

Gastric emptying and secretion in patients with diabetes mellitus

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EDITORIAL SYNOPSIS The gastric emptying rate tends to be slower in diabetics than in normal and peptic ulcer subjects.

The older workers claimed that the gastric secretion of acid was diminished in diabetes mellitus but more recent investigators have found conflicting results. Marks, Shuman, and Shay (1959), using Kay's augmented histamine test, found an acid secretory output in diabetics which differed little from the normal range. In contrast, Dotevall (1961a, b) found that acid output in diabetics was less than in normal subjects, and concluded that this lower secretory output was related to the higher blood glucose levels existing in diabetics (consistent with the depressant effect of glucose upon the secretion of acid by normal subjects and dogs, a result which has been claimed by a number of workers). This was not, however, confirmed by others. Glucose did not reproduce the marked suppressive effect of glucagon upon gastric secretion (Aylett, 1962), although blood glucose levels were comparable.

The investigation of gastric emptying in diabetics is of some interest, since in peptic ulcer subjects Aylett (1962) has shown a relationship between the rate of gastric emptying and change in the blood glucose level. It would be interesting to discover, therefore, whether diabetics with their higher range of blood glucose level would show a slow gastric emptying rate compared with that of normal or of peptic ulcer subjects.

Results are reported in a group of diabetic patients in whom gastric secretion and emptying rate were studied, using water test meals.

MATERIALS AND METHODS

Details of the modified Hunt test meal method have already been described (Aylett, 1962). The 'meals' consisted of 750 ml. of distilled water, marked with a known quantity of phenol red. A washout of 250 ml. of tap water preceded and followed the meal. The latter was poured into the stomach through a polythene stomach tube *in situ*. After allowing the meal to 'digest' for 20 minutes, the residue was recovered.

Estimations of phenol red and acid were done by the method of Hunt (1954), of chloride by the method of Sanderson (1952), and of potassium and sodium by flame photometry as described by King and Wootton (1959).

Thirty-two test meals were done in 18 diabetic subjects. It was hoped to give two test meals to each subject at widely differing blood glucose levels on the two occasions. However, this was seldom achieved in practice. Of the 18 patients studied, six were new and untreated before the first test meal. Of these, three patients had a second meal after a period of treatment with chlorpropamide. One of these three patients also had a past history of duodenal ulcer. Twelve of the remaining patients were diabetics already being treated for their condition. Of these, six were on soluble insulin, three on long-acting insulins, two on chlorpropamide, and one on insulin plus chlorpropamide. One patient was a mild, untreated diabetic. Of the 18 patients, one had severe retinopathy previously treated by pituitary ablation and was on a small maintenance dose of cortisone. Two had peripheral neuritis. One had intermittent vomiting attacks suspected to be due to gastroparesis (not proven). One patient had become diabetic following pancreatectomy for chronic pancreatitis.

RESULTS

BLOOD GLUCOSE LEVELS DURING TEST MEALS The mean venous blood glucose level during the meals was 191 mg. % (S.D. 93.0).

GASTRIC EMPTYING IN THE DIABETIC PATIENTS The mean volume of gastric contents emptied in 20 minutes was 468 ml. (Table I).

COMPARISON OF GASTRIC EMPTYING OF WATER MEALS IN DIABETIC PATIENTS WITH THE EMPTYING OF MEALS IN NORMAL AND IN PEPTIC ULCER SUBJECTS The test meals emptied a little more slowly in diabetics than did water meals in 16 normal and in 29 peptic ulcer subjects. Compared with the peptic ulcer subjects, this difference was significant. However, the difference from normal subjects was not statistically significant (Table I).

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The mean volume of gastric contents emptied for diabetic subjects corresponded closely to the mean volume of gastric contents emptied for oral glucose meals of 20 g./l. in a series of 11 normal and six peptic ulcer subjects, which were 467 and 484 ml. respectively (Table I). However, the blood glucose levels were not comparable, the mean level being higher in the diabetic subjects during water meals (mean = 191 mg.%) than in the normal or peptic ulcer subjects during these glucose meals (mean = 96.9 and 100 mg. % respectively).

TABLE I

GASTRIC EMPTYING AFTER WATER MEALS IN SERIES OF DIABETIC SUBJECTS COMPARED STATISTICALLY WITH SERIES OF NORMAL AND PEPTIC ULCER SUBJECTS

Meal	Mean Volume of Gastric Contents Emptied (ml.)			Difference Between Diabetic and Ulcer Subjects for Volumes of Gastric Contents Emptied
	Diabetic Subjects	Normal Subjects	Peptic Ulcer Subjects	
Water	468	520	559	Not significant
Water plus oral glucose (20 g./l.)	—	467	484	P < 0.05 > 0.025

GASTRIC SECRETION IN THE DIABETIC PATIENTS Excluding one patient with a past history of duodenal ulcer, the mean quantity of acid secreted in 20 minutes was 3.26 mEq., of chloride 6.65 mEq., of potassium 0.895 mEq., and of sodium 3 mEq. The mean volume of gastric secretion was 43.7 ml.

The mean concentration of potassium in the gastric secretion was 19.9 mEq./l. The mean concentration of sodium in the secretion was 76.1 mEq./l. (Table II).

COMPARISON OF GASTRIC SECRETION IN DIABETICS WITH SECRETION IN A SERIES OF NORMAL SUBJECTS The mean amount of acid and volume of gastric secretion was a little less in the diabetics than was obtained in a series of 16 normal subjects. The mean potassium output, however, was considerably reduced in the diabetics compared with normal subjects. The concentration of potassium in gastric secretion in the diabetics tended to be lower and the concentration of sodium a little higher than in the normal subjects (Table II).

The difference in output of acid between diabetic and normal subjects was not statistically significant. However, the difference in volume of gastric secretion was significant. The difference in output of potassium was highly significant. There was no significant difference in the concentrations of potassium and sodium in the secretion.

TABLE II

STATISTICAL COMPARISON OF GASTRIC SECRETION IN DIABETIC SUBJECTS WITH A SERIES OF NORMAL SUBJECTS

	Mean Values			Difference Between Diabetics and Normal Subjects
	Diabetic Subjects	Normal Subjects	Peptic Ulcer Subjects	
Quantity of H ⁺ (mEq.)	3.26	4.62	7.85	Not significant
Volume of secretion (ml.)	43.7	59.2	81.5	Significant (P < 0.05 > 0.025)
Quantity of K ⁺ (mEq.)	.895	1.63	1.55	Very significant (P < 0.01 > 0.005)
Concentration of K ⁺ in secretion (mEq./l.)	19.9	25.7	18.7	Not significant
Quantity of Na ⁺ (mEq.)	3.00	3.81	3.93	Significant (P < 0.1 > 0.05)
Concentration of Na ⁺ in secretion (mEq./l.)	76.1	68.0	53.3	Not significant

BLOOD GLUCOSE LEVELS IN DIABETICS IN RELATION TO GASTRIC FUNCTION When the amounts of acid secreted in water test meals in the diabetic subjects were plotted against the blood glucose levels 10 minutes after the start of the test meals it was apparent that there was no correlation.

Regression analysis showed no significant relationship between the log volume of contents emptied for test meals in the diabetics and the log blood glucose level 10 minutes after the start of the meal.

DISCUSSION

THE BLOOD GLUCOSE LEVELS The fasting blood glucose levels of the diabetics were mildly or moderately raised.

GASTRIC SECRETION IN THE DIABETIC SUBJECTS All except one out of 18 of the diabetics secreted some acid. In this patient achlorhydria was found in a water meal. In comparison none of the normal subjects showed achlorhydria.

The mean quantities of acid, chloride, sodium, and the volume of secretion produced by 17 diabetic subjects (excluding one patient with a past history of duodenal ulcer, in whom the amount of secretion corresponded to that in the peptic ulcer group) were a little below the mean quantities for the normal subjects. The difference between secretion in the two groups was not marked. However, the mean output of potassium in the diabetics was considerably below that for the normal subjects (Table II).

Many of the diabetics were from older age groups, while the series of normal subjects was predominantly of young adults. It is possible that if more normal subjects from older age groups had been

available for study then there might have been even less difference between secretory output in the two groups, since gastric secretion tends to diminish with advancing years in normal persons. It has been widely held that the gastric secretion of acid is below normal in diabetes mellitus. The origin of this view appears to stem largely from the interpretation of evidence obtained from Ewald type meals, in which the concentration of acid in gastric contents was low in diabetics. Hunt (1953) pointed out the fallacy of trying to deduce the secretory state of subjects from the acid concentration of Ewald type meals, since the concentration obtained is affected not only by secretory output, but also by the rate of gastric emptying of the meal. It therefore seems possible that the low acidities obtained by the earlier investigators might have been due in part to a slower rate of gastric emptying in diabetics.

In contrast, Marks *et al.* (1959), using the Kay augmented histamine test in 41 diabetic subjects, found the output of acid of the same order as that found by Kay (1953) and by Sircus (1958) in their normal subjects. Among the patients studied by Marks *et al.*, two were found to have achlorhydria, an incidence comparable to the present series. However, Dotevall (1961a), after investigating basal and maximal histamine secretion in 60 diabetic patients and comparing it in 30 control subjects, found a reduction of acid output for both types of secretion in the diabetics. Dotevall (1961a) suggested that disagreement of his results with those of Marks *et al.* (1959) might be due to the patients studied by Marks being predominantly the younger type of (insulin-sensitive) diabetic compared with a greater predominance of the older type of diabetic in Dotevall's series. In a further paper, Dotevall (1961b) gave results for gastric secretion in diabetics in Hunt type test meals. These meals were identical in volume with the meals given to diabetics in the present study, but substances were added to Dotevall's phenol red/water mixture and the timing of the meals also differed. Comparing the results for Dotevall's meals of saline with the present series using water only, the mean result for Dotevall's control subjects is higher, assuming the same rate of secretion over a 20-minute period; they would have produced a mean of 6.4 mEq. acid against 4.62 mEq. in this series. For Dotevall's diabetics, the results would differ little from the present series, *i.e.*, 3.40 mEq. in 20 minutes compared with a mean of 3.26 mEq. acid for this series. Thus there is a much greater contrast between secretory output in Dotevall's diabetics compared with his controls than in this series, in which the secretory output of the controls was less than the output in Dotevall's controls.

EFFECTS OF RAISED BLOOD GLUCOSE LEVEL ON GASTRIC SECRETION Glucose has been claimed to have a mild effect in suppressing gastric secretion in man and animals. This effect was inconstant and unconfirmed by many workers.

Dotevall (1961a, b), however, found that for basal secretion in diabetics, achylia was more common at blood glucose levels above 200 mg. % than for levels below 199 mg. % and concluded that this was due to the suppressant effect of glucose on gastric secretion. He also concluded that the lower amounts of secretion found in his series of diabetics, compared with those in normal subjects, was due to the diabetics' raised blood glucose level.

The present study did not show a clear-cut suppressive effect of blood glucose on the gastric secretion of acid. The secretory output of the diabetics was not markedly below that obtained from normal subjects (Table II). In addition, diabetics with the higher levels of blood glucose did not have a smaller secretory output than those with lower levels.

GASTRIC SECRETION OF POTASSIUM IN DIABETIC SUBJECTS It is interesting that in this series the secretion of potassium tended to be lower in diabetic than in normal subjects. Quastel (1960) showed that the rate of absorption of glucose from the small gut was related to the concentration of potassium in the gut lumen. It seems possible that in diabetic subjects a diminished output of gastric potassium entering the duodenum might limit to some extent the rate of absorption of ingested glucose. The normal concentration of potassium in gastric secretion is about four or five times more than in pancreatic juice. Previous investigators do not appear to have studied the secretion of potassium in diabetic patients.

GASTRIC EMPTYING IN THE DIABETIC SUBJECTS For water meals gastric emptying was somewhat slower in the diabetics studied than in series of normal and of peptic ulcer subjects (Table I). The possibility was raised whether gastric emptying might be slower in diabetics in response to their raised blood glucose level. In fact, the mean volume of gastric contents emptied for water meals in the diabetics corresponded closely with the mean volume emptied for oral glucose meals of 20 g./l. concentration in normal and peptic ulcer subjects (Table I). However, the mean blood glucose level in the non-diabetics, 10 minutes after the start of these glucose meals, was considerably lower than that for the diabetics 10 minutes after the start of the water meals. Such an explanation would, therefore, require the postulation of relative unresponsiveness of change in gastric emptying to change in blood glucose level in the

diabetics, in other words, they were 'habituated' to a raised blood glucose level. Against this explanation is the fact that regression analysis showed no significant correlation between the log blood glucose levels in the diabetics and the corresponding log volume of gastric contents emptied.

In the one diabetic subject, however, in whom there was a wide variation in blood glucose levels for the two test meals, emptying was rapid at a low, and slower at a high, blood glucose level: in the first meal the blood glucose level was 59 mg.% and volume of gastric contents emptied 689 ml., and in the second the level was 326 mg. % and the volume of gastric contents emptied was 544 ml. (This patient had, however, been treated by pituitary ablation for severe diabetic retinopathy and was on a small maintenance dose of cortisone in addition to insulin.)

The gastric emptying rate of diabetics might be influenced by the incidence of diabetic complications. For saline meals Dotevall (1961b), found a faster emptying rate in uncomplicated diabetics than in those with later complications. It is possible that any relationship between gastric emptying rate and blood glucose level in diabetic subjects might be masked in some cases by the presence of diabetic neuropathy causing gastroparesis. Previous workers (Malins and French, 1957; Campbell and Conway, 1960) have studied the gastric emptying rate by barium meal in selected diabetics having diarrhoea, vomiting, or neuropathy. In some cases slowing was found. The question was considered whether a few of the cases of apparent gastroparesis might be due to an inverse relationship between the gastric emptying rate and swings to high blood glucose levels in some unstable diabetics. However, where information is supplied in the literature about blood glucose levels at the time of gastric symptoms, there is no correlation with high blood glucose levels (Rundles, 1945; Kassander, 1958; Wooten and Meriwether, 1961). The possibility therefore, seems unlikely but further investigation might be warranted. In this series, slow gastric emptying was not clearly related to known diabetic complications.

SUMMARY

The blood glucose levels during water test meals after fasting in a series of diabetics (including treated and untreated subjects), were mildly or moderately raised but usually higher than the levels reached 10 minutes after ingestion of oral glucose meals in normal and in peptic ulcer subjects.

One out of 18 diabetics also had a duodenal ulcer, with levels of secretion comparable to those in the peptic ulcer series, while one diabetic patient had achlorhydria. The remaining diabetic patients show-

ed an acid secretory output a little below that of the normal subjects. No correlation was found between the height of the blood glucose level and the amount of acid secreted by the diabetics.

The output and concentration of potassium in the gastric secretion tended to be lower in the diabetics than in the normal subjects for water meals.

The gastric emptying of water meals tended to be slower in the diabetics than in the normal or peptic ulcer subjects. The mean rate of gastric emptying of water meals in the diabetics corresponded most closely to that for meals of 20 g./l. glucose in the normal and peptic ulcer subjects. There was no relationship between the rate of gastric emptying in diabetics and the level of blood glucose at the time of the meal.

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