PAPERS AND ORIGINALS

Prospectively randomised trial of proximal gastric vagotomy either with or without pyloroplasty in treatment of uncomplicated duodenal ulcer

C WASTELL, J COLIN, T WILSON, E WALKER, J GLEESON, R ZEEGEN

British Medical Journal, 1977, **2**, 851-853

Summary

A consecutive series of 100 men with uncomplicated duodenal ulcer was randomly divided into two groups: one group of 52 underwent proximal gastric vagotomy (PGV), the other group (48) underwent PGV with pyloroplasty (PGVP). Preoperative peak acid output (PAOP) was measured in all patients. Those with a higher preoperative PAOP were significantly more likely to develop recurrent ulceration. Three patients developed recurrent ulceration after PGV and seven after PGVP. Dumping was both more common and more severe after PGVP than PGV. An overall satisfactory result was achieved in 92% after PGV and 81% after PGVP.

We conclude that combining pyloroplasty with PGV has no appreciable advantages.

Introduction

Of all the different types of operation performed on patients suffering from duodenal ulcer, proximal gastric vagotomy (PGV) causes the least disturbance to the physiology of the stomach and duodenum. We report the results of a study to test whether PGV either with or without pyloroplasty is generally applicable to patients with duodenal ulcer.

Surgical Unit and Department of Gastroenterology, Westminster Hospital, London SW1P 2AP

C WASTELL, MS, FRCS, reader and honorary consultant surgeon
J COLIN, MS, FRCS, senior surgical registrar
T WILSON, FRCS, surgical registrar
E WALKER, FRCS, surgical registrar
J GLEESON, MRCP, FFR, consultant radiologist
R ZEEGEN, MRCP, consultant physician

Patients and methods

All male patients with uncomplicated chronic duodenal ulcer presenting for surgery between August 1970 and February 1974 were divided randomly into two groups at the time of the decision to operate. The first group (52 patients) underwent PGV, and the second group (48) underwent PGV with a modified Finney pyloroplasty (PGVP).

Preoperative investigation—All patients in whom chronic duodenal ulcer had been diagnosed by barium-meal examination and some who had been diagnosed by endoscopy were prepared as usual for laparotomy. We also measured peak acid output (PAOP) after stimulation with subcutaneous pentagastrin 9 µg/kg.

The operation—To ensure consistent technique, all operations were carried out by one person (CW). Proximal gastric vagotomy was performed as described.¹ An important point in the technique was the use of a four-bladed retractor.^{2,3} The dissection was such that the last visible major branch of the anterior and posterior nerve of Latarjet was preserved. At the upper end of the dissection 5-7 cm of oesophagus was cleared, and generally the posterior vagus was seen lying between the two crura of the diaphragm.

After operation—A nasogastric tube was not usually used, and the patients were started on sips of water within the first 24 hours. Between the eighth and 10th postoperative days a repeat PAOP estimation, a Hollander insulin test, and a limited barium-meal examination were performed. Most patients were discharged from hospital between the 10th and 14th postoperative days. Patients were seen for follow-up in the outpatient department at six weeks, three months, six months, one year, and thereafter annually. At each visit a standard questionnaire⁴ was filled out. An independent physician (RZ), who was unaware which of the two operations had been performed, noted the clinical findings quoted in this paper.

Results

There were no operative deaths, and the complication of necrosis of the lesser curve of the stomach was not seen.

Follow-up—The first patient underwent operation in August 1970 and the 100th in February 1974. The minimum follow-up period was therefore three years, and the maximum seven years. Three patients were lost to follow-up, two after PGV and one after PGVP.

Postoperative barium-meal examinations—Gastric peristalsis was radiologically normal. All patients had half-hour films that showed the stomach to be emptying satisfactorily.

Preoperative PAOP values were obtained for all patients. The mean preoperative PAOP for all patients was 37.8 mmol (mEq)/h ($\pm$ SD 13.7 mmol/h).

The insulin test was not performed in nine patients, and in 11 it was not continued for a second hour after the insulin had been given. Thirteen patients had a positive result, and 15 patients a late-positive response approximately two weeks after surgery.

RECURRENT ULCERATION

Recurrent ulcer as shown by barium-meal examination, endoscopy, or laparotomy occurred in three patients after PGV and in seven after PGVP. No recurrent ulcer occurred in patients with a preoperative peak acid output of < 30 mmol/h (table I). Seven of the 10 recurrences occurred in the 28 patients with a preoperative PAOP > 45 mmol/h.

TABLE I—Preoperative peak acid output (PAOP) in 100 patients who underwent operation for chronic duodenal ulcer, showing patients in whom ulcers subsequently recurred

Preoperative PAOP (mmol/h)	No of patients	No with recurrent ulcers
0-10	1	
10-20	11	
20-30	15	
30-40	32	2
40-45	13	1
45-50	10	2
50-60	13	3
60-70	3	1
70-80	2	1

Conversion: SI to traditional units—Gastric acid: 1 mmol = 1 mEq.

Analysis shows that those with a higher preoperative PAOP have a significantly greater chance of developing a recurrent ulcer ($\chi^2 = 11.07$; $P < 0.05$).

The mean age at entry to the trial of patients without recurrent ulceration ($42.3 \pm$ SD 13.1 years) was not significantly different from the mean age of those with recurrent ulceration (45.3 ± 11.0 years). Recurrent ulceration occurred in 10 patients (nos 8, 9, 10, 15, 16, 18, 44, 68, 69, and 94), and if this distribution is tested for skewness and kurtosis there is no strong evidence that recurrence occurs more frequently early in the series ($U = -1.77$; $P > 0.05$).

DUMPING AND DIARRHOEA

These symptoms are reviewed in table II. Patients who developed recurrent ulcers were not considered further from the point of view of symptoms. No difference in the incidence of symptoms can be shown between PGV and PGVP with the single exception of dumping.

TABLE II—Incidence and severity of symptoms after proximal gastric vagotomy (PGV) and PGV with pyloroplasty (PGVP)

Symptom	PGV (n = 47)			PGVP (n = 40)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Diarrhoea	3 (6%)	1 (2%)		3 (7.5%)	4 (10%)	
Dumping		3 (6%)		8 (20%)	1 (2.5%)	2 (5%)

This symptom was moderate in three patients after PGV, but mild in eight, moderate in one, and severe in two after PGVP ($\chi^2 = 12.49$; $P < 0.01$).

We defined diarrhoea as existing when a patient passed three or more stools per day or had undue urgency or looseness of stool. Three patients had mild diarrhoea after PGVP and PGV, one patient moderate diarrhoea after PGV, and four after PGVP.

Discussion

This series of patients was strictly consecutive and consisted of all patients who presented to one of us for surgery. No patient

was excluded because of unsuitability of temperament, because the ulcer diathesis appeared to be severe, or because the patient was too fat or too large for the operation to be carried out. Only one patient had to be excluded at the time of operation because of the finding of unsuspected gall stones. We thought that this approach would give an overall picture of the results that could be expected after this operation. We randomised the patients between PGV and PGVP because in 1970 it seemed necessary to see if drainage of the antrum was required.

The rate of recurrent ulceration after PGV reported by various workers varies from 1 to 22%.⁵⁻⁹ The rate that we report is therefore intermediate, being 6% after PGV and 14% after PGVP. Recurrent duodenal ulceration after vagotomy may be due to an incomplete denervation, an unsuspected Zollinger-Ellison syndrome, or for reasons unknown. In PGV the very nature of the dissection tends to result in a complete denervation, but the back of the oesophagus presents an area of especial difficulty. Grassi¹⁰ has described a branch of the posterior vagus that is easily missed which arises from above the hiatus and runs through the left crus of the diaphragm.

Lyndon *et al*¹¹ have shown that the acid response to insulin is higher after PGV if only 6 cm rather than 10 cm of the distal oesophagus is cleared at operation. Nevertheless, the recurrence rate was the same with both types of oesophageal dissection. In a preliminary study of a few patients Hallenbeck *et al*¹² showed that the recurrence rate in 39 patients with duodenal ulcer after PGV was greater than 15% if only 1-2 cm of the oesophagus was dissected, but that in 14 patients it was 7% when 5-7.5 cm was cleared. Varying the extent of the antral dissection has little effect on the postoperative insulin-stimulated acid secretion after PGV, but increasing the extent of the oesophageal dissection from 2 cm to between 5 and 7 cm results in a significant reduction.¹³

In our own series the length of the oesophageal clearance was roughly 5-7 cm, and at the end of the operation we could usually see the posterior vagus as it lay between the diaphragmatic crura. Complete denervation may not have been achieved, particularly early in the series. Nevertheless, recurrent ulceration was not significantly more common early in the series, and if more recurrences do occur they are likely to be in patients who underwent operation later.

Recurrence after PGV has been related to basal acid output measured immediately after operation.¹⁴ This finding was similar to that of Hood *et al*¹⁵ for other types of vagotomy. This relation, however, could not be confirmed in our patients. If the recurrent ulcers are grouped according to the preoperative peak acid output (table II) it is seen that no recurrence occurred at a level < 30 mmol/h. Only three recurrences were found in the 72 patients with a PAOP of less than 45 mmol/h, and it seems that there is a greater tendency for recurrence in those with a higher preoperative PAOP. This finding agrees with that of Robbs *et al*¹⁶ and Kronborg *et al*^{17, 18} for truncal vagotomy. Thus the preoperative PAOP has some predictive value in identifying patients at greater risk of recurrence.

Diarrhoea did occur after both PGV and PGVP, but in no patient was it severe. This contrasts with the usual overall incidence of around 25%, with between 2 and 5% of patients having severe diarrhoea after truncal vagotomy and drainage.^{4, 19, 20} Dumping was both more common and more severe after PGVP than PGV. The innervated antrum combined with widely patent gastric outflow tract predisposes to the syndrome, possibly because of rapid gastric emptying soon after food. More patients have this symptom after PGVP than after truncal vagotomy and pyloroplasty or gastrojejunostomy^{4, 19, 20, 21}—12 to 13% overall and 0.4 and 0.9% to a severe degree, respectively. The 6% incidence of moderate dumping after PGV in our series is therefore less than that occurring after truncal vagotomy and pyloroplasty and similar to the incidence found by others^{7, 8, 22} after PGV. Interestingly, Holle²³ always adds pyloroplasty to PGV, but records only two patients having mild or moderate dumping in a series of 338.

Vomiting of either bile or food occurred, but except for one patient after PGVP, was not severe. Postprandial fullness after PGV has been noticed by others,⁷⁻²² the incidence in these reports being similar to our figure of 23%. Other symptoms such as nausea, flatulence, epigastric pain, and heartburn caused few problems. One patient reported serious degrees of all four symptoms after PGV but no physical cause could be found. Dysphagia has also been reported to be troublesome after PGV. With the exception of the patient mentioned above, in which it occurred two years after operation, it posed no great problem and was only recorded in one patient to a mild degree after PGV.

When considering the overall result by means of the Visick grading, it is perhaps disappointing to find that only 39 (78%) and 36 (77%) patients had a grade I or II result after PGV and PGVP respectively. A further seven (14%) and two (4%) patients respectively had symptoms sufficient to remove them to grade III, but still with a satisfactory result. Beyond this, the grade IV results are due to recurrence after PGV and dumping or recurrence after PGVP. The single patient with a grade III unsatisfactory result after PGV was the same man who had severe symptoms without demonstrable physical cause; after PGVP such a result was due to dumping.

PGV itself can cure duodenal ulcers without imposing serious side effects such as diarrhoea, dumping, or vomiting. When combined with pyloroplasty the number of patients with dumping increases dramatically, and since there is no other advantage to the addition of gastric drainage it should not be combined with PGV. The problem of recurrent or persistent ulcers remains. Whatever the circumstances, some recurrent ulcers probably will occur, and the number may well be equal to or slightly above those occurring after either truncal or selective vagotomy and gastric drainage. Recurrent ulcers may be treated both medically and surgically, however, whereas dumping, diarrhoea, and vomiting usually cannot, and this is the most cogent argument in favour of PGV.

We should like to thank all those who have referred patients to us; Mrs J A G Goodwin for performing the statistical analyses; and Mrs A Johnston for typing the script. All the insulin and pentagastrin tests were performed by the late J I MacNaughton.

References

- Wastell, C, *et al*, *British Medical Journal*, 1972, **1**, 28.
- Goligher, J L, *British Journal of Surgery*, 1974, **61**, 337.
- Wastell, C, Wilson, T, and Pigott, H, *Proceedings of the Royal Society of Medicine*, 1974, **67**, 1183.
- Wastell, C, *Annals of the Royal College of Surgeons*, 1969, **45**, 193.
- Grassi, G, *et al*, *Surgery, Gynecology and Obstetrics*, 1973, **136**, 726.
- Liedberg, G, and Oscarson, J, *Scandinavian Journal of Gastroenterology*, 1973, **8** (suppl 20), 12.
- Amstrup, E, *et al*, *Annals of Surgery*, 1974, **180**, 279.
- Kronborg, O, and Madsen, P, *Gut*, 1975, **16**, 268.
- Jordan, P, *Archives of Surgery*, 1976, **111**, 370.
- Grassi, G, in *Surgery of the Stomach and Duodenum*, 3rd edn. Boston, Little, Brown, (in press).
- Lyndon, P J, Johnston, D, and Greenall, M J, *Gut*, 1975, **16**, 829.
- Hallenbeck, G A, *et al*, *Annals of Surgery*, 1976, **184**, 435.
- Joergensen, P M, Holst-Christensen, J, and Kronborg, O, *British Journal of Surgery*, 1977, **64**, 44.
- Holst-Christensen, J, *et al*, *British Journal of Surgery*, 1977, **64**, 42.
- Hood, J M, Spencer, E F A, and Macrae, K D, *British Journal of Surgery*, 1975, **62**, 665.
- Robbs, J V, Bank, S, and Marks, I N, *British Journal of Surgery*, 1973, **60**, 601.
- Kronborg, O, *Gut*, 1974, **15**, 714.
- Kronborg, O, and Madsen, R, *Scandinavian Journal of Gastroenterology*, 1976, **11**, 465.
- Cox, A G, Spencer, J, and Tinker, J, in *After Vagotomy*. London, Butterworths, 1969.
- O'Leary, J P, *et al*, *Annals of Surgery*, 1976, **183**, 613.
- Nelson, P G, *Medical Journal of Australia*, 1968, **2**, 522.
- Kennedy, T, *et al*, *British Medical Journal*, 1975, **2**, 301.
- Holle, F, *et al*, *Langenbecks Archiv für klinische Chirurgie, vereinigt mit Deutsche Zeitschrift für Chirurgie*, 1972, **330**, 197.

(Accepted 12 August 1977)

Maternal drug histories and congenital abnormalities

G GREENBERG, W H W INMAN, J A C WEATHERALL, A M ADELSTEIN, J C HASKEY

British Medical Journal, 1977, **2**, 853-856

Summary

We obtained drug histories for the first trimester of pregnancy for 836 mothers of congenitally malformed babies and for an equal number of control mothers of normal babies from the same doctors' practices. There was an association between the use of a hormonal pregnancy test and the subsequent birth of a malformed

baby. There was also a greater use of barbiturates by mothers of affected children compared with mothers of control babies, mainly accounted for by treatment of epileptic mothers with phenobarbitone. For all other drugs usage was similar in both sets of mothers.

Introduction

When in 1964 a Register of Adverse Reactions was established by the Committee on Safety of Drugs, based on the voluntary reporting of suspected adverse drug reactions, particular importance was attached to identification of possible teratogens. Although about 13 000 babies with visible malformations are born each year in England and Wales, only about 50 reports linking abnormalities with maternal use of drugs have been sent annually to the Committee on Safety of Medicines (CSM). Since so few reports were received it seemed likely that teratogenic effects would be missed, and a new method of surveillance was planned. The Office of Population Censuses and Surveys (OPCS) co-operated in a pilot study carried out in 1969, which showed the feasibility of a case-control survey. The major survey began in 1972.

Medicines Division, Department of Health and Social Security, London EC2A 1PP

G GREENBERG, BSC, MB, senior medical officer
W H W INMAN, MRCP, MFCM, principal medical officer

Medical Statistics Division, Office of Population Censuses and Surveys, London WC2B 6JP

J A C WEATHERALL, MB, MFCM, senior medical statistician
A M ADELSTEIN, FRCP, FFCM, chief medical statistician
J C HASKEY, MSC, statistician