

A LONG TERM STUDY OF THE IRON STATUS OF PATIENTS FOLLOWING VAGOTOMY

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The occurrence of anemia following partial gastrectomy is well recognised: the reported incidence ranges from three to 63 per cent¹. Iron deficiency is the commonest cause of the anaemia, deficiencies of either B12 or folic acid accounting for only a small number¹. With the advent of vagotomy and drainage as the routine treatment for duodenal ulcer it was hoped that anaemia would no longer be a significant problem. However, Wheldon and associates² found that truncal vagotomy with gastrojejunostomy resulted in anaemia in 43.5 per cent of males and 84 per cent of females after 15 years. There are no published data comparing the incidence of anaemia in the long term after the various types of vagotomy with or without drainage. The purpose of this study is to compare the iron status of patients after six different types of vagotomy and drainage.

PATIENTS AND METHODS

Four hundred and seventy-five patients were investigated; these comprised six prospectively studied groups of post vagotomy patients totalling 421. The three categories of vagotomy, truncal (TV), selective (SV) and proximal gastric vagotomy (PGV) were studied. The groups were sub-divided depending upon the accompanying drainage procedure; either gastrojejunostomy (GJ) or pyloroplasty (P).

Seventy patients with no known gastrointestinal disease and with comparable age and sex distributions to their counterparts were studied as controls. These patients had simple conditions such as inguinal herniae, varicose veins or benign breast lumps. Furthermore, 54 patients after partial gastrectomy (PG) were investigated as a form of quality control. If no evidence of anaemia or iron deficiency was found in this group, the study would be invalid. All patients were tested at least five years after operation. The male to female ratio of 3:1 was similar in all groups. The details and designation of the groups are shown in Table 1.

TABLE 1
Patients studied more than 5 years after Gastric Surgery

<i>Group</i>		<i>Male</i>	<i>Female</i>	<i>Total</i>	<i>MEAN OF FOLLOW-UP (years)</i>
Truncal Vagotomy and Gastrojejunostomy	TVGJ	99	35	134	7.7
Truncal Vagotomy and Pyloroplasty	TVP	13	5	18	5.5
Selective Vagotomy and Gastrojejunostomy	SVGJ	27	4	31	11.9
Selective Vagotomy and Pyloroplasty	SVP	69	18	87	8.3
Proximal Gastric Vagotomy and Gastrojejunostomy	PGVGJ	76	23	99	6.5
Proximal Gastric Vagotomy	PGV	39	13	52	5.5
Partial Gastrectomy	PG	36	18	54	11.9
Controls	CONTROLS	53	17	70	—
	TOTAL	412	133	545	
		(75.6%)	(24.4%)		
		Chi ² =5.62; 7 D.F.			
		N.S.			

Serum iron and total iron binding capacity (TIBC) were measured by the method of Young and Hicks³. Normal ranges were 14-29 $\mu\text{mol/l}$ and 45-72 $\mu\text{mol/l}$ respectively. A percentage saturation of iron of less than 15 was regarded as an index of iron deficiency. Serum ferritin was determined by radioimmunoassay⁴ using an antibody against human spleen ferritin raised in the rabbit. The normal mean concentration is higher in men than in women with a range between 12 and 250 $\mu\text{g/l}$ ⁵. Ferritin shows a log-normal distribution⁶ and for this reason the geometric mean values were used. In our laboratory these values are 100 $\mu\text{g/l}$ for men and 60 $\mu\text{g/l}$ for women; 10 $\mu\text{g/l}$ is regarded as the lower limit of normal in both sexes⁷. Haemoglobin was determined by standard techniques, the normal range being 13-18 g/dl for men and 12-16 g/dl in women.

STATISTICAL METHODS

A one-way analysis of variance was used to investigate whether the mean levels of the various postoperative iron status parameters differed significantly between any of the groups. When this test confirmed the existence of significant differences, the Newman-Keuls test⁸ was used to determine which groups could be considered to differ from one another. The test calculates a minimum difference value; groups whose mean levels differ by at least this value may be considered to be significantly different at the conventional $P < 0.05$ level or greater (Tables 2, 3, 4). Because of the considerable variation in length of follow-up both within and between groups (Table 1) it was necessary to establish whether any of the

parameters showed a tendency to alter with time. Were such a tendency to exist, any differences between the groups could not be unambiguously ascribed to the influence of operation type. The existence of time trends was investigated by correlating the serum iron, TIBC, percentage iron saturation, ferritin and haemoglobin levels with the number of years between the initial operations and the date of the sample collection. These correlations were derived for each group in order to avoid confounding the influences of operation type and time. Variations in percentage with anaemia and percentage with low ferritin between groups were tested using the conventional Chi-squared test.

RESULTS

Of the 35 correlations of iron status parameters with time examined only one, the serum iron level in PG patients, showed a significant tendency to alter with duration of follow-up ($P < 0.025$). The conventional level of statistical significance ($P < 0.05$) implies that on average an apparently significant result will appear once in every twenty tests even when no true relationship exists, thus this single significant result from a total of 35 tests is not unexpected and is of little consequence. Therefore it is concluded that there is no evidence to suggest that iron status after vagotomy alters significantly during the period of investigation. This further implies that the variations in length of follow-up between the groups will not exert any influence on the levels of the parameters. Any inter-group differences can therefore be unequivocally ascribed to the influence of the types of vagotomy.

TABLE 2
Mean Values for Iron, TIBC and Percentage Saturation

Group	Iron	TIBC	% Saturation
1. TVGJ	18.68 (28)	79.21 (23)	26.04 (23)
2. TVP	17.97 (69)	69.97 (62)	27.26 (60)
3. SVGJ	19.43 (93)	79.44 (87)	25.24 (87)
4. SVP	20.74 (112)	72.51 (102)	29.87 (102)
5. PGVGJ	16.44 (18)	76.80 (10)	20.40 (10)
6. PGV	20.98 (52)	73.33 (48)	29.91 (47)
7. PG	15.52 (52)	77.99 (46)	21.49 (45)
8. CONTROLS	19.30 (67)	65.98 (64)	29.36 (61)
F	3.08	5.86	3.67
	7,483 D.F.	7,434 D.F.	7,427 D.F.
	$P < 0.01$	$P < 0.001$	$P < 0.001$
Minimum difference for intergroup significance	4.37	8.72	6.90

Serum iron values are given in Table 2. The difference between PGVGJ and PGV was significant ($P < 0.01$); no group differed from the controls though the levels after both PGV and SVP were significantly higher than those of PG. TIBC (Table 2) was significantly higher in all three gastrojejunostomy groups (TVGJ, SVGJ and PGVGJ) than in the controls. It was also significantly higher in the PG group ($P < 0.001$) compared to controls. The percentage iron saturation in both PGVGJ and PG groups was significantly lower than the controls.

TABLE 3
Ferritin and Frequency of Low Values

Group	Mean Values ($\mu\text{g}/1$)	% of Group with Low Ferritin ($< 20\mu\text{g}/1$)
TVGJ	94.50 (14)	21.4
TVP	65.43 (35)	14.3
SVGJ	53.88 (57)	29.8
SVP	61.91 (55)	26.5
PGVGJ	79.78 (9)	33.3
PGV	93.31 (39)	17.9
PG	49.85 (34)	39.7
Controls	89.11 (27)	18.5
F	2.55 7,262 D.F. $P < 0.05$	$\text{Chi}^2 = 814$ 7 D.F. N.S.

Minimum difference 40.2
for intergroup
significance

Mean levels of ferritin and the percentage of patients with values below $10\mu\text{g}/1$ are shown in Table 3. The ferritin levels of TVGJ and PGV were significantly higher than the PG group ($P < 0.05$). However, none of the vagotomy groups differed from the controls.

Haemoglobin levels are shown in Table 4. The mean level of $13.87\text{ g}/\text{dl}$ after TVGJ did not differ from the controls but was significantly lower than PGV. The differences between PG on the one hand and PGV and the controls were highly significant ($P < 0.001$). The percentage of individuals with anaemia is based on a lower limit of normal of $13\text{ g}/\text{dl}$ for men and $12\text{ g}/\text{dl}$ for women. According to these criteria, there was anaemia in 4.3 per cent of the control group and 31.5 per cent of PG. The Chi-squared test confirmed the existence of very highly significant differences between the groups ($\text{Chi}^2 = 32.242$ with 7 degrees of freedom

TABLE 4

Haemoglobin and Frequency of Anaemia

<i>Group</i>	<i>Haemoglobin Mean Values (g/dl)</i>	<i>% anaemic (men 13 g/dl, women 12 g/dl)</i>
TVGJ	13.87 (31)	22.6
TVP	14.23 (85)	14.1
SVGJ	14.13 (97)	14.4
SVP	14.47 (129)	7.7
PGVGJ	14.12 (17)	5.9
PGV	14.96 (50)	4.0
PG	13.23 (54)	31.5
Controls	14.67 (69)	4.3
F	6.46	Chi ² =32.24
	7,524 D.F.	7 D.F.
	P<0.001	P<0.001
Minimum difference for intergroup significance	0.82	

P<0.001). The trend was from 22.6 per cent after TVGJ through 14.4 per cent after SVGJ to 4 per cent after PGV.

There are theoretical reasons for expecting a difference between the two drainage procedures, therefore they have been compared in Table 5. The TIBC (P<0.001) and the percentage saturation (P<0.01) alone exhibit significant differences, both favouring pyloroplasty.

TABLE 5

Comparison of Gastrojejunostomy and Pyloroplasty

	<i>GJ</i>	<i>P</i>	
Haemoglobin (mean)	14.07 (145)	14.38 (214)	t=1.77, N.S.
Anaemic (%)	15.17 (145)	10.38 (214)	Chi ² =1.49, N.S.
Ferritin (mean)	63.90 (80)	63.28 (90)	t=0.07, N.S.
Iron Deficient (%)	28.75 (80)	21.11 (90)	Chi ² =1.15, N.S.
Fe (mean)	18.89 (139)	19.68 (181)	t=0.88, N.S.
TIBC (mean)	79.17 (120)	71.55 (164)	t=4.14, P<0.001
% Saturation (mean)	24.99 (120)	28.91 (162)	t=2.63, P<0.01

DISCUSSION

The frequency of anaemia in the PG group (31.5 per cent) was close to the average prevalence found by Deller & Witts. All parameters indicated a poor iron status after PG so that the "quality control" was acceptable.

The study set out to measure the patients' iron status in as many ways as practicable, including the use of a ferritin assay which theoretically is the best method. Walters⁹ established that each microgram per litre of circulating ferritin represents 8 mg of storage iron, thus providing a relationship for ready estimation of the body's stores. Using this formula the mean total body iron of the PGV group and controls would be approximately 700 mg, substantially greater than the 400 mg of the PG group. Ferritin immunoassay has certain real advantages. The result may be obtained from a serum sample of 0.05 ml and it can demonstrate impending abnormality before iron stocks are exhausted. The highest mean ferritin level was found in the TVGJ group. There is no ready explanation for this anomaly but the group comprised only 1.4 patients and the results were influenced by two high ferritin levels of 260 and 300 $\mu\text{g}/\text{l}$ respectively. The finding of 11.1 per cent of low ferritin levels in the controls is at first surprising but it should be remembered that iron deficiency is by no means uncommon; figures of 22 per cent for women and 6 per cent for men have been recorded¹⁰. Low haemoglobin values were found in 4.3 per cent of the controls. Ferritin depletion antedates iron deficiency anaemia so it is consistent that low ferritin results were found in more than 10 per cent of our controls.

Studies of the results of serum iron revealed no significant difference in any of the vagotomy groups. On the other hand, TIBC was higher in all three gastrojejunostomy groups compared to those who underwent pyloroplasty. These results are at variance with the levels obtained for serum iron and ferritin and would suggest the existence of a compensatory mechanism following gastrojejunostomy. Apart from the partial gastrectomy group, the percentage iron saturation was low only after PGVGJ, a small group of 10 patients.

On examination of haemoglobin levels there appeared to be a trend favouring PGV but none of the vagotomies differed significantly from the controls.

There are theoretical reasons for expecting poor iron absorption after vagotomy and drainage. The operations cause rapid gastric emptying and intestinal hurry. Whether vagal denervation of the duodenum, as in truncal vagotomy, influences iron absorption is not known. When the duodenum and proximal jejunum is by-passed, impairment of absorption can be expected¹¹. Our data give limited support to this concept. The proportion of anaemia is much less than in either Wastell's¹¹ or Wheldon's² series.

The study indicates that iron deficiency and anaemia are not a major problem after any type of vagotomy. There is no tendency for iron status to deteriorate with time. There is limited evidence to suggest that gastrojejunostomy may cause anaemia and that vagotomy with drainage fares worse than proximal gastric vagotomy without drainage. There is no clear evidence that selective vagotomy with either type of drainage fares better than truncal vagotomy.

SUMMARY

THE iron status of 421 patients from five to 15 years after six types of vagotomy with and without drainage was measured and compared with a group of 70 controls and 54 patients after partial gastrectomy. Serum iron, total iron binding capacity, percentage saturation, haemoglobin and ferritin were measured.

The possibility of deterioration with time between five and 15 years was investigated but not found in any of the vagotomy groups.

There was no gross iron deficit after any type of vagotomy. The results of proximal gastric vagotomy were similar to the controls. The more sophisticated the surgery, i.e. the lesser the extent of denervation, the better was the iron status of the patient.

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