Biologic Gastric Emptying Time in Diabetic Patients, Using Tc-99m-Labeled Resin-Oatmeal With and Without Metoclopramide

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Biologic gastric emptying time (BGET) was measured in 24 patients with severe diabetes mellitus complicated by vascular damage and peripheral or sensory neuropathy. This population had a BGET of 192 ± 32.9 min (mean ± s.e.m. normal 40–85 min). Patients with diabetic gastroenteropathy had prolongation of BGET to 295 ± 45 ($p < 0.05$). Metoclopramide significantly shortened BGET in this subgroup to 101 ± 40 min, with return to normal values in eight of the 12 patients given the drug. The Tc-99m-labeled resin-oatmeal test meal used as described in this study provides a reliable measure of BGET and of the response to metoclopramide.

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Determination of the gastric emptying time is of interest in diabetic gastroenteropathy because of the gastric atony that may accompany other signs and symptoms of visceral neuropathy (*1*). Nausea and vomiting of distressing degree often accompany this condition and determination of a prolonged gastric emptying time provides the gastroenterologist with objective evidence of physical disorder. In addition to establishing the presence of abnormal gastric function, the gastric emptying study can be combined with pharmacologic intervention to assess the likelihood that a therapeutic agent under test will improve gastric emptying. The purpose of this preliminary note is to report our experience with measurements of the biologic gastric emptying time (BGET) in diabetic patients being investigated for complaints considered to be possibly the result of diabetic gastroenteropathy. The effect of metoclopramide (*2,3*) (Fig. 1), a dopamine antagonist that stimulates gastric motility independently of vagal innervation (*4*), was evaluated in half of the patients studied.

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MATERIALS AND METHODS

There were 24 diabetic patients for whom complete data were available. The ages ranged from 22 to 64 yr (mean 39); there were 13 women and 11 men. Tc-99m-labeled triethylenetetramine (TETA) polystyrene resin is prepared locally by treating the chlormethylated copolymer of styrene and divinylbenzene with triethylenetetramine. The resulting polystyrene–polyamine resin chelates Tc-99m from aqueous solution (approximately $10^{-9}M$) with high efficiency. The labeled resin is nonabsorbable, does not adhere to gastric mucosa, releases less than 2.0% of the radioactive label when incubated with simulated gastric juice (USP) at 37°C for 25 hr, and loses less than 0.2% of the radioactivity during its passage through the entire gastrointestinal tract (*5*). The Tc-99m-labeled resin was mixed with 4 oz. of cooked oatmeal obtained from the hospital dietary department and ingested by the patient without added sugar or liquid, following an overnight fast.

Immediately after ingestion of the test meal, the patient was placed supine under a multicrystal gamma detector system* coupled to a dedicated minicomputer that acquires and stores data at a rate of one frame per minute. In selected patients, metoclopramide,† 10 mg,

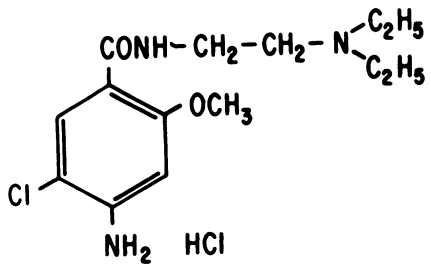

FIG. 1. Structure of metoclopramide hydrochloride.

was injected i.v. at 1-1.5 hr after the test meal.

To circumvent variations in absolute count rate because of incomplete consumption of the test meal, variations in body build, or variations in the anatomic location of the stomach, the initial count rate recorded from the region selected over the stomach was used as 100% of activity for the point of origin of the time-activity curve (TAC). This procedure minimizes variations that might otherwise seriously affect the counting statistics.

On completion of data acquisition, the TAC was generated and plotted on semilog paper. In instances where the TAC did not approximate a straight line, the curve was drawn biphasically. The biologic half-time of gastric emptying (BGET) was calculated from monophasic TACs using the equation $Tb = Tp \times Te/Tp - Te$, where Tb represents BGET in minutes, Tp represents physical half-life of Tc-99m in minutes, and Te represents the experimentally observed gastric emptying half-time in minutes. In the case of biphasic TACs, the BGET was obtained by taking the intercept of the observed gastric emptying curve with a line representing the physical decay of Tc-99m, 50% of total counts administered being taken as the origin. Representative uncorrected time-activity curves are shown in Fig. 2.

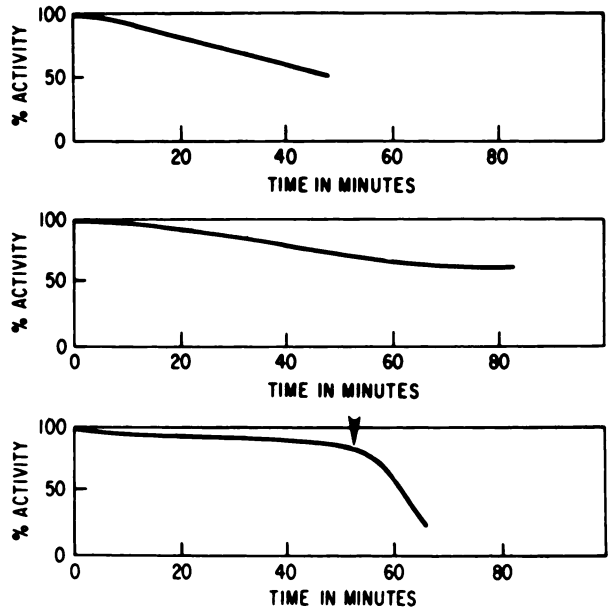

FIG. 2. Top: normal gastric emptying in diabetic patient (No. 19). Center: prolonged gastric emptying in diabetic patient (No. 14). Bottom: prolonged gastric emptying in diabetic patient (No. 10) showing response to injection of metoclopramide (arrow). To yield BGET, the curves must be corrected for physical decay of Tc-99m.

RESULTS

In normal volunteers the BGET range in our institution was previously established as 45 to 60 min by this method (*6*). Continued use of the method in a variety of clinical conditions has led to a widening of the range to 40–85 min, which, we believe, defines more adequately the range of normal as seen clinically. The diabetic population (Table 1) as a whole had prolonged BGET, 192 ± 32.9 s.e.m. The 12 patients studied with metoclopramide were selected prospectively by the referring clinicians; they had significantly longer BGET than the overall diabetic group: 295 ± 45 ($p < 0.05$). Metoclopramide reduced the BGET significantly in this subgroup to 101 ± 40 ($p < 0.001$). Statistical comparisons are by the t-test (*7*). It is of interest that patients either responded dramatically (as in Case 9) or not at all (Case 13). Clinically the BGET was considered to provide a useful diagnostic test for the presence of gastric

TABLE 1. BIOLOGIC GASTRIC EMPTYING TIME IN DIABETIC PATIENTS

Patient	Age	Sex	BGET (before drug) min	BGET (after drug) min
1	29	F	272	—
2	36	F	400	83
3	34	M	436	436
4	59	F	22	—
5	47	F	51	—
6	34	F	29	—
7	44	F	37	—
8	36	F	26	—
9	30	F	418	23
10	53	F	450	6
11	31	F	108	—
12	54	M	402	33
13	32	M	300	300
14	35	M	196	43
15	64	M	58	—
16	26	M	350	—
17	32	F	200	39
18	54	F	180	180
19	27	F	48	—
20	43	M	16	—
21	42	M	196	24
22	31	M	308	27
23	29	M	60	25
24	22	M	48	—

atony and to provide a useful measure of its responsiveness to metoclopramide administration.

DISCUSSION

All diabetic patients reported here had severe diabetes mellitus, with complications such as diabetic retinopathy, neurogenic bladder, male impotence, peripheral neuropathy, chronic renal failure, or diabetic gangrene of the lower extremity. Most had juvenile onset of the disease, but adult onset was clearly documented in several. While the majority were insulin-dependent, at least one patient with abnormal BGET and response to metaclopramide had never needed insulin. It appears from this series that neither the type of diabetes mellitus (juvenile onset as opposed to adult onset) nor the insulin requirement of the patient serves as a completely adequate predictor of the risk of diabetic gastroenteropathy.

Previous investigators have reported variable success in measuring the gastric emptying time in diabetic patients. The older work in this area is reviewed by Scarpello and coworkers (*8*), who studied a series of 29 patients with a test meal containing Tc-99m-labeled sulfur colloid mixed with potatoes. They found no statistically significant difference in gastric emptying time between diabetics (with or without gastroenteropathy) and normal controls, and suggested some possible compensatory mechanism whereby diabetics are able to maintain normal gastric emptying despite denervation of the stomach. We wonder whether micelles may not have formed and adhered to the gastric mucosa, as has been seen with other colloidal radiopharmaceuticals exposed to gastric juice (*5*). Such complex formation would considerably decrease the sensitivity of the test.

The test meal used in our studies of BGET has certain desirable characteristics: it simulates ordinary food, thereby increasing patient compliance, and it is semisolid, avoiding the problem of rapid gastric transit of liquids (*9*). Since the majority of our patients experienced postprandial symptoms, we felt that measurement of the BGET with a semisolid test meal would give more useful results. This agrees with Campbell and coworkers, who demonstrated a clear difference in the gastric emptying patterns of two simultaneously administered markers, one (In-113m DTPA) labeling the liquid component of the test meal, and the other (Tc-99m sulfur colloid) labeling the solid component. They were able to demonstrate conversion of the gastric emptying time to normal for both components following metoclopramide administration in two patients studied with this drug (*10*).

In summary, diabetic gastroenteropathy is a complication rendering management of the diabetic patient more difficult. Correct diagnosis helps the clinician to select proper therapy, including the possible administration of metoclopramide. The BGET reported here provides a reliable measure of gastric motility in the diabetic patient, and the response of an atonic stomach to metoclopramide can be accurately assessed as part of this test procedure.

FOOTNOTES

* System 77, Baird Atomic Co.
† Reglan, A. H. Robins Co.

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REFERENCES

1. ALMY TP: Disorders of motility. In *Textbook of Medicine.* Beeson PB, McDermott W, Eds. Philadelphia, W. B. Saunders Company, 1975, pp 1193-1194
2. CONNELL AM, GEORGE JD: Effect of metoclopramide on gastric function in man. *Gut* 10: 678-680, 1969
3. ROBINSON OPW: Metoclopramide—a new pharmacological approach? *Postgrad Med J* (July Suppl) 49: 9-12, 1973
4. Reglan Injectable (Metoclopramide Hydrochloride) package insert. Richmond, Virginia: A. H. Robins Company, 1978
5. THEODORAKIS MC: Preparation and evaluation of a polystyrene resin as a Tc-99m carrier: a new radiodiagnostic agent for gastric emptying time in humans. Ph.D. Thesis, Lexington, Kentucky: University of Kentucky, 1975, pp 18-32
6. DIGENIS GA, BEIHN RM, THEODORAKIS MC, et al: Use of ^{99m}Tc labeled triethylenetetramine-polystyrene resin for measuring the gastric emptying rate in humans. *J Pharmacol Sci* 66: 442-443, 1977
7. SWINSCOW TDV: Statistics at Square One. VII. Statements of probability. *Br Med J* 2: 33-34, 1976
8. SCARPELLO JHB, BARBER DC, HAGUE RV, et al: Gastric emptying of solid meals in diabetics. *Br Med J* 2: 671-673, 1976
9. CHAUDHURI TK: Use of ^{99m}Tc-DTPA for measuring gastric emptying time. *J Nucl Med* 15: 391-395, 1974
10. CAMPBELL IW, HEADING RC, TOTHILL P, et al: Gastric emptying in diabetic autonomic neuropathy. *Gut* 18: 462-467, 1977