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Medical Treatment of Peptic Ulcer Disease: Is It Truly Efficacious?

MARK A. GOLDBERG, M.D.

The prevalence of active peptic ulcer disease in the United States is in the range of 1.5 to 2 percent. The annual incidence of peptic ulcer disease is approximately 0.3 percent. Thus, about 4 million Americans have peptic ulcer disease at any given time, and about 350,000 new cases of peptic ulceration are diagnosed yearly. In addition, roughly 5 to 10 percent of the population will be affected by peptic ulcers during their lifetime. Clearly, peptic ulcer disease is a medical problem of significant magnitude in the United States [1].

In response to this problem, a research effort of vast proportions has been brought to bear on this issue. Over the past decade, numerous well-controlled, randomized, double-blind trials have been conducted to establish the efficacy of the medical treatment of peptic ulcer disease. Treatment strategies have centered on (1) neutralizing gastric acid, (2) inhibiting secretion of gastric acid, (3) enhancing mucosal defenses, and (4) preventing recurrence. To this end, numerous studies investigating the efficacy of antacids, H_2 receptor antagonists (cimetidine and, more recently, ranitidine), and sucralfate have been conducted. In 1977, Peterson et al [2] showed that large doses of antacids can accelerate the healing of duodenal ulcers. Ippoliti et al [3] demonstrated this increased rate of healing is comparable to that produced by cimetidine. A review of the literature indicates that in controlled, randomized, double-blind studies, both sucralfate and cimetidine are efficacious (and comparable) in significantly increasing the rate of healing of duodenal ulcerations [4]. More recently, a new H_2 receptor antagonist, ranitidine, has been shown to have an efficacy similar to that of sucralfate, cimetidine, and large doses of antacids [5,6].

Furthermore, cimetidine [7] and ranitidine [8] have been shown to be efficacious in preventing the recurrence of duodenal ulcers.

With respect to the medical treatment of gastric ulcers, Isenberg et al [9] showed that cimetidine significantly hastened the healing of benign gastric ulcers compared with placebo but not compared with a low-dose antacid regimen (not even antacids administered as needed were given to the group receiving placebo). In addition, high-dose antacids [10] and ranitidine [11,12] have been shown to be comparable to cimetidine in their ability to heal gastric ulcers, whereas the efficacy of sucralfate is less well documented [13]. Ranitidine [12,14] also seems to be efficacious in preventing the recurrence of gastric ulcers, whereas the efficacy of cimetidine [15] is less clear.

Largely as a result of studies such as those just mentioned, a billion dollar industry has developed to supply the various pharmacologic agents used in the medical treatment of peptic ulcer disease. But are these drugs, in fact, truly efficacious? Clearly, they accelerate the healing of most peptic ulcers. However, why do physicians treat peptic ulcer disease? I believe that the generally accepted reasons are: (1) to alleviate symptoms; and (2) to prevent complications (hemorrhage, perforation, and obstruction). With respect to preventing the complications of peptic ulcer disease, no well-controlled, randomized, double-blind study has shown that the medical treatment of peptic ulceration decreases the incidence of hemorrhage, perforation, or obstruction. Perhaps these complications occur in those ulcers refractory to medical therapy or perhaps they are evident primarily at the time of presentation when they do occur. In fact, in a historical perspective, McKay and

McArdle [16] have noted no difference in the incidence of perforation before and after the introduction of cimetidine in the West of Scotland.

Even in their ability to alleviate symptoms, drugs seem to be of marginal utility. The high-dose antacid regimen utilized by Peterson et al [2] was not more effective than placebo in relieving ulcer symptoms (patients in both treatment groups were given antacid tablets to take as needed for relief of ulcer pain). A large American, multicenter, double-blind study on the use of cimetidine in the treatment of duodenal ulcers (both the group receiving cimetidine and the group receiving placebo were given antacids as needed to control pain) was performed by Binder et al [17]. In their study, both the patients receiving cimetidine and the patients receiving placebo were predominantly pain-free after the first week of therapy, and significant differences were no longer present. Even during the first week of therapy, statistically significant differences in symptom relief were small. In addition, in several multicenter, double-blind studies [18,19], ranitidine proved no better than placebo in relieving symptoms of duodenal ulcers. Similarly, sucralfate seems to be minimally efficacious with regard to symptom relief. In the largest American study to date, a multicenter, double-blind trial of sucralfate and placebo in the treatment of duodenal ulcers conducted by McHardy [20], decreases in diurnal and nocturnal ulcer pain occurred consistently over time in both groups. Only at the end of Week 4 did a statistically significant difference exist in favor of sucralfate, and this was only for diurnal ulcer pain. With respect to symptom relief from gastric ulcers, neither cimetidine [9] nor ranitidine [11] appears to be more efficacious than antacids given as needed. These small differences with regard to symptom relief in groups receiving treatment and groups receiving placebo should not be surprising, since the natural history of peptic ulcers is to heal and to recur.

With respect to preventing the recurrence of duodenal and gastric ulceration, the H_2 receptor antagonists are effective. However, once these medications are discontinued, patients return to their baseline predilection. Furthermore, no data have documented the value of this prophylaxis in preventing complications of peptic ulcer disease, and no data exist on complications of long-term use of these medications.

In light of the data just summarized, let us ask once again: Is the medical treatment of peptic ulcer disease efficacious? Efficacy is defined as the ability to produce intended results. The intended result in the treatment of ulcers is to relieve pain symptoms and to prevent the complications of hemorrhage, perforation, and obstruction. The current medical treatments do not convincingly produce any of these results; they simply heal ulcers more quickly than antacids given as needed. Hence, I conclude that the current medical therapies for gastric and duodenal ulcers have not been proved to be efficacious. Perhaps the majority of patients with peptic ulcer disease could be managed just as well (but much less expensively) with antacids given as needed.

We must be extremely careful when we discuss the efficacy of medical treatment. We must be sure that we are asking the proper questions. With respect to the medical treatment of peptic ulcer disease, millions of dollars have been spent on research, and a billion dollar industry has been allowed to blossom, but we have not yet even posed the proper question: Does the medical treatment of peptic ulcer disease provide increased symptom relief or prevent the complications of peptic ulcer disease? This will be a difficult question to answer, but perhaps it is time that we focus our research efforts on the appropriate issues.

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