

Therapeutic Applications of Vagotomy

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The treatment of the peptic ulcer disease involves several options. The present discussion deals with the long-term management with emphasis on the application of vagotomy. Eradication of *Helicobacter pylori* is the treatment of choice in ordinary peptic ulcer patients. Exceptions are non-steroidal, anti-inflammatory drug-induced ulcers and the Zollinger-Ellison syndrome.

Failures to eradicate *H. pylori* in old or unfit duodenal ulcer patients and most gastric ulcer patients will lead to intermittent antisecretory treatment or continuous maintenance treatment. Maintenance treatment will usually mean lifelong treatment, and optimal results are probably obtained with a full-dose antisecretory regime.

Failures to eradicate *H. pylori* in young and fit duodenal ulcer patients is the group of patients to whom proximal gastric vagotomy can still be recommended as an elective surgical procedure. The proximal gastric vagotomy should preferably be performed with the laparoscopic technique. Evidence is presented that completeness of vagotomy is of clinical importance. The completeness of vagotomy can be tested and defined.

INTRODUCTION

The therapeutic strategy for peptic ulcer patients has changed dramatically in the last few years. Previously, most patients were treated with intermittent courses of antisecretory drugs, due to the chronically recurrent pattern of the ulcer disease. Antisecretory treatment with histamine H₂-antagonists resulted in high healing rates and a relatively fast symptom relief. These results were further improved with the introduction of omeprazole, the first proton pump inhibitor. Patients with frequent recurrences or repeated complications were recommended one out of two prophylactic regimens. Surgery was recommended to young and otherwise fit patients, while maintenance antisecretory treatment was recommended to older and unfit patients, as well as to those who refused surgery. Elective gastric resection or vagotomy in combination with a drainage procedure has, however, mostly been abandoned because of unpredictable postgastrectomy syndromes in 10-15 percent of cases. Elective proximal gastric vagotomy is still a conceivable option in duodenal ulcer patients because this procedure does not result in any postgastrectomy syndrome, but it does result in a relatively high recurrence rate if used in patients with gastric ulcers.

The therapeutic strategy has, however, been completely changed with a discovery that eradication of *Helicobacter pylori* will cure the peptic ulcer disease in most patients. Eradication of *H. pylori* is, therefore, the primary therapeutic choice today. The following discussion will deal with available alternatives for long-term management of the peptic ulcer disease with emphasis on the application of vagotomy.

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ERADICATION OF *H. PYLORI*

In peptic ulcer patients, eradication of *H. pylori* is a first-hand choice in most patients [1]. Exceptions are patients with Zollinger-Ellison syndrome and probably patients on non-steroidal anti-inflammatory drug medication. Apart from these exceptional patients, practically all patients with recurrent peptic ulcer disease have *H. pylori* infection, and they are candidates for *H. pylori* eradication. However, a patient with a first-time peptic ulceration should be tested for the presence of *H. pylori* infection before considering eradication therapy.

There are, however, some problems with the eradication therapy. At present, there are two alternatives: the triple therapy (bismuth and two antibiotics) or omeprazole twice daily with one antibiotic (usually amoxicillin). Both therapies are successful in just above 80 percent of patients, but the triple therapy results in more side-effects and, therefore, less compliance. How do we handle the remaining 20 percent? It seems reasonable to add at least another eradication trial with a different antibiotic combination to the twice-daily dose, antisecretory proton pump inhibitor, where most experience involves omeprazole. Whatever the outcome, there will be a number of patients in whom even a repeated eradication trial will fail. Furthermore, some peptic ulcer patients will be re-infected with *H. pylori* after a successful eradication. The re-infection rate is claimed to be surprisingly low, but the long-term results are unknown. Those peptic ulcer patients still having the *H. pylori* infection should be managed by a different strategy.

ANTISECRETORY TREATMENT

Intermittent treatment

Most peptic ulcer patients who have had unsuccessful eradication treatment have rather infrequent symptomatic episodes (i.e., fewer than one to two episodes each year). These patients can be easily managed by intermittent treatment over four to six weeks. Antisecretory drugs are most efficient. Proton pump inhibitors are superior to histamine H₂-receptor antagonists, both with regard to healing rates and fast symptom relief.

Continuous maintenance treatment

Some peptic ulcer patients who have had unsuccessful eradication of *H. pylori* have a more severe disease with more or less continuous symptoms or repeated complications and may not be suitable for surgery or willing to accept surgery. A typical example is the older patient who has had repeated peptic ulcer bleedings and has other severe, concomitant disease. Such patients should be given continuous maintenance treatment.

There is vast experience with continuous maintenance treatment with histamine H₂-receptor antagonists such as cimetidine, ranitidine, famotidine and nizatidine. Traditionally, the maintenance dose has been half the dose used for healing a peptic ulcer. The recurrence rate during half-dose maintenance treatment with any of the histamine H₂-receptor antagonists has been up to 25-30 percent for the first 12 months. This recurrence rate is much lower than that obtained during placebo treatment but certainly is not satisfactory. The same rather poor results have been obtained during half-dose maintenance treatment with omeprazole [2, 3]. Consequently, there seems to be a case for more potent medical prophylaxis in the maintenance therapy for peptic ulcer (e.g., a full-dose antisecretory regimen).

There are no reports of full-dose maintenance treatment with histamine H₂-receptor antagonists. There are, however, some reports of full-dose maintenance treatment with omeprazole [4, 5]. In these studies, the recurrence rate during the first 12 months has reached a more satisfactory level of about 10 percent. This recurrence rate seems to remain stable over a prolonged period of full-dose maintenance treatment with omeprazole [4]

and is thus comparable with the recurrence rate after proximal gastric vagotomy for duodenal ulcer.

INDICATIONS FOR SURGERY

The indications for elective surgery for peptic ulcer disease have been completely changed. Previously, the main indication was "failure of medical therapy." This is obviously no longer valid. Almost all peptic ulcers can now be healed by medical therapy, but it is a question of choice of drug and dosage. At present, elective surgery is an alternative to continuous life-long, full-dose maintenance, antisecretory, therapy for relatively young and otherwise fit patients. A prerequisite is that the surgical procedures should have good long-term results and exceptionally low mortality and morbidity. Proximal gastric vagotomy for duodenal ulcer seems to be an acceptable procedure, although it results in too high a recurrence rate of 30-35 percent when performed for pyloric or prepyloric ulcers [6, 7]. The surgical procedures for gastric ulcers involve a gastric resection or vagotomy with a drainage operation. Since these procedures will result in severe and unpredictable postgastrectomy syndromes in 10-15 percent of the patients, the indication for this type of elective operations should be very restrictive.

Closure of a duodenal ulcer perforation can usually be performed by laparoscopic surgery. Additional proximal gastric vagotomy might be considered in a young patient with a short perforation history and severe recurrent ulcer disease [8]. Bleeding from a peptic ulcer can be stopped in 90-95 percent of patients by endoscopic techniques. When open surgery is required for a bleeding ulcer, vagotomy might be considered in addition to stitching the bleeding vessel in a young patient with severe recurrent ulcer disease. The stitching can sometimes be performed via an incision in only the duodenal bulb of a patient with a duodenal ulcer, but often a pylorotomy is needed.

Elective proximal gastric vagotomy

The number of proximal gastric vagotomies performed in recent years has been reduced to a very low figure. With the indications stated above, there will be a place for a few proximal gastric vagotomies, particularly since they now can be performed as a laparoscopic procedure. It is, however, absolutely essential that the vagotomy should result in a minimal number of incomplete vagotomies. The technique used for laparoscopic vagotomy should not be allowed to jeopardize the completeness of vagotomy just because it is a laparoscopic procedure. Therefore, it seems reasonable that the laparoscopic proximal gastric vagotomy should be performed in exactly the same way as during open surgery. If modifications in the surgical technique are introduced, they must be evaluated with regard to the frequency of incomplete vagotomies obtained.

Test for completeness of vagotomy

Traditionally, the insulin test has been used. This test, however, entails some risk. Furthermore, it results in a number of false-negative results because of extravagal inhibition of gastric acid secretion and false-positive results because of extra-vagal release of gastrin [9]. After proximal gastric vagotomy, 80 patients were tested both with sham-feeding and an intravenous dose of 0.2 IU insulin/kg body weight. Divergent results were obtained in 30 patients. A positive sham-feeding test and a negative insulin test were obtained in 12 patients, and four of these accepted further testing. The four patients had a mean acid increase of 2.34 mmol/30 min on sham-feeding, while 0.2 IU insulin/kg body weight only increased the acid output by 0.07 mmol/30 min. Repeating the insulin test with a reduced dose of insulin to 0.1 IU/kg resulted in a marked increase of acid output by 1.11 mmol/30 min. Thus, the ordinary dose of insulin had obviously produced a false negative result.

Five patients with a negative sham-feeding response (0-0.5 mmol/30 min) and a positive response to insulin at a dose of 0.2 IU/kg (1.31 mmol/30 min) accepted further testing. The insulin test was repeated with the same dose of insulin, but in addition, the beta-adrenergic antagonist propranolol was injected at a dose of 0.1 mg/kg. This time the insulin test resulted in an increase of acid output of only 0.1 mmol/30 min. The reason for the design of the experiment was that insulin hypoglycemia is known to induce liberation of epinephrine from the adrenals, and intravenous infusion of epinephrine has been shown to release gastrin in man [10]. This extra-vagal release of gastrin should be blocked by a beta-adrenergic antagonist. In any case, the insulin test produced a false-positive result in these five patients. Therefore the simple, reproducible and safe sham-feeding test seems to be a more reliable postoperative test for completeness of vagotomy than the insulin test

The criterion for incompleteness of vagotomy

Different criteria for incompleteness of vagotomy have been published previously. They all lack the necessary information about the spontaneous oscillations of the basal acid secretion in subjects with an unequivocal vagotomy. Therefore, we studied 10 patients who had been subjected to resection of the esophagus and reconstructed with an esophago-gastric anastomosis. The operation certainly resulted in transection of all vagal innervation to the stomach. The oscillations of basal acid secretion were studied over a three-hr period. The difference (plus two standard deviations) between the highest and lowest recorded 15-min output was 0.6 mmol [11]. Subsequent sham-feeding produced no further increase of the acid output. Furthermore, the oscillations in basal acid secretion were also studied in 20 duodenal ulcer patients after proximal gastric vagotomy. Early postoperative tests had shown them to be presumably completely vagotomized and they had been asymptomatic for seven to 10 years. The difference (plus two standard deviations) between the highest and lowest recorded 15-min output was again 0.6 mmol. Consequently, a reasonable criterion for incompleteness of vagotomy is an acid response to sham-feeding which exceeds the lowest basal secretion by more than 0.6 mmol/15 min.

Is completeness of vagotomy of clinical importance?

The recurrence rate after proximal gastric vagotomy is highly variable with a range of 10-40 percent. The impact of complete vagotomy on recurrence rate is uncertain. The role of completeness of vagal denervation in determining the long-term outcome after proximal gastric vagotomy for duodenal ulcer disease was studied by relating the early postoperative acid response to sham-feeding to the subsequent ulcer relapse rate observed during a mean follow-up period of 7.5 years (five to 15 years) in 98 patients [12]. The relapse rate for the whole group was 11 percent. Within five years after the operation, 23 percent of those with an incomplete vagotomy had an ulcer relapse, while only three percent of those with a complete vagotomy had a relapse. This difference is significant. However, four patients with a complete vagotomy had an ulcer relapse more than five years after the operation. Obviously, a complete vagotomy implies a low risk for ulcer relapse.

IS THERE A PLACE FOR THE CLASSICAL DRAGSTEDT OPERATION?

Some patients present with a long fibrous stenosis of the postpyloric region after innumerable courses of short-term medical treatment for duodenal ulcer. In this particular case, a truncal vagotomy with a gastroenterostomy, Dragstedt's classical operation [13], seems most appropriate. A similar operation, truncal vagotomy with pyloroplasty and stitching of a bleeding ulcer, is often the simplest solution to treat a bleeding juxtapyloric ulcer that could not be handled by endoscopic techniques. Proximal gastric vagotomy is, however, the most frequent vagotomy procedure for duodenal ulcer, and selective vagotomy with

antrectomy or pyloroplasty is probably the most frequent surgical procedure for pyloric-prepyloric ulcers.

CONCLUSION

Eradication of *H. pylori* is the therapeutic strategy of choice in ordinary peptic ulcer patients. Exceptions are non-steroidal, anti-inflammatory, drug-induced peptic ulcers and the Zollinger-Ellison syndrome. In patients with frequent recurrences or repeated complications, and in whom repeated attempts to eradicate *H. pylori* have failed, proximal gastric vagotomy is a prophylactic procedure to consider in young and fit duodenal ulcer patients, particularly if it can be performed as a laparoscopic procedure. Such a procedure should be performed in a surgical department with a high success rate in performing complete vagotomies.

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