A Modified Form of Insulin (Hollander’s) Test for Determination of Completeness of Vagotony

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Abstract
In order to improve its diagnostic as well as predictive value, the classical insulin (Hollander’s) test was modified and then performed in postvagotomy patients. Twenty-five patients with chronic duodenal ulcer undergoing vagotony were studied pre- and post-operatively. Another group of 15 patients, who had earlier undergone vagotomy but returned with symptoms suggestive of recurrent ulcer, were also studied. All collection errors were accounted for. The stimulated gastric juice volume (expressed as peak and 2 h values) was used for interpretation of results. The reduction in post-operative stimulated volume (V0) was compared with pre-operative values in order to assess the adequacy of vagotony.

The lower 95% confidence limits of stimulated gastric juice volume in the 25 pre-operative patients were 163-1 ml/h for V0 peak and 137-8 ml/h for V0 ½-2 h. The post-operative V0 peak correctly predicted the status of vagotony in all patients. Four patients were predicted to have undergone incomplete vagotony as the values were above the cut-off point and all these developed recurrent ulcer on follow-up. Similarly the status of vagotony in all those patients having symptoms of recurrent ulcer was correctly defined. All those eight patients who actually had recurrent ulcer had stimulated values above the cut-off point. V0 ½-2 h values were not as predictive.

It is suggested that the peak gastric juice volume ought to be used in analysing the results of the insulin test.

Key words: Vagotomy, recurrent ulcer, modified insulin test, pyloric ligation, duodenal reflex, pure gastric juice.

Introduction
Vagotomy alone or in combination with a drainage procedure is the operation of choice in the surgical management of chronic duodenal ulcer. Recurrent ulcer because of incomplete vagotony constitutes a major problem with this surgery. Various intraoperative as well as postoperative tests have been described for assessing the completeness of vagotony.1,2

Hollander1 used insulin induced hypoglycemia to assess the adequacy of vagotomy. The original test however went into disrepute because of poor correlation between the test results and the clinical outcome of vagotony. The test as originally described had many pitfalls, viz, gastric juice collection errors, difficulties in interpretation of the test and variability of basal acid secretion leading to poor reproducibility.4,5 Many workers have since tried to improve the interpretation of the test and have suggested different criteria and methods of conducting the test.6,7 In the present study an attempt has been made to improve further the methodology of the test as well as to simplify its interpretation with the aim of giving a greater predictive value to the test in patients undergoing surgery. Gastric juice volume instead of acidity has been used for interpretation of results as the titrable acidity has been found to be influenced greatly by duodenal reflux and is hence likely to affect the accuracy of the test.8

Material and Methods
Forty patients with chronic duodenal ulcer who were to undergo vagotomy with or without drainage or had vagotony in the past were selected for the study. A modified form of insulin stimulated gastric secretory test was performed in all of them.

Twenty-five patients (Group I) had insulin stimulated gastric secretion studies before and after operation. There were 21 males and 4 females with age ranging from 20 to 52 years. Patients with diabetes mellitus, cardiovascular problems and gastric outlet obstruction were excluded from the study. The diagnosis of chronic duodenal ulcer was confirmed by barium meal examination and/or endoscopy and subsequently at surgery. The indication for surgery in all these cases was intractability and failure of medical treatment. Ten patients gave history of hematemesis. Fifteen patients underwent highly selective vagotomy without drainage, three patients underwent truncal vagotomy and gastrojejunostomy, and truncal vagotomy with pyloroplasty was performed in seven patients.

Group II consisted of 15 patients with chronic duodenal ulcer (12 males, 3 females), who had undergone vagotomy in the past and presented with symptoms suggestive of recurrent ulceration. Three patients had proximal gastric vagotomy and the rest had truncal vagotomy and drainage performed as primary surgery.

Procedure: All patients refrained from tobacco and any medication for 24 hours before the test. After overnight fasting a lubricated double lumen nasogastric
tube was passed into the stomach and the position of the tube adjusted with the help of the water recovery test. During the test, patients were asked not to swallow their saliva.

Phenol red solution of 0.15 g/dl concentration was injected through the small lumen at a constant rate of 1.0 ml every 10 minutes with the help of a slow injector. Before this infusion was started, the first standard of phenol red was collected in a vial over a 10 min period. Gastric juice was aspirated continuously through the larger lumen of the tube with the help of a low pressure (5 mm Hg) suction machine by interposing a conical flask. Air was pumped intermittently into this lumen with a sphygmomanometer bulb to keep its holes patent. The first 30 min aspirate was discarded to allow for adequate equilibration of phenol red in the stomach. The next three 10 min samples were collected as basal secretion. Insulin 0.2 units/Kg body weight was being injected intravenously as a bolus dose. Thereafter 10 min samples of gastric juice were collected for the next 2 hours. Two blood samples were taken at 10 min intervals before insulin injection to estimate fasting blood glucose levels. After insulin injection, blood glucose levels were monitored every 15 min for the next 2 hours. Hyperglycemia with blood glucose of less than 50 mg/dl was considered adequate. The second standard of phenol red was collected over 10 min after completion of the test.

Phenol red concentration was measured using a spectrophotometer. The absorbance value was determined in the two standards for making necessary corrections. The amount of phenol red recovered in one collection period (10 min) was expressed as a fraction of the amount infused during that period. The pyloric loss was calculated with the help of the

\[ \text{Pyloric loss} = \frac{1 - R}{R} \times V, \]

where \( R \) = recovery fraction, and \( V \) = volume of sample in ml.

The amount of duodenal reflux for each 10 min period was calculated by using a formula which is based on the difference in sodium ion concentration in the duodenal and gastric juice. The

\[ V_\text{k} = 7.34Q_{\text{Na}} - 0.0712V_{\text{w}} - 1.281, \]

where \( V_\text{k} \) = volume of duodenal reflux, \( Q_{\text{Na}} \) = output of sodium ions in a given period, and \( V_{\text{w}} \) = volume of gastric juice corrected for pyloric loss.

In each 10 min sample of gastric juice, sodium and potassium ions were measured by flame photometer and chloride ions were measured by chloride meter. Hydrogen ion concentration in each 10 min aspirate was titrated with 0.1N HCl for titration with phenol red as indicator. Potassium, hydrogen and chloride ion concentrations were used to countercheck the accuracy of sodium concentration, as the sum of cations (sodium, potassium and hydrogen) and anions (chloride) is equally balanced.

Expression of results: Pure gastric juice volume (Vg) was calculated for each 10 min period by adding pyloric loss to and subtracting duodenal reflux from the recovered volume. The results were expressed in ml/h as peak (Vg peak) and 1-2 hour (Vg 1-2 h) values. Peak value was the sum of three consecutive highest 10 min samples multiplied by 2. Half to two hour value was defined as the sum of the nine 10 min samples from half hour to two hours after insulin administration divided by 1.5. For these two indices mean and lower 95% confidence limits (mean minus two standard deviations) of Vg in the pre-operative group was taken as the cut-off point for interpreting the results of the post-operative studies.

Results

Pre-operative Vg peak values in Group I ranged from 157.9 ml/h to 597.9 ml/h, with a mean of 300.5 ml/h. The lower 95% confidence limit was 163.1 ml/h. Vg 1-2 h ranged from 145.8 ml/h to 498.7 ml/h with a mean of 246.9 ml/h. The lower 95% confidence limit was 137.8 ml/h.

In these patients, the test was repeated around the 14th post-operative day. Post-operative Vg peak ranged from 31.75 ml/h to 278.57 ml/h and Vg 1-2 h values from 31.03 ml/h to 252.54 ml/h. Four of these patients had Vg peak more than the cut-off point (lower 95% confidence limit: 163.1 ml/h) as calculated from the pre-operative data, indicating that these patients had an incomplete vagotomy (Fig 1). Four patients also had post-operative Vg 1-2 h values above the cut-off level (Fig 2).

At follow up 6 months to 2 years later, four patients developed clinical or investigative evidence of recurrent ulceration. Vg peak predicted correctly the status of vagotomy in all these patients, while indicating the adequacy of vagotomy in the remaining 21 patients.

Vg 1-2 h value, however, incorrectly predicted as having had complete vagotomy one of the four patients who developed recurrent ulcer; on the other hand one of the 21 asymptomatic patients was erroneously predicted as having undergone incomplete vagotomy.

The Vg peak values in Group II patients ranged from 57.9 ml/h to 524.60 ml/h and Vg 1-2 h values from 29.33 ml/h to 415.54 ml/h. Eight of these patients had Vg peak values above the cut-off point in Group I, indicating inadequate vagotomy (Fig 1). Seven had Vg 1-2 h values above the cut-off point (Fig 2).

A recurrent ulcer was later diagnosed by endoscopy and/or surgery in eight patients in this group.

Vg peak correctly predicted the presence of recurrent ulceration in all these eight patients as well as no ulceration in those seven patients who had some other pathology for their symptoms. Vg 1-2 h correctly predicted recurrent ulcer in 7 of 9 patients; the status of vagotomy was, however, incorrectly defined in one patient.

Discussion

In this study the volume rather than titrable acidity was used for the interpretation of the results and was
found to be more specific. Hollander, who first introduced the insulin test in 1946 to assess the adequacy of vagotomy, based his results on acidity. The incidence of incomplete vagotomy as per Hollander's criteria has varied from 15% to 50%. In contrast, the incidence of actual development of recurrent ulceration has ranged from 5% to 10%. It is this discrepancy that has prompted many workers to modify the procedure of the test and/or the interpretation criteria to improve the results.

Different doses of insulin have been suggested for achieving significant hypoglycemia. The dose of insulin used in this study was 0.2 units per kg body weight. During the test all patients experienced hypoglycemic symptoms in the form of thirst, sweating, hunger and occasionally headache and restlessness. Only one patient developed severe hypoglycemic symptoms in the form of extrasystoles at the end of the test, which disappeared with intravenous glucose administration when the test was over. Blood sugar values of less than 50 mg/dl only have been accepted as the threshold value for the test. This varied from 15 mg/dl to 20 mg/dl in our patients.

Basal secretion has been found to be extremely variable. Its use in Hollander's test for interpretation of vagal stimulation, therefore, is yet another fallacy. To overcome this problem, gastric juice volume rather than acidity was calculated and compared to determine the adequacy of vagotomy.

The post-operative insulin test results in Group I patients, using V0 peak as interpretation criterion, had predicted the likelihood of developing recurrent ulcer in all 4 patients who at follow-up developed recurrent ulcer. In the remaining 21 patients the status of vagotomy was defined as complete and none of them developed recurrent ulcer later. V0 1-2 h secretion values gave an incorrect result in 2 patients.

The accuracy of V0 peak for diagnosis was proven in all those 8 patients who actually had recurrent ulcer in Group II. The remaining 7 patients neither had recurrent ulcer nor were considered to have had an incomplete vagotomy as per test results. V0 1-2 h secretion again failed to identify incomplete vagotomy in one patient who had recurrent ulcer.

It is therefore our opinion that the extent of reduction in stimulated volume, when used as an interpretation criterion of post-operative insulin test, is more accurate in defining the status of vagotomy.

References
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