

GASTROENTEROLOGY



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DUODENAL ULCER: WHY DOES TREATMENT OFTEN FAIL?

Duodenal ulcer rarely presents a diagnostic problem because its symptoms are so well known and roentgenologic facilities are so readily available. Nevertheless, it remains a disease of major importance not only because of its high incidence (approximately 10% of Americans at some time in their lifetime have a duodenal ulcer) but also because there are still too many unnecessary therapeutic failures and recurrences.

Why do these failures occur? There are three main reasons, I believe. At the risk of controversy, I would like to discuss them—and suggest alternative methods of treatment that have proven practical

for me. The first stems from the *common misconception that diet regulation alone is sufficient management*. Of course, from a common-sense standpoint the ulcer patient should avoid spices, gas-forming foods and other irritants in the diet. Since coffee, chewing gum and tobacco may stimulate gastric secretion, their use should also be restricted and, if possible, discontinued. Except in the very acute cases, however, strict control of diet actually plays a minor role in therapy. Furthermore many patients have a reluctance to accept it. I have seen exacerbation of symptoms in numerous patients who, after struggling with strenuous long-term diets, finally

rebelled against the entire treatment and ended up with no regimen at all, to their obvious detriment.

A second reason for treatment failure is *improper use of anticholinergic and antisecretory drugs*. The rationale for curtailing acid secretion is a sound one, for it is based on laboratory and clinical knowledge of peptic ulceration. Of course, the primary cause of duodenal ulcer is not known, and all we can say with certainty is that the ulcer is the end result of a pathological process in which the gastroduodenal mucosa fails to withstand the digestive action of acid gastric juice. Surely, then, gastric acid is an indispensable factor in the formation of duodenal ulcer. When gastric acidity is effectively and completely neutralized or abolished, as by therapeutic irradiation of the gastric mucosa, a duodenal ulcer will heal and remain healed as long as the acid is completely neutralized or absent. In short, I have never seen the dictum "no acid, no ulcer" refuted.

Why Anticholinergics Fail

If the benefits of controlling acid secretion are so widely recognized, why do anticholinergics and antisecretory agents sometimes fail? Usually, I have found this is because the agents were not sufficiently individualized: the dose is inadequate or it has not been given long enough.

Underdosage seems to occur exceptionally often with anticholinergic drugs. These drugs, widely used since they were introduced 10 years ago, selectively inhibit the parasympathetic ganglia and/or the terminal nerve end-

ings (or act on the parietal cells themselves to decrease or abolish gastric acid production). Ideally, the drug we choose should be capable of both achieving and maintaining inhibition of gastric secretion. There are a number that will do this, but to succeed they must be used in the dose that is effective not in the "average" patient, but in the person being treated. Also, no anticholinergic will be equally effective in all persons; sometimes a patient will respond much more favorably to one than to another. Thus, both the dosage and the drug must be individualized.

Testing a Drug's Effectiveness

Usually the average recommended dose is used but if the clinical results are not good then one must use a different method. Thus, when greater accuracy is needed, as in the chronic patient, one can test the effectiveness of an anticholinergic agent quite simply in the following manner. A Rehffuss tube is passed into the stomach, and a one-hour, fasting, basal gastric collection is obtained. The gastric juice is titrated in order to determine the amount of free acid present. A solution of antisecretory drug is then instilled through the tube into the stomach and the tube is clamped off. One hour later, after the drug has passed into the small intestine and after absorption has begun, continual gastric aspiration is resumed. One can then determine quite accurately how such gastric acidity has decreased and whether anacidity has occurred. The duration of effectiveness of the drug can also be determined in this way. By using the results of objective tests such as this, it is possible to individualize, to a high degree, the dosage of antisecretory drugs.

Proper Use of Antacids

A third—and equally important—reason for treatment failure occurs with improper use of *antacids*, the sheet anchor of duodenal ulcer therapy. Many drugs such as calcium carbonate, combinations of aluminum hydroxide and magnesium compounds, or dihydroxy aluminum aminoacetate will neutralize stomach acidity. But all too often they are not given in amounts large enough to be effective, and underdosage is as much the rule as it is the exception. It is usually necessary to give 1 to 2 Gm. of antacid, in each dose.

In addition, studies in our laboratory have shown, as one might expect from the known emptying time of the stomach, that only rarely does an antacid neutralize stomach acid for longer than half an hour to 45 minutes. Therefore, to provide the necessary environment for healing, the patient should, at least during the first week or two of therapy, take an antacid every half hour or every hour during the day. For some, several doses are necessary at night. (Four ounces of milk, a dietary item most patients will accept, can also be used effectively to neutralize gastric acidity and can be alternated with other antacids for variety.) Beginning the second week and continuing for approximately 2 to 3 weeks, the antacid may be taken every 2 hours.

Prolong Treatment with Antacids

After approximately one month of this regimen, medication may be taken in the mid-morning, mid-afternoon, an hour after supper, and at bedtime. This program should be continued for at least 3 to 6 months in patients with early acute ulcers and in patients who do not secrete a large amount of acid. However, in those who secrete a large amount of acid and/or give a history of recurrences, I feel quite strongly that antacids must be taken for several years or until the patient's life is stabilized. Once he has regular hours and regular habits so that he is relatively free from emotional stress and strain, the antacid can be omitted. But treatment should be resumed whenever stress recurs.

By the way, some patients during this therapy develop constipation and require a laxative; magnesium carbonate (1-4 Gm. daily) is excellent for this purpose, since it is an antacid, too.

To summarize, I would like to repeat that probably the most important measure in managing duodenal ulcer, and preventing recurrence, is to provide *adequate* and *prolonged* control or neutralization of gastric juice. In general, the drugs which do this are as safe as they are effective. Under such therapeutic circumstances, there is little to lose if treatment is vigorous, but much to be lost if it is inadequate.

QUESTIONS AND ANSWERS

Q. *Don't emotional factors account for much of the difficulty in treating duodenal ulcer?*

A. Yes, as we all know, emotional stress, tension, strain, worry, and other psychic difficulties may precipitate—and perpetuate—duodenal ulcer. We can make the patient aware of these factors and, as a result of this awareness, he may be able to modify or even to eliminate some of them. But mild sedation is useful because it may decrease psychic stimulation and thereby reduce psychically-stimulated gastric secretion. Some patients respond well to barbiturates, meprobamate, or other tranquilizers. But usually it is impossible for anyone to avoid all or even a significant portion of the circumstances in his life that may cause tension especially if he is to be gainfully employed. In fact, his tensions may not be abnormal; only his reaction to them—the ulcer—can be considered so. It is not generally possible to use medication to completely eliminate tension over long periods of time. For this reason, the more specific measures such as anticholinergics and antacids are all the more important.

Q. *Does the occurrence of side effects with anticholinergics indicate that the medication is causing an adequate reduction of gastric secretion?*

A. No. The rule of thumb method for using anticholinergics indicates only that the patient is receiving all he can comfortably take, not that the dose is adequate. Even gastric secre-

tion values obtained in a fasting stomach are not necessarily indicative of the amounts of acid that may be secreted when the patient is eating. This is one of the reasons antacid therapy is so important, for we do know that given in the doses and in the frequency recommended, adequate control of acidity is usually achieved.

Q. *Are you saying that dietary control alone can never succeed in healing a duodenal ulcer?*

A. No, because many ulcers will heal without any treatment. But in chronic or recurrent ulcer patients, diet is of little importance.

Q. *How often do you find surgery necessary for duodenal ulcer?*

A. Surgery should be reserved for the complications of duodenal ulcer such as massive hemorrhage or perforation. The truly resistant case is rare. In any case, surgery is not necessary in more than 5-10% of all patients.

Q. *There has recently been some evidence that when given hourly, certain popular antacids cause an excessive intake of sodium for patients with heart disease or cirrhosis. Is this problem so rare that it is only of academic interest, or do you consider it a frequent problem?*

A. In my experience this is not a frequent problem, especially since I do not find it necessary to give antacids hourly for more than several weeks.