy was 9 cm from the distal margin of the tubular esophagus. Twelve of these 13 patients had reflux symptoms. Five patients had a history of significant gastrointestinal bleeding. Four patients had experienced esophageal strictures, and eight had esophageal ulcers. These patients were all studied subsequent to ulcer healing. Three patients had undergone antireflux surgery many years prior to the diagnosis of Barrett's. Twelve of 13 patients had endoscopic esophagitis. All 13 patients had a positive response to acid perfusion, and none had any primary esophageal motor disorder. Technical difficulties did not allow inclusion of all patients in all statistical analyses. Therefore, if diminished sample sizes are used, they are denoted along with mean and standard deviation estimates.

Study Protocol. A detailed explanation of the study protocol has been previously published (4). All subjects were studied in the sleep laboratory with monitoring of electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), and electrocardiogram (ECG). These measures were used to determine stages of sleep and wakefulness by standardized criteria (9). Esophageal pressures were monitored with two transducers (5 cm apart) along with esophageal pH using a specially designed and engineered catheter (Konigsburg Instruments, Inc., Pasadena, California). The catheter was placed through the nose and positioned in the esophagus 5 cm above the manometrically determined lower esophageal sphincter (LES). A series of two to five infusions of 15 ml of 0.1 N HCl (warmed to 38°C) were conducted in the supine position during sleep. In addition, one similar acid infusion was conducted prior to the beginning of the sleep study while the subject was awake and in the supine position. The waking infusion was accomplished without the subject's knowledge in order to simulate the conditions occurring with infusions during sleep.

Study Measures. The acid clearance interval was determined by assessing the time from the drop in pH to below 4 until the pH again returned to 4. Arousals from sleep were polygraphically determined by the appearance of alpha or beta EEG activity within 10 min of the acid infusion. The arousal latency time was established as the interval between the drop in the distal esophageal pH to a value less than 4 to the point at which an arousal response was first polygraphically observed. Spontaneous reflux is defined as a drop in pH to below 4 not associated with an acid infusion (4).

Parameters of esophageal motility were also measured with subjects awake and asleep. A primary esophageal contraction wave (PEC) was defined by the presence of a burst of activity from the submental EMG associated with the act of swallowing followed within 7 sec by a propagated peristaltic contraction wave. Secondary peristalsis (SP) was identified whenever a normal peristaltic contraction complex occurred that was not preceded within 7 sec by a burst of activity from the submental EMG indicative of a swallow. Nonpropagated waves were defined when swallowing occurred with no contraction waves following within 7 sec or if a wave were to be observed at only one particular transducer site. Simultaneous contraction waves were identified when nonperistaltic simultaneous contraction waves were noted within 7 sec after a swallow. Total swallows (TS) were determined by adding primary, nonperistaltic, and simultaneous contractions.

In order to clearly present the current data, it is necessary to describe some of the results from a previous investigation since the current data analysis and presentation are similar to those described in one of these prior studies (4). First, acid infused into the esophagus will provoke arousal responses from sleep in asymptomatic controls significantly more often than water infusions (4). Further, rapid and efficient acid clearance associated with acid infusions during sleep is accompanied by an arousal response and subsequent swallowing responses which occur during polygraphically identified awaking. The greater the amount of wakefulness in the acid clearing interval, the more rapid the acid clearance time (4). That is, waking and acid clearance time are have a high positive correlation, and thus the discussion of acid clearance itself must include concomitant consideration of the arousal response and the degree of waking attained during the acid clearance interval. A similar study in normals revealed that if subjects aroused from sleep with acid infusion remained awake for more than 30% of the acid clearing interval, they could eliminate acid from the esophagus as efficiently as while fully awake (4). All statistical tests in the present study employed Student's t test. Since the data appeared to deviate substantially from a normal distribution, an arcsin transformation was used to normalize the data in order to justify the use of a conventional parametric statistic.

RESULTS

The mean LES pressure in patients with Barrett's esophagus was significantly less than that of the controls (10 ± 5 vs. 18 ± 7 mm Hg, respectively (P <