Consequences of Nighttime Heartburn – Quality of Life and Sleep Disturbances

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Not uncommonly clinicians observe that patients who are effectively treated for severe heartburn will spontaneously report that they are sleeping better in addition to achieving a resolution of their substernal burning. Such reports from patients have focused attention on the relationship between gastroesophageal reflux (GER) during sleep and the extent to which this phenomenon will result in disturbances of sleep and its attendant complications. In the recent past, sleep as a physiologic and phenomenological issue was essentially ignored with regard to its role in the pathogenesis of disease. With the evolution of sleep laboratories from purely research facilities documenting physiologic and psychological changes associated with sleep, to clinical laboratories, which document important physiologic changes in individuals complaining of a variety of sleep-related problems, an awareness of the relationship between sleep and various gastrointestinal phenomena has rapidly emerged. More recently, there has been a particular focus on the issue of nighttime heartburn as related to the consequences of sleep disturbance and reduction in the quality of life.

Gastroesophageal reflux disease (GERD) is a highly prevalent disorder that affects a substantial proportion of the population in the United States and western countries. Fifteen percent of US adults experience symptoms of GERD, the most common of which are heartburn and regurgitation, at least once a week. [1] Gastroesophageal reflux (GER) occurs via several mechanisms which result in a diminution of the normal barrier between the stomach and the esophagus, the lower esophageal sphincter (LES) (Fig 1). This may occur via a chronic decrease in the resting LES pressure or via what is termed a transient LES relaxation. The LES normally decreases to the intragas-

• More than 60 million people experience heartburn at least once a month and 25 million suffer from heartburn daily.

• About 1/2 of pregnant women experience heartburn at least once a month and about 1/4 report symptoms daily.

• Infants and children can also have heartburn, which may result in vomiting, coughing and other respiratory problems.

Source: American Gastroenterological Association poll
tric pressure levels with swallows. This creates a “common cavity” and allows ready access of the acidic gastric contents to the esophageal mucosa. The most notable stimulus for these transient decreases of the LES is gastric distention. Thus it is easy to understand why most episodes of GER occur post prandially. It has been established that this is the most common mechanism of GER either during waking or during sleep. The fact that symptoms of heartburn are readily treated with either antacids, histamine-2 receptor antagonists (H2 blockers), and more recently proton-pump inhibitors, have obscured the frequency and importance of the symptom of nighttime heartburn. Thus, until recently, clinicians would rarely, if ever, inquire about the frequency, characteristics, and consequences of nighttime heartburn.

NIGHTTIME HEARTBURN AND SLEEP DISTURBANCES – ISSUES IN PREVALENCE AND QUALITY OF LIFE

Several studies have recently focused attention on both quality of life and the sleep disturbance as consequences of nighttime heartburn. In general such studies define nighttime as the time when the patient lays down to attempt to go to sleep until waking in the morning occurs. Among the first observations regarding the relationship between nighttime heartburn and sleep disturbance, was a report by Janson and colleagues [2] describing the results of a survey of the general population in several Scandinavian countries. In this study, the authors found a significant relationship between the occurrence of nighttime heartburn at least once a week, and daytime sleepiness, daytime tiredness, and snoring. Symptoms of GER were associated with daytime sleepiness (odds ratio 2.6), daytime tiredness (odds ratio 4.5), and disrupted breathing (odds ratio 3.8). The relationship between snoring and GER at least one night per week showed an odds ratio of 2.75. Subsequently, an epidemiologic study was conducted by Farup and colleagues [1] which described the impact of nighttime heartburn on health-related quality of life. In this study, nighttime heartburn was described as a common symptom in patients with frequent daytime heartburn. The authors reported that 74% of those individuals with frequent heartburn had symptoms of nighttime heartburn. It was also noted that subjects who reported nighttime heartburn were significantly more impaired with regard to quality of life than subjects who reported daytime symptoms only. This was observed particularly for the physical and mental component subscales.

This surprising prevalence of nighttime heartburn has been replicated in a more recent study by Shaker and colleagues. [3] This study involved a nationwide telephone survey of 1000 adults experiencing heartburn at least once a week conducted on behalf of the American Gastroenterological Association;
It is important also to recognize and understand that the basic phenomenology of sleep alters the response to the acid mucosal contact which results from GER. Under normal circumstances during waking, acid mucosal contact is associated with an orchestrated set of secretory and motor responses in the esophagus. With acid mucosal contact there is a reflexive increase in salivation which, when swallowed into the distal esophagus, acts as a buffer to neutralize the acidic mucosa. In fact, studies have shown that the actual bicarbonate concentration of the saliva is altered by the acidity of the refluxate. The most typical symptom of GER, heartburn, is noted to be the direct result of acid mucosal contact and is a “signal” to the patient that some response is required. Coupled with the increase in salivation, this triggers a set of progressive swallowing responses. As noted in Fig 2 these responses are typically diminished during sleep. Salivation is nearly absent during sleep and swallows are markedly decreased. No heartburn is noted unless there is an awakening from sleep, since heartburn is a waking conscious experience. The combination of these alterations in acid mucosal responses during sleep leads to a marked prolongation of mucosal acid contact time associated with sleep related GER.

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This is an important concept since numerous studies from our laboratory and others have indicated that sleep related GER is an important determining factor in the development of the complications of GER such as esophagitis and the respiratory complications of GER such as the exacerbation of bronchial...
asthma [4]. The prolongation of acid mucosal contact time facilitates the back diffusion of hydrogen ions into the esophageal mucosa which leads to the mucosal damage noted in patients with esophagitis. In addition, sleep has been demonstrated to facilitate the proximal migration of very small amounts of acid infused into the distal esophagus. [5] This alone creates a risk for aspiration of acid into the larynx and tracheobronchial tree. Thus, sleep itself alters responses to GER and episodes of GER disrupt sleep. This interactive effect makes the issue of nighttime heartburn a particularly clinically relevant issue.

**Therapeutic Resolution of Symptoms and Impact on Quality of Life**

An epidemiologic study of general symptomatic GERD patients (n=6215) also revealed similar results in terms of there being diminished quality of life in this patient cohort. [6] Kulig and colleagues found that the generic quality of life of these patients was diminished, and that quality of life was significantly improved in patients with both erosive and nonerosive GERD, as well as Barrett’s esophagus, after 2 weeks of treatment with esomeprazole. This study indicates that quality-of-life measures can be substantially and significantly improved quickly with appropriate resolution of symptoms. This study did not address the issue of nighttime GERD.

Other studies have more formally documented the presence of sleep disturbances in patients with nighttime GERD, as well as response to treatment. For example, results from a randomized clinical trial involving patients with both nighttime heartburn and sleep disturbance were recently published by Johnson and colleagues. [7] This multicenter, randomized, double-blind, placebo-controlled trial included adults with GERD-associated sleep disturbances and moderate to severe nighttime heartburn, as noted by a subjective patient diary. Patients received either esomeprazole 40 mg, 20 mg, or placebo once daily for 4 weeks. Outcome variables were the relief of nighttime heartburn, the change in the PSQI global score, and changes in work productivity as assessed by the Work Productivity and Activity Impairment questionnaire. A significantly higher percentage of patients reported relief (no heartburn on 6 of 7 nights), and complete resolution (no heartburn on 7 nights) of symptoms with treatment compared with placebo. There was no significant difference between the 40 mg and 20 mg doses of esomeprazole; approximately 50% of treated patients had relief of nighttime heartburn symptoms compared with approximately 13% on placebo. Approximately 82% of patients in the treatment arms reported relief of GERD-associated sleep disturbance compared with 55% on placebo. The PSQI data, which measures general sleep quality, showed significant improvement to nearly normal levels in both treatment groups. It was documented that approximately 16 work hours were lost due to GERD-related sleep disturbances at baseline; this was improved to approximately 12 hours subsequent to treatment. Using an average total employee compensation cost of $24.59, the cost of hours saved per patient per week was approximately $290.00 in the 2 treatment groups.

### Lifestyle Modifications to Avoid Nighttime Heartburn

1. Avoid food ingestion for at least 2.5-3 hours before bedtime.
2. Avoid alcohol for at least 4 hours prior to bedtime.
3. Sleep with the upper body slightly elevated;
4. Try to sleep on the left side.
5. OTC H-2 blockers 1 hour prior to bedtime.
6. Avoid food, beverages and medicines that weaken the sphincter muscle and may damage the esophageal lining. These include:
   - Chocolate
   - Peppermint
   - Fried and fatty foods
   - Coffee
   - Carbonated beverages
   - Alcoholic beverages
   - Citrus fruits and juices
   - Tomato products
   - Pepper
   - Vinegar
   - Ketchup and mustard
7. Lose weight, if overweight.
8. Stop or decrease smoking to help the LES (sphincter) muscles work better.

Table 1
Indeed, results of a recent Internet survey showed that GERD-related symptom severity was strongly associated with work impairment, and that nighttime GERD was associated with substantially greater work impairment, as was symptom severity. [8] In a smaller study using polysomnography to define sleep parameters rabeprazole 20mg qd was shown to improve subjective sleep measures without any change in the objective sleep measures. [6]). Pantoprazole is the only PPI with an indication for nighttime heartburn, but there are no outcome studies on treated patients with nighttime heartburn and sleep disorders.) Other lifestyle measures may also be helpful in controlling nighttime GER, and these are noted in Table 1. Perhaps the most important is to avoid sleeping within 2 hours of eating a meal. The gastric distension resulting from a meal will, as noted earlier, predispose to the occurrence of transient decreases of the LES and subsequent GER.

OBSTRUCTIVE SLEEP APNEA

Patients with obstructive sleep apnea (OSA) share risk factors for GERD such as obesity. Heartburn is a symptom commonly observed in patients with obstructive sleep apnea (OSA). Patients with both GER and OSA have been shown to have significantly poorer quality of life compared with patients with OSA alone. [9] It is clinically well established that OSA is associated with a profound degree of daytime sleepiness, depression, and irritability — all of which are factors that weigh heavily in diminishing the quality of life. GER exacerbates to an even greater degree the quality of life in this patient population (i.e., those with sleep disorders).

CONCLUDING REMARKS

In conclusion, it appears that the occurrence of nighttime heartburn is a symptom that clearly mitigates quality of life and work performance. Patients with nighttime heartburn consistently report that these nighttime symptoms disturb them more than their daytime heartburn, and the resultant disturbance in sleep and the impaired daytime performance takes its toll in terms of the quality of daily life in these patients. It is also evident that although there are many causes of sleepiness, nighttime heartburn is indeed associated with reports of disturbed sleep, and in a majority of such patients, sleep disturbances and quality of life can be markedly improved by eliminating the symptoms of nighttime heartburn.

REFERENCES


