

## 10 Masking of Disease

The proposed OTC availability of Ome, as well as the current OTC availability of antacids and H<sub>2</sub>RAs for the self-treatment of heartburn, has given rise to some concern that their use may result in a delayed diagnosis by masking symptoms of serious diseases. These conditions include Barrett's esophagus with dysplasia, esophageal cancer and gastric malignancy. However, for treatment of occasional or episodic heartburn, the availability of antacids and H<sub>2</sub>RAs for OTC use appears to be safe and has not resulted in an increased incidence of undiagnosed or a delayed diagnosis of esophageal or gastric malignancy.<sup>129</sup>

### 10.1 Heartburn Symptoms

Heartburn is defined as a burning sensation that rises upward in the substernal area, and is often aggravated by food.<sup>130</sup> About 80% of the patients who did not seek medical attention used antacids to relieve their symptoms.<sup>131</sup>

Patients with a long history of severe and frequent heartburn and acid regurgitation may have a higher risk of developing adenocarcinoma of the esophagus.<sup>132-134</sup> However, in a nationwide population-based case-control study conducted in Sweden from 1995 through 1997, only 216 cases of adenocarcinoma of the esophagus were collected.<sup>135</sup> This suggests that the incidence of cancer is very low even in this group with chronic severe heartburn.

It is uncertain whether medical or surgical therapy reduces the risk of developing esophageal adenocarcinoma.<sup>134,135</sup> In the case-controlled trial of 196 patients with adenocarcinoma of the esophagus, H<sub>2</sub>RAs did not increase the incidence of cancer.<sup>134</sup>

If heartburn symptoms become chronic and persistent, it would suggest that GERD is present. Long standing GERD may lead to complications such as severe EE, esophageal stricture formation, and the development of Barrett's esophagus. Although Barrett's esophagus is found in up to 10% of patients with chronic GERD and is associated with adenocarcinoma of the esophagus, at least one large epidemiological trial suggests that evidence of Barrett's esophagus is found in only 38% of patients diagnosed with esophageal adenocarcinoma.<sup>134,135</sup> However, clinical symptoms may not correlate with the development of complications or more serious disease. In fact, many patients with esophageal carcinoma present with symptoms caused by the tumor itself, with little knowledge of how long Barrett's esophagus preceded the development of the cancer. It has been noted that patients with Barrett's esophagus seem to suffer fewer reflux symptoms than those with uncomplicated reflux.<sup>131,136</sup> This was demonstrated in a trial in Olmsted County, Minnesota, in which the prevalence of Barrett's esophagus based on endoscopy was 22.6 per 100,000 while at autopsy it was 17 times higher at 376 per 100,000.<sup>137</sup> In addition, studies suggest that it can take more than 20 years for an adenocarcinoma to develop in patients who have Barrett's esophagus.<sup>138</sup>

Short segment Barrett's esophagus (SSBE) is more prevalent than the long segment Barrett's esophagus (LSBE) and also has a greater association with adenocarcinoma of the esophagus.<sup>139,140</sup> However, diagnosing SSBE at endoscopy appears to be less reliable than diagnosing LSBE, with a positive predictive value of only 25% (LSBE positive predictive value = 55%).<sup>140</sup>

## 10.2 Endoscopic Findings

Endoscopic studies of the OTC target population with heartburn symptoms indicate that there is a very low incidence of serious disease. Studies evaluating the prevalence of Barrett's esophagus and malignancies in patients with heartburn are presented in Table 10.1. In general, the incidence of Barrett's esophagus and esophageal or gastric cancer in patients undergoing endoscopy for dyspepsia (including heartburn) is very low.

Trial (Authors)	Number of patients	Mean duration of heartburn (years)	Number (%) of cases			
			Esophagitis (Grade II or greater)	Barrett's esophagus	Gastric cancer	Esophageal cancer
Corder AP et al. <sup>131</sup>	143	10	33 (15)	6 (4)	0	0
Robinson et al. <sup>129</sup>	155	11	73 (47)	9.0 (6)	0	0
Protocol SKF 92334/B0025 <sup>141,142</sup>	208	9.6	5 (2.4)	2 (1.0)	0	0
Pappa KA et al. <sup>143</sup>	234	Minimum of 5 episodes per month	9 (3.8)	Not mentioned	0	0

## 10.3 Approaches in the Management of Heartburn

Guidelines from the American Society for Gastrointestinal Endoscopy suggest that a patient with uncomplicated heartburn symptoms be given an initial trial of treatment before considering further diagnostic evaluation.<sup>235</sup> Endoscopy should be performed promptly if alarm symptoms are present. Upper endoscopy for patients with predominantly reflux symptoms and no accompanying alarm symptoms does not appear to be of value and usually will not influence management.<sup>236</sup>

The American College of Gastroenterology recommends empiric therapy in patients with heartburn, or GERD.<sup>144</sup> If drug therapy and lifestyle modifications are unsuccessful, or if the disease is recurrent, endoscopy or other diagnostic tests are recommended. The College further recommends that endoscopy be reserved for patients with alarm symptoms, patients who show no response to medical therapy, and for those who require continuous therapy.<sup>145</sup>

The population who are targeted to use omeprazole for treatment or prevention of occasional or episodes of self-limiting heartburn should not be under any undue risk.

If an otherwise healthy person with uncomplicated heartburn were to consult a clinician and not self-medicate with an over-the-counter product, an empiric course of therapy with a histamine H<sub>2</sub>-receptor antagonist or proton pump inhibitor in conjunction with lifestyle changes would be in keeping with the standard of practice.

In order to avoid the risk of possible complications that may occur with longstanding chronic and persistent heartburn, consumers should be made aware of the indications, dosage and duration of therapy of over the counter heartburn medication they intend to use. In addition, they should have a clear understanding of when to seek medical attention. This information should be clearly labeled with explicit instructions that are understandable by all potential users. The proposed labeling for over-the-counter omeprazole does instruct users to seek medical advice if they need to take their medication as directed continuously for more than 10 days. Labeling for the OTC H<sub>2</sub>-receptor antagonists also instructs consumers if they have taken this medication for fourteen days to seek medical attention before taking any further medication. The label will also clearly highlight alarm symptoms and that the presence of any of these additional symptoms must warrant prompt medical attention before continuing self-treatment.

#### **10.4 Conclusions**

The availability of H<sub>2</sub>-receptor antagonists for the self-treatment of heartburn has not increased the incidence of serious complications. Similarly, the use of omeprazole for over-the-counter medication for occasional or episodic heartburn is unlikely to pose an increased health risk or mask other diseases.

Consumers should continue to be aware of the significance of chronic heartburn, the proper use of OTC medications for heartburn, and when to seek medical attention for their symptoms.

The risk of esophageal or gastric cancer in individuals with heartburn symptoms is very low and would not be expected to be increased by OTC use of omeprazole. From the data presented, there is no evidence to justify investigating every consumer who has heartburn.