Leading article

Antacids and duodenal ulcer

It is strange that despite all the laboratory studies and clinical trials of ulcer healing drugs during the last 10 years, progress of knowledge about antacid therapy has been remarkably slow. It is not that the subject is esoteric, for antacids remain high in the rankings of drugs prescribed in hospitals and in general practice and of course they transcend professional medical practice by joining such items as Elastoplast, aspirin and Dettol as basic constituents of the household medicine cabinet. Yet we are still rather vague about how and when they should be prescribed, even for a disorder as precisely defined as duodenal ulcer. The physician must nevertheless make a decision about antacid usage every time a patient is started on medical therapy for duodenal ulcer and give further advice when the acute ulcer healing phase of the chosen therapy is completed. His recommendations must take account of the side-effects of antacids which are perhaps more substantial than generally appreciated, especially if large doses are used.1

In the United Kingdom, at least, there is widespread support for a treatment regime in which antacids are used for symptom relief, while an H₂ antagonist, or other ulcer healing drug is used to 'treat the ulcer'. It is well known that antacids given in sufficient quantity will themselves be sufficient to allow a duodenal ulcer to heal, but in the main clinicians appear to have accepted this as a piece of interesting information, rather than something relevant to clinical practice. In fact the present use of antacids in duodenal ulcer owes more to the design of the many trials of H₂ antagonists than to critical analysis of information about antacids themselves. The clinical trials of cimetidine and ranitidine almost all involved patients taking ad lib antacids and, with a few exceptions, showed that antacid requirements fell as the patient's ulcer progressed towards healing. Thus the recommended pattern of therapy emerged — antacids should be used symptomatically and concurrently with the H₂ antagonist. Occasional challenges to this comfortable line of thinking have come along, such as evidence that antacids impair the bioavailability of cimetidine3 and ranitidine,4 but the reality has been that most patients obtain acceptable symptom relief soon after the regime is begun, and in due course their ulcers heal. The system works, so why change it?

It is only when the literature about antacid therapy is examined that our ignorance of the subject is exposed. Twenty years ago, Myhill and Piper5 published their paper 'Antacid therapy of peptic ulcer — a mathematical definition of an adequate dose', in which they argued for hourly administration of antacid sufficient to neutralise 50 mmol of acid in men with duodenal ulcer and 26 mmol in women. Ten years later, Fordtran6 recommended neutralising capacity for 80 mmol acid hourly in duodenal ulcer patients. Although the arguments in favour of such high doses found
more favour in the United States than in the United Kingdom, the debate essentially reflected uncertainty whether antacid treatment was given to neutralise acid, or whether the purpose was to relieve symptoms. In 1977 the well known study of Peterson et al\(^7\) then established beyond doubt that antacid therapy could heal duodenal ulcers, when 1008 mmol of acid neutralising capacity was given daily as seven doses of 30 ml liquid antacid. More recently antacid regimes of more modest neutralising capacity have also been found more effective than placebo in healing duodenal ulcers.\(^8\)\(^9\)

En passant, one may observe that reference to neutralising capacity now seems obligatory in papers published about antacids, and reviews of the subject often make comparisons by tabulating the neutralising capacity of antacids given in various clinical trials. Neutralising capacity of antacids is now usually determined according to the method of Fordtran et al\(^10\) which involves in vitro titration of the antacid to pH3 and it is often forgotten that in describing the method, the authors stated ‘the choice of pH3 as an end point for the in vitro test has no physiological or pathological significance; it is simply the in vitro end point that empirically was found to correlate best with in vivo antacid potency’. If, in fact, one chooses pH values of 4 or 4.5 for such titrations (which Fordtran and his colleagues did not examine) the relative potency of several commonly used antacids is rather different from that seen with the pH3 definition. When comparing studies which have used different antacids, it is sensible to remember that neutralising capacity, as presently defined, is not a measurement with any intrinsic biological significance.

If antacid therapy is to be used for control of symptoms, rather than healing of ulcers, it would be helpful to have knowledge of its effectiveness. Here, there is some discrepancy between the beliefs held by many clinicians and the evidence of formal investigation. Sturdevant et al\(^11\) comparing pain relief in duodenal ulcer patients given a single dose of antacid or placebo found a slight advantage for the antacid, but it fell short of statistical significance. Littman et al\(^12\) also failed to show any convincing difference between single doses of antacid or placebo in relief of ulcer pain, whereas two other studies showed a small advantage for the antacid.\(^13\)\(^14\) The conclusion to be drawn from all four studies is that one dose of antacid has, at best, no more than a modest effect in acute relief of ulcer pain. It would be wrong, however, to use these observations as a reason for abandoning the conviction held by many clinicians that antacids are effective relievers of symptoms in duodenal ulcer. Patients with ulcer pain do not take single doses of antacid – they take repeated doses as the pain recurs and perhaps other doses according to advice given and the effects of such treatment may bear little relationship to the effects of a single dose taken in isolation. Clearly, some patients with duodenal ulcer do not gain pain relief from antacid and it is not unusual to hear a patient say that his antacid used to relieve the pain, but no longer works. We have very little understanding of the basis of pain in duodenal ulceration and until there is evidence to the contrary, it is reasonable to accept the clinical impression that in some patients modest doses of antacid therapy seem to provide symptom relief, while in others they do not. It seems unlikely that so many patients would persist with antacid medication and apparently be satisfied with it, if its benefits were simply those of a placebo.

In this issue, Kumar et al\(^15\) report a beautifully simple and
straightforward trial which provides additional information pertinent to therapy of duodenal ulcer. They have shown that healing of ulcers with antacid treatment does not need enormous doses – six daily doses of 15 ml, each representing a neutralising capacity of 34.5 mmol, was sufficient to heal 85% of ulcers within four weeks. Double this dose produced a similar healing rate, but also resulted in an unwanted disturbance of bowel function, while half the dose was not so effective in achieving healing. The optimal dose produced good relief of ulcer pain over the four week period of treatment and the results support the existence of a direct relationship between pain relief and ulcer healing.

Thus antacid therapy at practicable doses does heal duodenal ulcers. One may perhaps be a little cautious before accepting that its effect on patients in India will be precisely matched in western Europe, because there is much evidence of international variation in ulcer healing with medical treatment, but the results are similar to those reported from Hong Kong and from Norway, when the amounts of antacid used were comparable. Moreover, the finding of a dose-response relationship is consistent with commonsense and provides a basis for judgement of the optimum dose, by balancing efficacy against side-effects. Of course, there is some practical disadvantage in a daily treatment regime which requires six daily doses and no one would suggest that these observations are reason enough to abandon other ulcer healing drugs. For some patients, however, antacid therapy of this sort will be appropriate and in those parts of the world where political, economic, or logistic considerations limit the range of drugs available, it may be useful to know that the effectiveness of this simple antacid regime compares favourably with all other drugs promoted at present for healing of duodenal ulcer.

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References


