Omeprazole: Is it the Answer of Peptic Ulcer Disease?

Waquaruddin Ahmed (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Omeprazole, the acid pump inhibitor, is a new approach to the regulation of gastric acidity. Its discovery has led to new insights into the mechanism of gastric secretion, pathogenesis of certain gastrointestinal tumours and the development of new treatments for peptic ulcer. Recently this product has been marketed in Pakistan with promising results, but is yet to be evaluated in terms of long term safety and efficacy. Omeprazole inhibits acid secretion by inhibiting H+/K+ -AT Pase enzyme in the parietal cell. A single 20mg dose of omeprazole inhibits acid secretion by 65% after 4-6 hours and by 25% after 24 hours, but with subsequent doses inhibition increases, reaching a plateau after 4 doses. When the treatment is stopped, secretion returns to the pretreatment levels in 3 days without rebound phenomenon. The long term administration of omeprazole causes inhibition of gastric acid secretion leading to an increased plasma gastrin concentration, which, in turn, produces carcinoid tumours of the body of stomach and hyperplasia of certain oxyntic mucosal endocrine cells, the entero chromaffin-like cells in experimental animals. These results led the Food and Drug Administration to restrict the length of omeprazole treatment to 8 weeks except in patients with Zollinger Ellison syndrome. Initial studies examining the efficacy of omeprazole in the healing of duodenal ulcer indicate 20mg/day as the most effective minimum dose. All doses of more than 10mg/day showed healing rates of 90-100% at 4 weeks. Later randomized controlled trials of omeprazole (20 mg/day) and H2 receptor antagonists (ranitidine 300 mg/day) showed healing rates of 42-83% and 34-65% respectively at 2 weeks, while 82-97% and 63-96% respectively at 4 weeks. This shows a significant advantage for omeprazole both at 2 and 4 weeks. Other studies lasting for 6-8 weeks and with doses of more than 20 mg/day have shown even larger differences in favour of omeprazole. However, no significant difference was found in the healing rates both at 2 and 4 weeks in a similar study conducted at our centre, appearing in this issue of JPMA. In the same study we could not find any significant difference in the rate of pain relief, while in the earlier studies omeprazole has been shown to be more effective in relieving symptoms as compared to H2 receptor antagonists. Omeprazole has also shown its efficacy in the healing of resistant duodenal ulcers - which failed to heal after at least two months of treatment with H2 receptor antagonists in standard or high doses. The healing rates with 40 mg omeprazole/day reached up to 98% at 4-8 weeks in these cases. Although few follow-up studies have demonstrated similar relapse rates in omeprazole and H2 antagonists treated cases but most of others have shown less recurrence (41-44%) with omeprazole as compared to ranitidine (50-60%), in six months. However, the relapse rate was significantly higher (100%) in the former group as compared to the latter (90%) within three months in our series appearing in this issue of the journal. Gastric ulcer like duodenal ulcer, also responded better with omeprazole as compared to H2 receptor antagonist. Meta-analysis showed that 20 mg omeprazole/day was significantly better than H2 receptor antagonists only after 8 weeks and 30-40 mg of omeprazole after 4 weeks therapy. Resistant gastric ulcers not healing with H2 receptor antagonists showed healing up to 96% with 40 mg omeprazole/day at 8 weeks. Although omeprazole offers a little advantage over H2 receptor antagonists for large and resistant gastric ulcers, the rate of relapse was similar. In contrast to the slight advantage of omeprazole in the healing of duodenal and gastric ulcer, omeprazole is much more effective than H2 receptor antagonists for the relief of symptoms and healing of refluxoesophagitis. The healing rate up to 74% and 87% with omeprazole vs 43% and 56% with ranitidine has been reported at
4 and 8 weeks respectively.\textsuperscript{28-30} Omeprazole 40 mg has also shown better healing rates in resistant oesophagitis (90\%) than ranitidine 300 mg B.D. (47\%)\textsuperscript{31}, but unfortunately 80-90\% of the healed oesophagitis relapses within 6 months after cessation of therapy.\textsuperscript{29,32} Inspite of high relapse rates omeprazole has its real advantage in the treatment of patients with oesophagitis and Zollinger Ellison syndrome who failed to respond with H2 receptor antagonists even in higher doses and longer duration.\textsuperscript{33,34} The benefits of omeprazole therapy have to be weighed against its potential risks. Cases of gynecomastia and impotence are emerging due to its inhibitory effect on the synthesis of adrenal steroids.\textsuperscript{35} It interacts with the cytochrome P-450 system in the liver and inhibits metabolism of some drugs like warfarin,\textsuperscript{36} phenytoin,\textsuperscript{37} diazepam,\textsuperscript{38} antipyrine and aminopyrine.\textsuperscript{39} Long term treatment may produce sufficient hypergastrinemia to cause hyperplasia of enterochromaffin-like cells and possibly carcinoid tumours in some patients.\textsuperscript{41} Marked anti-secretory effect of omeprazole increases the bacterial-cell counts and nitrosamine levels in the stomach.\textsuperscript{41} Such changes could theoretically lead to an increased risk of both gastric cancer and gastrointestinal infections especially in tropical countries where helminthic, protozoal and bacterial infections are common due to poor hygienic conditions. Although this magic drug has proven its efficacy in the rapid healing of all types of peptic ulcer disease, its high cost, rapid relapse and potential risks of developing adverse effects has to be balanced against the risk/benefits of other treatments.

References
12. Banthan, LCD., Bianchi-Porro, 0., Bose, K et at A comparison of two differentdoses of omeprazole
15. Archambault, A.P., Pare, P., Bailey, R.J. et al Omeprazole (20 mg daily) versus cimetidine (1200 mg daily) in duodenal ulcer healing and pain relief. Gastroenterology, 1988;94:1130-34.