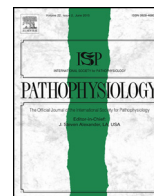




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Review

Gastroesophageal reflux disease: A clinical overview for primary care physicians

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ABSTRACT

Objective: GERD is among the most common outpatient disease processes encountered by clinicians on a daily basis. This review provides insights about how to approach GERD in terms of disease management and treatment.

Methods: Review articles were searched using PUBMED and MEDLINE using criteria that included English language articles published in the last 5 years concerning studies carried out only in humans. The key words used in the searches were GERD, PPI, and erosive esophagitis. Recommendations from the American College of Gastroenterology are also included in this manuscript.

Results: The search resulted in ~260 articles. The manuscript brings together and presents the results of recent recommendations from professional societies and recently published review articles on GERD.

Conclusion: GERD is one of the most common diagnoses made by gastroenterologists and primary care physicians. It is important to recognize the typical and atypical presentations of GERD. This paper helps primary care physicians understand the disease's pathophysiology, and when, how, and with what to treat GERD before referring patients to gastroenterologists or surgeons.

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Contents

1. Definition	00
2. Epidemiology	00
3. Clinical manifestation	00
4. Pathophysiology and risk factors	00
5. Complications	00
6. Diagnosis	00
7. Management	00
8. Non-pharmacologic intervention	00
9. Pharmacologic intervention	00
10. Comparing H2RA AND PPI	00
11. Comparing PPI	00
12. Refractory GERD and resistance to PPI	00

1. Definition

Gastroesophageal reflux disease (GERD) is one of the most common diagnoses made by both primary care physicians and gastroenterologists [1].

The Montreal Classification provides the most recent consensus definition of GERD. It defines GERD as heartburn symptoms or complications resulting from the reflux of gastric contents into the esophagus, up to the oral cavity, and lungs [4]. GERD is fur-

Abbreviations: GERD, gastroesophageal reflux disease; NERD, non-erosive disease; ERD, erosive disease; LES, lower esophageal sphincter; PPI, proton pump inhibitor; H2RA, histamine receptor antagonists; ATPase, adenosine 5'triphosphatase; EE, erosive esophagitis; NNT, number needed to treat; QOL, quality of life; GABA, γ -aminobutyric acid; EoE, eosinophilic esophagitis; ENT, ear, nose and throat; LINX, trade mark.

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13. Surgery.....	00
14. Adverse effects associated with PPI.....	00
15. Summary and conclusion.....	00
Grant support.....	00
Disclosure.....	00
Authors' contributions	00
References.....	00

ther classified into two subgroups. The first subgroup is GERD with heartburn symptoms but without endoscopic evidence of mucosal erosions (Non-Erosive Reflux Disease or NERD). The second subgroup is GERD with heartburn symptoms accompanied by objective evidence of erosions (Erosive Reflux Disease or ERD) [5].

Functional heart burn also falls under endoscopic negative disease, however it is important to note that it is a distinct entity from NERD. NERD is defined as typical reflux symptoms without evidence of reflux disease in endoscopy but abnormal acid exposure on the impedance-pH monitoring and is responsive to PPI. [84,85]. Functional heart burn on the other hand, as defined by Rome IV classification, is a retrosternal burning discomfort or pain refractory to anti-secretory therapy without presence of GERD, histopathologic abnormality, motility disorder or structural abnormality for at least three months with symptoms onset at least six months prior to the diagnosis. [86]

2. Epidemiology

In ambulatory care settings, GERD accounts for 17.5% of all digestive diseases recorded [2]. Sandler et al. reported that the annual incidence of GERD as the primary diagnosis by primary care providers in the United States was 4.6 million [3]. This number would rise as high as 9.1 million when considering GERD among the top three diagnoses during those encounters. GERD has a significant impact on both direct and indirect healthcare costs. The direct cost include office visits, diagnostic tests, treatments and hospital admissions, representing 9.3 billion dollars of the total amount of money spent on health care in the United States [3]. The indirect cost include missed work, decreased productivity while at work due to GERD related symptoms, and impaired daily living activities [3].

Estimates of the prevalence of GERD are primarily based on the presence of heartburn and/or acid regurgitation symptoms [6–8]. However, heartburn or acid regurgitation symptoms are not always present in patients with endoscopic evidence of esophagitis or Barrett’s esophagus [9]. A recent systematic review of 16 epidemiological studies found the prevalence of GERD to be 18.1% – 27.8% in North America, 8.8% – 25.9% in Europe, 2.5% – 7.8% in East Asia, 8.7% to 33.1% in the Middle East, 11.6% in Australia and 23% in South America [7]. Two different population studies from the UK and the USA, showed the incidence of GERD to be around 5 per 1000 person years [7]. Another population based survey from the United States found that up to 22% of the participating population reported heartburn symptoms, while 16% reported acid regurgitation. Heartburn and regurgitation was considered clinically significant if symptoms occur at least twice weekly, which were present in 6% and 3% respectively [8].

3. Clinical manifestation

The cardinal symptoms of GERD are troublesome heartburn and or regurgitation [11]. Heartburn is caused by the contact of refluxed material with the sensitized or ulcerated esophageal mucosa and perceived as burning behind the breast bone or retrosternal area whereas regurgitation is sensing the gastric content into the oral

cavity [87]. Heartburn mostly occurs during the postprandial state [4]. Persistent heartburn causes esophagitis, which manifests as dysphagia and is suggestive of peptic stricture. Dysphagia has been noted as the sole presentation of GERD in one-third of the patients [10]. GERD can manifest as either esophageal or extra-esophageal symptoms [87]. Esophageal or typical symptoms of GERD are heartburn, regurgitation, and chest pain or epigastric pain while extra-esophageal symptoms or atypical presentations are cough, laryngitis, asthma and dental erosion syndromes [87]. Furthermore, according to Montreal definition of GERD, without symptoms of heartburn and or regurgitation, there is no causal relationship between GERD and unexplained asthma and laryngitis. In addition to this, typical GERD symptoms can develop after exercise [86]. Some patients who complain of poor sleep are found to have heartburn and regurgitation at night time or during their sleep [87]. It is not clear if symptoms of odynophagia, water brash, hyper salivation and globus sensation are directly related to GERD [12,87].

4. Pathophysiology and risk factors

Reflux can be both physiologic and pathologic [1]. Physiologic reflux mostly occurs during the postprandial state, is transient, does not occur during sleep, and does not result in reflux symptoms [1]. The pathologic reflux is related to transient loss of pressure in the lower esophageal sphincter (LES) [10,29]. Transient loss of pressure in the LES is diagnosed when persistent LES relaxation occurs, lasting more than 10 s, with the absence of swallow within 4 s before and 2 s after the onset of the event, and presence of active crural diaphragm inhibition [87,88]. Lower esophageal sphincter (LES) tone and activity of crural diaphragm maintains the gastroesophageal junction (GEJ) pressure, in turn LES tone is maintained by the activity of neurotransmitters released by vagus nerve and by the stimulation of enteric nervous system [87–89]. LES relaxes as a neurogenic reflex in response to swallowing food leading to increased intra-gastric pressure and volume [90]. Various risk factors have been attributed to transient hypotension of the LES, such as diet and lifestyle (smoking, alcohol), abdominal obesity, infiltrative disease (e.g. scleroderma), myopathy associated with chronic intestinal pseudo-obstruction, medications (anticholinergics, smooth muscle relaxants such as β-adrenergic agents, aminophylline, nitrates, calcium channel blockers, and phosphodiesterase inhibitors), surgical damage to the LES, and esophagitis [10,15]. Among these risk factors, obesity accounts for 50–70% of patients with reflux symptoms, and 15% of the obese patients also have hiatus hernia (HH) [83]. The mechanism related to development of reflux symptoms in obese patients is thought to be secondary to chronic increased intra-abdominal pressure, which in turn results in an ineffective LES, delayed gastric emptying, and HH [84].

5. Complications

The various complications of GERD described in the literature are divided into three broad categories: esophagitis, peptic stricture, and Barrett’s esophagus (the last two are consequences of long standing esophagitis) [10,13]. Esophagitis is caused by constant irritation of the mucosal surface of the esophagus and subsequent loss

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