

Sleep disturbances and hypnotic medication use in relation to risk of Barrett's esophagus and esophageal adenocarcinoma

Anastasia Shnitser MD, Abhik Roy MD, Sidney Cohen MD and Anthony J DiMarino MD

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Thomas Jefferson University Hospital

BACKGROUND

The incidence of esophageal adenocarcinoma (EA) has increased more rapidly than any other cancer (with the exception of malignant melanoma) in the United States over the past 30 years. Gastroesophageal reflux disease (GERD) is the strongest risk factor for the development of Barrett's esophagus, which in turn leads to the rise of most EA's. In a large portion of persons with sleep disorders, perhaps as high as 30%, GERD is a major causal or contributing factor. It has been proposed that the use of hypnotics for the treatment of sleep disorders may exacerbate the damaging effects of refluxate on the esophageal epithelium by reducing the frequency and effectiveness of normal clearance mechanisms (figure 1).

PURPOSE

Our study was developed to track prior use of hypnotic sleep aids in patients diagnosed with Barrett's esophagus and/or esophageal adenocarcinoma.

REFERENCES

- DiMarino AJ, Banwait KS, Eschinger E et al. The effect of gastro-oesophageal reflux and omeprazole on key sleep parameters. *Aliment Pharmacol Ther* 2005; 22: 325-329.
- Johnson DA, Orr WC, Crawley JA et al. Effect of esomeprazole on nighttime heartburn and sleep quality in patients with GERD: a randomized, placebo-controlled trial. *Am J Gastroenterol* 2005; 100: 1914-1922.
- Gagliardi GS, Shah AP, Goldstein M et al. Effect of Zolpidem on the sleep arousal response to nocturnal esophageal acid exposure. *Clin Gastro and Hep* 2009; 7: 948-952.
- Adachi K, Fujishiro H, Yuki M, et al. Predominant nocturnal acid reflux in patients with Los Angeles grade C and D reflux esophagitis. *J Gastroenterol Hepatol* 2001; 16: 1191-1196.
- Orr WC, Goodrich S, Fernstrom P et al. Occurrence of Nighttime Gastroesophageal Reflux in Disturbed and Normal Sleepers. *CGH* 2008; 6: 1099-1104.

METHODS

We performed a retrospective chart review using ICD-9 codes for Barrett's esophagus and EA to identify patients with confirmed histologic diagnoses of these conditions. Patients that met study criteria were queried by telephone to obtain a history of hypnotic medication use over the 10 years prior to the diagnosis of Barrett's esophagus or EA. Hypnotic medications included both benzodiazepines and non-benzodiazepines (such as zolpidem, zaleplon, and trazodone). In addition, we obtained an accurate history regarding their acid reflux symptoms and treatment.

Figure 1: Pathophysiology of hypnotic medications effect on disordered sleep.

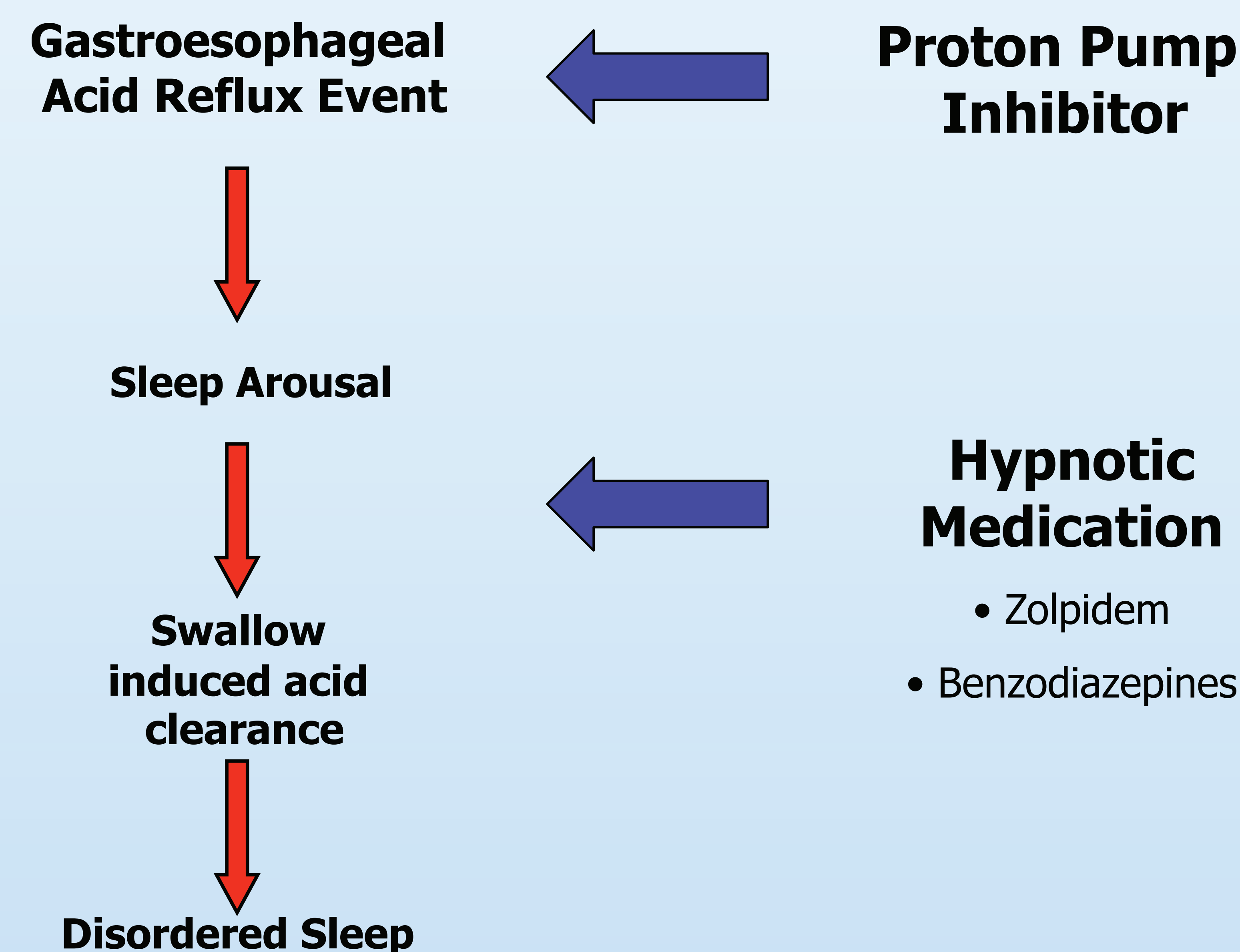


Table 1: Characteristics of Study Participants on Sleep Aids at the time of diagnosis with BE or EA.

	Diagnosis	Symptoms	Acid suppression	Sleeping Aids
61F	BE, no dysplasia	Acid reflux	PPI (Nexium)	Zolpidem and Duloxetine
52F	BE, no dysplasia	Acid reflux	PPI (Nexium)	Zolpidem
74M	BE, no dysplasia	Acid reflux	PPI (Prilosec)	Zolpidem
62M	BE, no dysplasia	Nocturnal acid reflux	None	Alprazolam
69M	BE, no dysplasia	Indigestion	Calcium carbonate (Tums) PRN	Clonazepam
37M	BE, no dysplasia	Acid Reflux	None	Doxylamine (Unisom)
55M	EA arising from BE	Acid Reflux	PPI (Protonix)	Zolpidem
70M	BE, no dysplasia	Acid Reflux	PPI (Nexium)	Zolpidem
44F	BE, no dysplasia	Acid Reflux	Famotidine PRN	Zolpidem and Quetiapine
66M	BE, no dysplasia	None	PPI (Nexium)	Clonazepam and Quetiapine
60M	BE, no dysplasia	Acid Reflux	PPI (Nexium)	Diphenhydramine and Fluoxetine
51F	BE, no dysplasia	Acid Reflux	None	Trazodone, Bupropion and Escitalopram
70M	BE, no dysplasia	Dysphagia	None	Temazepam
85M	BE, no dysplasia	None	None	Diphenhydramine

CONCLUSION

These studies indicated several important findings:

1. Sleep aid usage is lower than expected in the general population (some publications estimate that upwards of 25% of Americans use sleeping aids) suggesting that in this study patients with Barrett's have less disordered sleep as compared to historical population.
2. Some patients with disordered sleep and Barrett's are on sleep aids but not acid suppression medication suggesting that disordered sleep and GERD with Barrett's should be carefully evaluated for PPI management in conjunction with sleep aid usage.