Annals of Nuclear Medicine Vol. 18, No. 6, 533–535, 2004

Usefulness of measuring the gastric emptying time in a case of brittle diabetes

Taner ERSELCAN,* Hakan ALAGÖZLÜ,** Ferhan CANDAN*** and Bulent TURGUT*

**Department of Nuclear Medicine,*
***Department of Emergency Medicine-Division of Internal Medicine,*
*and ***Department of Internal Medicine,*
Cumhuriyet University School of Medicine, Sivas, Turkey

Gastric emptying time measurement by radionuclide study, although quite informative, is rarely remembered in clinical practice. We presented a patient with brittle diabetes who had multiple emergency admissions due to hypoglycemia under routinely prescribed insulin therapy. She had severe gastroparesis, which was determined by scintigraphic gastric emptying study (gastric half-emptying time = 260 min for a mixed meal). She had not presented to the emergency service for two years because of only a slight change the timing of her insulin administration time (after meal instead of before meal) in the light of gastric-emptying study.

Key words: brittle diabetes, gastric emptying, scintigraphy, hypoglycemia

INTRODUCTION

"Brittle diabetes" is a term used to describe an uncommon subgroup of insulin-dependent diabetes mellitus (IDDM), usually seen in young females and characterized by glycemic instability of any type leading to life disruption, and recurrent and/or prolonged hospital admissions.[1,2] Brittleness may be in the form of hyperglycemic brittleness causing recurrent ketoacidosis or hypoglycemic brittleness leading to unconsciousness or an occasional combination of both (mixed brittleness).[1,3–5] Such patients are costly in terms of health care resources due to multiple emergency admissions.

Hypoglycemic brittleness occurs due to a mismatch between the action of insulin and absorption of nutrients.[1,6] In such patients gastroparesis should be remembered. Gastroparesis is a disorder in which the stomach takes too long to empty its contents and it is most often a complication of uncontrolled IDDM due to vagal nerve damage. At least 20 percent of patients with IDDM develop gastroparesis, which makes stomach-emptying unpredictable, with glycemia in turn becoming more difficult to control.[7,8]

Diabetic gastroparesis can be easily assessed by measuring the gastric-emptying time for which, scintigraphic technique is considered to be the non-invasive gold standard for both solid and liquid meals.[9]

CASE

A 24-year-old woman who had a 12-year history of type 1 diabetes mellitus was admitted to our hospital's emergency service in March 2000 because of an episode of disorientation. She had an episode of slurred speech, and lethargy. She had already presented to the emergency service many times due to hypoglycemia. The patient had been admitted 4 or 5 times per year since 1998 because of hypoglycemic events. Although she had been treated with insulin and diet therapy, glycemic control had been fluctuating and was poor. On admission, a blood glucose value of 38 mg/d*l* was obtained before the administration of 50 m*l* bolus of 50% glucose. Her mentation cleared immediately and neurologic signs disappeared. An order was written to continue 5% glucose in water at 100 m*l*/hour. The blood tests showed the following results: Hemoglobin; 13.3 g/d*l*, hematocrit; 39%, white blood cell count; 7400/mm^3, platelets; 224.000/mm^3, hemoglobin

Received November 12, 2003, revision accepted April 7, 2004.

For reprint contact: Taner Erselcan, M.D., Department of Nuclear Medicine, Cumhuriyet University School of Medicine, P.K. 806 Sivas, TURKEY.

E-mail: erselcan@cumhuriyet.edu.tr

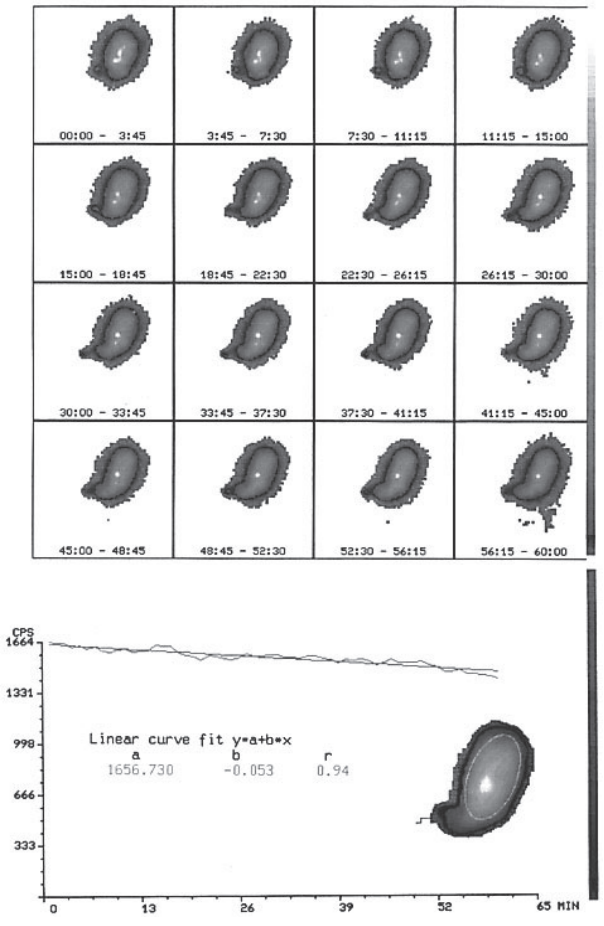

Fig. 1 The composite dynamic serial images of gastric-emptying study in the presented case and curve fitting (r; regression coefficient), by which half-emptying time was measured as 260 min.

A_{1C} (HbA_{1C}) level; 22%, sedimentation rate; 16 mm/h, total protein; 7.3 g/d*l*, plasma albumin; 4.9 g/d*l*, blood urea nitrogen; 11 mg/d*l*, plasma creatinine; 0.9 mg/d*l*, total cholesterol; 223 mg/d*l*, triglycerides; 126 mg/d*l*, total bilirubin; 0.8 mg/d*l*, aspartate aminotransferase; 16 IU/*l*, alanine aminotransferase; 14 IU/*l*, lactate dehydrogenase; 260 IU/*l*, alkaline phosphatase; 85 IU/*l*, sodium; 135 mEq/*l*, potassium; 4.5 mEq/*l*, chloride; 96 mEq/*l*. No abnormality was observed in blood gas or in urine analysis. She has been taking human insulin as 14 units of NPH insulin and 12 units of regular insulin at 7 AM, and 8 units of NPH insulin and 6 units of regular insulin at 5 PM since the onset of her diabetes.

In the presented case, causative problems were considered, and these comprised alcohol abuse, renal failure, liver disease, thyroid hormone excess or deficiency, adrenal insufficiency along with Somogyi phenomenon, factitious insulin overdose and gastroparesis.[10] We eliminated the Somogyi phenomenon by the known blood glucose level, which had been determined previously at 3 AM. Also, blood levels of thyroid and adrenal hormones had already been normal. She had no alcohol, drug abuse or factitious insulin overdose. From the point of view of gastroparesis, gastric-emptying time was measured by scintigraphy. In scintigraphic gastric emptying study, a standard mixture meal of 300 kcal, prepared as described in a multicenter study, was applied in the present case.[11] The test meal has a solid and liquid component, consisting of an omelet with two eggs and 150 m*l* of orange juice. 18 MBq (0.5 mCi) technetium-99m labeled macroaggregates of human serum albumin (LyoMAA, Malinckrodt Medical, Netherlands) was added to the omelet and mixed during the cooking. After an overnight fast, the patient ingested the omelet and drank the orange juice in the morning and image acquisition started immediately thereafter. While the patient was in the semi-sitting position in front of the single head gamma camera (Orbiter, MIE, Germany), dynamic imaging was performed with a low energy all purpose collimator using 64 × 64 matrix size, as one image per 15 second, during 60 minutes. The stomach activity was outlined by a region of interest and the time-activity curve was generated. A linear fit operation was applied to calculate the half-emptying time (T_{50}), for which the normal value is 100 ± 20 min.[11] The half-emptying time measured as 260 min in the presented case (Fig. 1). In this regard, we recommended her to take insulin after meals rather than before meals.

One year later, the patient's glycemic control improved, and her HbA_{1C} level decreased to 7.2%. She did not experience hypogylcemia again within two years.

DISCUSSION

For more than 30 years, scintigraphic gastric emptying test by using radioisotope labeled meal has become the method of choice for the measurement of gastric emptying in clinical practice. Measurement of gastric emptying with scintigraphic techniques which is non-invasive, uses a physiologic meal, delivers a low radiation dose and is quantitative, is the most physiologic study available for studying gastric motor function.[11] This technique gives reliable measurements and is highly reproducible. Scintigraphic gastric emptying time measurement has been used as a screening test for the diagnosis of gastric dysmotility in different gastrointestinal and metabolic disorders.[12] Factors that effect gastric emptying are type of food, the volume of the meal and its caloric content, osmolality, acidity and chain length of fatty acids in the meal. According to the literature, recent findings suggest differences in gastric emptying time between gender, age, menopause and patient positioning.[11]

Recently, in a multicentre study the scintigraphic gastric emptying by low fat meal has also been studied. Median values (95th percentile) for percent gastric retention at 60, 120, and 240 min have been reported as 69% (90%), 24% (60%) and 1.2% (10%) respectively.[13]

Gastric emptying time measurement by radionuclide

study, although quite informative, is unfortunately rarely remembered in clinical practise. We presented a patient with brittle diabetes who had multiple emergency admissions due to hypoglycemic attacts under routinely prescribed insulin therapy. She had severe gastroparesis, which was determined by scintigraphic gastric emptying study (gastric half-emptying time = 260 min for a mixed meal). In this case, the gastric half-emptying time was too long according to the reported values for mixed solid-liquid meal in the literature.[11]

An insulin treatment regimen can be devised, which would provide relatively stable control of blood glucose values for most patients with diabetes. A small subgroup of patients, however, experience extremely erratic patterns of glycemic control, with large fluctations in glucose levels for no obvious reason. These patients are usually said to have "brittle" diabetes. These patients either have marked and often incapacitating excursions of blood glucose levels on a daily basis or have frequent decompensations in their glycemic control, often with recurrent ketoacidosis and/or hypoglycemia that significantly interferes with their lifestyle.[1,4,10]

The problem of hypoglycemic brittleness is heterogenous, with a number of causes. The Somogyi phenomenon, alcohol abuse, thyroid hormone excess or deficiency, renal insufficiency, adrenal insufficiency and cirrhosis are often overlooked as causes of erratic glycemic control; however, none of these was associated with the presented case. Also, diabetic gastroparesis can lead to erratic absorption of nutrients from the gastrointestinal tract, making it extremely difficult to coordinate insulin administration with meals. The presented case obviously had gastroparesis that was diagnosed with gastric emptying scintigraphy. Accordingly changing the timing of insulin administration helped to the control gastroparesis. Prokinetic drugs can bring about rapid improvement in gastric emptying, but after 4–5 weeks of therapy, emptying (especially solid phase) seems to return to the pretreatment state.[8,14] Therefore, we recommended her to take insulin only after meals rather than before meals without using prokinetic medication. A recent report has also shown that acceleration of gastric emptying as a treatment strategy was not found to be beneficial for brittle diabetes in patients with type 1 diabetes.[15]

Brittle diabetic patients impose a considerable burden on hospital, social, and family resources due to multiple emergency admissions. Therefore, brittle phenomenon together with scintigraphic gastric-emptying study in diabetic patients should be kept in mind. We concluded that advising only a slightly change in insulin timing would help in such patients without any prokinetic medication. The presented case showed at the same time that a simple and non-invasive study of scintigraphic gastric-emptying time measurement would be of great benefit for diabetic patients suspected to have the brittle phenomenon.

REFERENCES

1. Gill G, Lucas S. Brittle diabetes characterised by recurrent hypoglycemia. *Diabetes Metab* 1999; 25: 308–311.
2. Gill GV, Lucas S, Kent LA. Prevalence and characteristics of brittle diabetes in Britain. *QJM* 1996; 89: 839–843.
3. Selam JL. How to measure glycemic instability? *Diabetes Metab* 2000; 26: 148–151.
4. Tattersall R, Gregory R, Selby C, Kerr D, Heller S. Course of brittle diabetes: 12 year follow up. *BMJ* 1991; 302: 1240–1243.
5. Kent LA, Gill GV, Williams G. Mortality and outcome of patients with brittle diabetes and recurrent ketoacidosis. *Lancet* 1994; 344: 778–781.
6. Farrell FJ, Keeffe EB. Diabetic gastroparesis. *Dig Dis* 1995; 13: 291–300.
7. Hackelsberger N, Piwernetz K, Renner R, Gerhards W, Hepp KD. Postprandial blood glucose and its relation to diabetic gastroparesis; a comparison of two methods. *Diabetes Res Clin Pract* 1993; 20: 197–200.
8. Barkin JS, Robbins EG, Stein B. Diabetes and GI System. In *Ellenberg and Rifkin's Diabetes Mellitus*. Porte D, Rifkin H, Sherwin RS, Ellenberg M (eds). 5th ed. Appleton & Lange, 1998: 1183–1207.
9. Mearin F, Malagelada JR. Gastroparesis and dyspepsia in patients with diabetes mellitus. *Eur J Gastroenterol Hepatol* 1995; 7: 717–723.
10. Rosenzweig JL. Principles of Insulin Therapy. In *Joslin's Diabetes Mellitus*. Kahn CR, Weir GC (eds). 13th ed. Philadelphia; Lea & Febiger, 1994: 460–484.
11. Gryback P, Hermansson G, Lyrenas E, Beckman KW, Jacobsson H, Hellstrom PM. Nationwide standardisation and evaluation of scintigraphic gastric emptying: reference values and comparisons between subgroups in a multicentre trial. *Eur J Nucl Med* 2000; 27: 647–655.
12. Donohoe KJ, Maurer AH, Ziessman HA, Urbain JL, Royal HD. Procedure guideline for gastric emptying and motility. Society of Nuclear Medicine. *J Nucl Med* 1999; 40: 1236–1239.
13. Tougas G, Eaker EY, Abell TL, Abrahamsson H, Boivin M, Chen J, et al. Assessment of gastric emptying using a low fat meal: establishment of international control values. *Am J Gastroenterol* 2000; 95: 1456–1462.
14. Erbas T, Varoglu E, Erbas B, Tastekin G, Akalin S. Comparison of metoclopramide and erythromycin in the treatment of diabetic gastroparesis. *Diabetes Care* 1993; 16: 1511–1514.
15. Lehmann R, Honegger RA, Feinle C, Fried M, Spinas GA, Schwizer W. Glucose control is not improved by accelerating gastric emptying in patients with type 1 diabetes mellitus and gastroparesis; a pilot study with cisapride as a model drug. *Exp Clin Endocrinol Diabetes* 2003; 111: 255–261.