Ranitidine or omeprazole in the treatment of gastric and pre-pyloric ulceration?

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THE REPORT IN THIS EDITION OF THE JOURNAL BY PARÉ and colleagues (page 7) summarizes the results of the Canadian arm of a large multicentre trial of omeprazole versus ranitidine in the treatment of gastric and prepyloric ulceration (1). This paper raises the question of which agent is now the drug of choice. In arriving at an answer there are three factors to consider: safety, efficacy, and cost.

SAFETY
The safety of ranitidine is well established. Unwanted effects are uncommon and there has been no suggestion of carcinogenic potential of this drug. The introduction of omeprazole, on the other hand, was subject to considerable debate given the development of carcinoids in rats (2). However, evidence is accumulating that omeprazole does not cause tumours in humans even when used at high doses over prolonged periods of time (3,4). It is unlikely that short term use in humans will cause tumour development. In terms of safety, therefore, there is little to choose between these medications when used for short periods.

EFFICACY
The efficacy of ranitidine and omeprazole needs to be considered from the point of view of both symptom relief and ulcer healing. In the study by Paré et al no significant difference in symptom relief was found between the two drugs. In the multicentre study of Walan et al (1) omeprazole 40 mg daily was superior to ranitidine in producing symptomatic relief at two weeks but not thereafter. Also, omeprazole 20 mg daily healed 89% of ulcers, and at a dose of 40 mg daily, 96%. The results for omeprazole were essentially the same in the Canadian trial presented in this issue. However, ranitidine at a dose of 150 mg bid healed 85% of ulcers in the multicentre trial but only 71% in the Canadian group, an unusually poor response (5-7). On the basis of the multicentre study there is no difference in efficacy between low dose omeprazole and standard ranitidine therapy. A similar result has been previously reported by Classen et al (8). High dose omeprazole is more effective than either lower dose omeprazole or ranitidine.

The average costs as quoted by three large pharmaceutical chains in Halifax for eight weeks’ treatment with oral ranitidine 150 mg bid, omeprazole 20 mg daily, and omeprazole 40 mg daily were $120, $186 and $352, respectively. The makers of omeprazole have recently announced a reduction in price of approximately 25% making the projected cost (actual cost is not yet available) for eight weeks of omeprazole 20 and 40 mg, $140 and $264, respectively. In terms of cost there is little to choose between standard H2 blocker therapy and low dose omeprazole, high dose omeprazole is more than twice as expensive.

How should the high cost of omeprazole 40 mg daily be balanced with its increased efficacy? At first glance the cost of high dose omeprazole seems unjustifiable. However, failure
of an ulcer to heal after eight weeks of therapy requires a further course of treatment and yet another endoscopy. The cost of endoscopy is not simply the fee paid to the physician but also the cost to the hospital budget which has been estimated at the Victoria General Hospital in Halifax to be approximately equal to the endoscopic fee. On the other hand it is clear that the majority of patients do not require such intensive and expensive therapy since 80 to 90% of patients will have their ulcers heal on conventional H₂ blocker therapy or with the comparably priced omeprazole at a dose of 20 mg daily (5-8).

ANY SOLUTION?

How then do we resolve the question? One approach would be to use a longer period of conventional therapy with H₂ blockers before reassessing the ulcer. Healing rates of 96% have been reported for standard ranitidine therapy when used for 12 weeks (9). Another possibility would be to use higher doses of H₂ blockers, such as 300 mg bid, but this will cost almost as much as high dose omeprazole. Perhaps a more cost effective approach would be to use standard H₂ therapy or omeprazole 20 mg in patients who should respond well, and reserve the more effective and expensive therapy for patients expected to have more resistant ulcer disease. The multicentre trial (1) and the paper by Paré and colleagues provide some information in this regard. Patients who continued on nonsteroidal anti-inflammatory drugs (NSAIDs) fared poorly on conventional ranitidine therapy; only 53% healed their ulcers. Treatment with high dose omeprazole resulted in healing in 95% of these patients – a clinically and statistically significant difference. It seems reasonable to use high dose omeprazole in this subgroup.

OTHER FACTORS

Age, sex, smoking and ulcer site did not influence healing rate, but ulcer size did. It would be of clinical interest to know whether a subgroup of patients can be defined, based on ulcer size, which should receive intensive therapy. The Danish Omeprazole Study Group (10) found that ulcers greater than 12 mm in diameter showed more pronounced healing when treated with omeprazole 30 mg daily than with cimetidine 1 g daily.

There is no shortage of drug trials of anti-ulcer therapy, but the emphasis of these trials is on showing that one agent is as good as, or better than, another. These trials provide useful information to clinicians wishing to treat peptic ulcer disease successfully but they could provide even more useful information if equal emphasis was given to analysing and discussing treatment failures. In this regard the paper by Paré is a useful addition to the literature.

Based on these studies it appears that for most patients it does not matter, either clinically or economically, whether standard H₂ blocker therapy or low dose omeprazole is used. In patients with gastric and prepyloric ulcers who need to continue on NSAIDs, high dose omeprazole may be appropriate. Hopefully in the future further subgroups will be defined, permitting rational use of this effective, but expensive, therapy.

REFERENCES
