New Assessment of the Completeness of Vagotomy and the Selection of Operation for Duodenal Ulcer Based upon Gastric Pepsin Secretion

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KAMEYAMA, J., SEKINE, T. and SATO, T. *New Assessment of the Completeness of Vagotomy and the Selection of Operation for Duodenal Ulcer Based upon Gastric Pepsin Secretion.* Tohoku J. exp. Med., 1980, 130 (2), 183-188 — On the basis of the study of gastric pepsin secretion before and after operation for duodenal ulcer, the assessment of the completeness of vagotomy and the selection of operation were attempted. Vagotomy with pyloroplasty that results in a post-operative peak pepsin output (PPO) after insulin stimulation of less than 100 mg tyrosine/hr may well be considered as representing complete vagotomy. In view of the evaluation of ulcer recurrence, this criterion was confirmed to be a more reliable index compared with the criteria based upon gastric acid secretion. Therefore, concerning the selection of operation for duodenal ulcer on the basis of gastric pepsin secretion, we propose the following criteria: Vagotomy with pyloroplasty should be indicated for patients with an insulin-stimulated preoperative PPO less than 500 mg tyrosine/hr; vagotomy with hemigastrectomy for those with 500-1250 mg tyrosine/hr; and distal gastrectomy such as Billroth I operation for those with over 1250 mg tyrosine/hr. ——— gastric pepsin secretion; duodenal ulcer; recurrent ulcer; assessment of the completeness of vagotomy; selection of operation

In order to preserve the physiological function of the stomach as much as possible, various types of operation for duodenal ulcer have been devised. Although many reports dealt with gastric acid secretion in duodenal ulcer, a few reports are available for gastric pepsin secretion. The present study was thus undertaken to investigate gastric pepsin secretion before and after operation for duodenal ulcer. Based on the results of gastric pepsin secretion, the assessment of the completeness of vagotomy, and then the selection of operation were studied.

PATIENTS AND METHODS

The subjects comprised 71 patients with duodenal ulcer (62 male and 9 female, with a mean age of 38 years) from 1974 to 1978 in our Department. Vagotomy with pyloroplasty (V+P) was performed on 42 patients and vagotomy with hemigastrectomy (V+H) on 17 patients, but the remaining 12 patients were not operated on. Postoperative studies were made 4 weeks after operation. No recurrence of ulcer was noted on x-ray or endoscopic examination in any case. Moreover, 3 cases of ulcer recurrence after vagotomy with

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pyloroplasty were scrutinized according to the criteria on the basis of gastric pepsin secretion as well as gastric acid secretion.

Gastric analysis was made using regular insulin (0.2 U/kg, intravenously) as gastric secretory stimulant. Pepsin concentration was determined by the human gastric pepsin assay proposed by the Japanese Society of Gastroenterology (Committee of the Japanese Society of Gastroenterology 1974). The peak pepsin output (PPO) was obtained from two consecutive 15-min samples of the highest value after stimulation and expressed as mg tyrosine/hr.

The lowest level of blood sugar after insulin stimulation was less than 50 mg/100 ml in all cases, favorably corresponding to the insulin test (Hollander 1948).

In statistical analysis, the measured values were expressed as mean $\pm$ s.e. The regular distribution of preoperative PPO was determined by using Shapiro-Francia's method.

RESULTS

Insulin-stimulated gastric pepsin secretion before and after operation

Gastric pepsin secretion began to increase within 15–30 min after insulin injection, i.e. 15–30 min earlier than the acid secretory response, and continued to be increased even after 120 min. The mean value of preoperative PPO in all duodenal ulcer cases was 387.9 mg tyrosine/hr. The mean value of preoperative PPO in the cases of V+H (422.2 mg tyrosine/hr) was higher than in the cases of V+P (374.8 mg tyrosine/hr). On the other hand, the mean value of postoperative PPO in the cases of V+H (32.5 mg tyrosine/hr) was lower than in the cases of V+P (80.6 mg tyrosine/hr). The average reduction rate in V+H (92%) was higher than that in V+P (80%) (Table 1, Fig. 1).

Fig. 1. Pepsin secretion (PPO) before and after operation. $\square$, before operation; $\blacksquare$, after operation; %, average reduction rate.

Distribution of preoperative PPO

Preoperative PPOs after insulin stimulation were evaluated whether they showed the regular distribution or not. Skewness and kurtosis of the measured values were

TABLE 1. *Pepsin secretion (PPO) before and after operation*

Type of operation	PPO (mg·tyrosine/hr)		Average reduction rate (%)
	Before	After	
V+P	374.8±87.4	80.6±15.8	80
V+H	422.2±33.6	32.5±23.7	92
Mean±s.e.			

1.57 and 6.17, respectively, and the measured values did not show a good regular distribution. However, skewness and kurtosis of the values after natural logarithmic transformation were 0.25 and 2.93, respectively. These transformed values showed more favorably a regular distribution than the measured values. After natural logarithmic transformation, the mean value of preoperative PPO (m) and its standard deviation (σ) were 5.88 and 0.41, respectively.

Assessment of the completeness of vagotomy based upon gastric acid secretion and gastric pepsin secretion

The insulin test after V+P was performed in 42 cases without recurrent ulcer and 3 cases with recurrent ulcer. The criterion of Ross and Kay (1964) for the completeness of vagotomy, which is based upon the measurement of gastric acid secretion, is widely accepted as the most reliable means. Of 42 cases without recurrent ulcer, 7 showed early positive response. However, no recurrence of ulcer was noted in these 7 cases on x-ray or endoscopic examination. On the other hand, 3 cases with recurrent ulcer did not show early positive response (Fig. 2). Therefore, there was no relationship between the criterion of Ross and Kay and

Fig. 2. Postoperative pepsin secretion (PPO) with and without recurrent ulcer. Criterion of Ross and Kay. ●, early positive response; ○, late positive or negative response.

the recurrence of ulcer. Of 42 cases without recurrent ulcer performed V+P, 32 had PPO less than 100 mg tyrosine/hr. The remaining 10 (24%) had a postoperative PPO more than 100 mg tyrosine/hr. However, all of the 3 recurrent ulcers had a postoperative PPO more than 100 mg tyrosine/hr (Fig. 2).

DISCUSSION

In order to preserve the physiological function of the stomach as much as possible, various types of operation, especially vagotomy, have been devised for duodenal ulcer. However, it has been pointed out that recurrent ulcer occurred after incomplete vagotomy. From the point of view of ulcer recurrence, it would be an important problem whether vagotomy was performed completely or not. In reference to criteria for the completeness of vagotomy, Hollander (1948) first advocated the criterion based upon the measurement of gastric acid secretion. Clinically, this criterion was not related with ulcer recurrence. Thereafter Ross and Kay (1964) proposed a modified criterion, and it is widely accepted as the most adequate and reliable one for the completeness of vagotomy. In the present study, we examined 3 cases of recurrent ulcer after vagotomy and pyloroplasty according to the criterion of Ross and Kay (1964). None of these cases showed an early positive response. Further, of 42 cases, 7 showed an early positive response, revealing no recurrence of ulcer on x-ray or endoscopic examination. There was no relationship between the criterion of Ross and Kay (1964) and the recurrence of ulcer. Therefore, it seemed that the criterion of Ross and Kay based upon gastric acid secretion would not be available for the purpose of the assessment of the completeness of vagotomy.

Gastric acid and pepsin are the most important aggressive factors in ulcer formation (Alphin et al. 1977; Nagamachi and Skoryna 1977). However, Hirschowitz and Sachs (1965), Rosato et al. (1971), Roland et al. (1974) and Kameyama and Sekine (1978) reported that the pepsin secretion was more intimately related with vagal innervation than the acid secretion. Limbosch et al. (1971) and Kameyama et al. (1978) reported that the pepsin secretion after insulin stimulation provided a more reliable index to the completeness of vagotomy than did the acid secretion. Therefore, the assessment of the completeness of vagotomy based upon gastric pepsin secretion was examined. As mentioned above, all of recurrent ulcers had a postoperative PPO more than 100 mg tyrosine/hr, but no recurrence of ulcer was found in patients with less than this value. Recently, Faber et al. (1974), using insulin-stimulated PAO for assessing the completeness of vagotomy, performed natural logarithmic transformation of the measured values and stated that the transformed values were more favorable for the statistical analysis since they showed an accurately regular distribution. According to Faber's idea, we examined the distribution about the measured values of preoperative PPO after insulin stimulation and found that they did not show a good regular distribution. However, after natural logarithmic transformation, the transformed values of preoperative PPO showed more an accurately regular distribution than the measured

values. Therefore, we performed the statistical analysis in terms of natural logarithmic transformation. As for no recurrence of ulcer, first we considered the range of preoperative PPO to be the 99% tolerance limit. Secondly, we considered that a postoperative PPO must be lower than the lowest range of preoperative PPO. Thus, the lowest range of preoperative PPO after natural logarithmic transformation ($m-3\sigma$) was 4.65. This value corresponded to the measured value of 104.9 mg tyrosine/hr. For convenience sake, we counted this value as 100 mg tyrosine/hr. From the point of view of clinical observation and statistical analysis, vagotomy with pyloroplasty that results in a postoperative PPO after insulin stimulation of less than 100 mg tyrosine/hr may well be considered as representing complete vagotomy.

The selection of operation for duodenal ulcer based upon gastric pepsin secretion was examined. As mentioned above, a preferable postoperative PPO must be under 100 mg tyrosine/hr. Since the average reduction rate of PPO was 80% after V+P and 92% after V+H, such a preferable postoperative PPO would be attained by V+P in patients who have a preoperative PPO less than 500 mg tyrosine/hr, and by V+H in those who have a preoperative PPO less than 1250 mg tyrosine/hr. In view of the preservation of the physiological function of the stomach as much as possible, we propose the following criteria: V+P should be indicated for patients with an insulin-stimulated preoperative PPO less than 500 mg tyrosine/hr, and V+H for those with 500–1250 mg tyrosine/hr. For those with a PPO over 1250 mg tyrosine/hr, distal gastrectomy such as Billroth I operation, after which the average reduction rate of PPO is more higher than after V+P and V+H (Kameyama and Sekine 1978), should be indicated, though none of our patients had a preoperative PPO more than 1000 mg tyrosine/hr.

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