Gastric emptying time in patients with primary hypothyroidism

Primer hipotiroidili hastalarda mide boşalma zamanı

Dr. Hakkı KAHRAMAN[1], Dr. Nadir KAYA, Dr. Arif DEMİRÇALI, Dr. İrem BERNAY, Dr. Fulya TANYERİ

Ondokuz Mayıs Üniversity, Medical Faculty, Department of Internal and Nuclear Medicine, Samsun

ÖZET: *Hipotiroidili hastaların çoğunda, gastrointestinal motilitenin yavaşlaması sonucu meydana gelen semptomlar önemli bir sorun oluşturmaktadır. Yaptığımız bu çalışmada, radyoizotopik metod kullanılarak hipotiroid hastaların mide boşalma zamanı hesaplandı.*

İlk kez tanı konulan ve ortalama yaşı 43 (yaş aralığı 38-50) olan, daha önce hiç tedavi edilmemiş 15 primer hipotiroidili hasta (13'ü kadın, 2'si erkek) çalışma programına alındı. Hastaların üst gastrointestinal sistemleri endoskopik ve radyolojik yöntemlerle incelendi. Mide çıkışında obstrüksiyonu olanlar dışlandı. Kontrol grubu ise gastrointestinal patolojisi ve hormonal bozukluğu olmayan 12 sağlıklı kişiden oluşturuldu. Bu kişilerin ortalama yaşı 45'di (yaş aralığı 35-55).

Çalışmaya alınan kişilerin mide boşalma zamanı (t 1/2), 1 mCi Tc99-sülfür kolloid ile işaretlenmiş semisolid gıda verildikten sonra, epigastrik bölgeden sayım yapılarak hesaplandı. Ortalama mide boşalma zamanı (t 1/2) hipotiroid hastalarda 112.13±48.96 dakika, kontrol grubunda ise 57.87±6.38 dakika olarak bulundu. Hipotiroid hastaların mide boşalma zamanı kontrol grubuna göre belirgin olarak uzundu ($p<0.001$). Mide boşalma zamanı ile serum TSH düzeyi arasında anlamlı bir ilişki yoktu.

Sonuç olarak, hipotiroidili hastaların mide boşalma zamanının tayininde radyoizotopik çalışmanın kolay, hızlı ve güvenilir olabileceği kanısına varıldı.

Anahtar kelimeler: **Gastrik motilite, hipotiroidi, mide boşalma zamanı**

SUMMARY: *Symptoms due to slowing of gastrointestinal motility constitute an important problem in most patients with primary hypothyroidism. In this study, gastric emptying time was calculated by radioisotopic method in patients with primary hypothyroidism.*

Fifteen hypothyroid patients (2 male, 13 female) participated in the study. Mean age was 43 (range 38-50) years. Only patients who were recently diagnosed and not yet recewing replacement therapy were included in the study. Radiologic and endoscopic examination of the upper gastrointestinal tract were made. Patients with gastric outlet obstruction were excluded. Twelve healthy and euthyroid persons with no detectable gastrointestinal pathology were examined as control group. The mean age of this group was 45 (range 35-55) years.

Patients and control group received a semisolid meal containing 1 mCi Tc 99-sulphur colloid and measurements were made from epigastrium. Mean gastric emptying time (t 1/2) was 112.13±48.96 minutes in hypothyroid patients and 57.87±6.38 minutes in the control group. Gastric emptying time of the hypothyroid patients was significantly different from the control group ($p<0.001$). There was no correlation between gastric emptying time and serum TSH levels.

We concluded that radioisotopic study is a safe, rapid and reliable method in determining gastric emptying time in patients with primary hypothyroidism.

Key words: **Gastric motility, hypothyroidism, gastric emptying time**

GASTROINTESTINAL motility and serum thyroid hormon levels are closely related. Motor hyperactivity is found in patients with thyrotoxicosis, despite hypoactivity in hypothyroid patients (1-4). Gastrointestinal system symptoms like flatulence and constipation are frequently present in patients with hypothyroidism as a result of reduced motor activity (5). Delay in gastric emptying time is another indicator of motor hypoactivity in hypothyroidism (1,2,6-10). In delayed emptying, gastric content may provoke nausea and vomiting in some patients and may lead to phytobezoar formation if the phenomenon persists for a long time (11,12).

Although inspection from a gastric fistulae, persistent intubation tests, radiological procedures and radioisotopic tests have been used as various diagnostic tools to determine gastric emptying time (GET), radiological methods have been pre-

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Table 1. *Basal laboratory values of hypothyroid patients*

Triiodothyronine (T3)	81.08 ± 37.06	ng/dl
Thyroxine (T4)	2.51 ± 2.03	mg/dl
Free T3 (fT3)	1.83 ± 1.33	pg/ml
Free T4 (fT4)	0.35 ± 0.24	ng/dl
Thyroid-stimulating hormone (TSH)	87.24 ± 44.70	mIU/ml
Creatinine phosphokinase (CPK)	922.92 ± 983.88	U/L
Lactic dehidrogenase (LDH)	562.56 ± 264.42	U/L

ferred in most hypothyroid patients for many years (9,13). Barium can affect gastric motility by itself due to its unphysiological properties (10). Scintigraphic examinations using radio-labeled foods have been widely used in many diseases that affect gastric motility (10,13-15). The best results among these techniques were obtained by the most physiological semi-solid food labelling. This method has not been previously used to examine hypothyroid gastroparesis. The aim of this study was to investigate the value of this physiologic and noninvasive diagnostic method in hypothyroid gastroparesis.

MATERIALS and METHODS

Fifteen recently diagnosed as primary hypothyroid patients (2 male and 13 female), with the exception of subclinical ones, were included in the study. The mean age was 43 years (range 21-67 years). All drugs which may affect gastric motility were discontinued at least 10 days previous to study. All patients were evaluated by radiological and endoscopic techniques to rule out gastric outlet obstruction.

Twelve healthy people with no gastrointestinal or hormonal pathology constituted the control group. The mean age of this group was 45 (range 35-55) years.

Patients and control subjects received a standard semisolid meal marked with 1 mCi $T_c^{99\,m}$ sulfur colloid (SC) and sequential images were obtained from epigastric region using a gamma-camera (Phillips, Gammadiagnost-Tomo). Using the acquired data, time-activity curves were generated. Gastric emptying half-times (t 1/2) were calculated from time-activity curves (Fig. 1).

All data were expressed as Mean±SD, and the statistical evaluation of the data was performed using Mann-Whitney U test and regression analysis.

RESULTS

The mean time interval between the beginning of the symptoms and the diagnosis of hypothyroidism was 27.82±22.97 months. All hypothyroid patients' basal laboratory values are shown on Table 1. Mean gastric emptying half-time (GEHT) (t

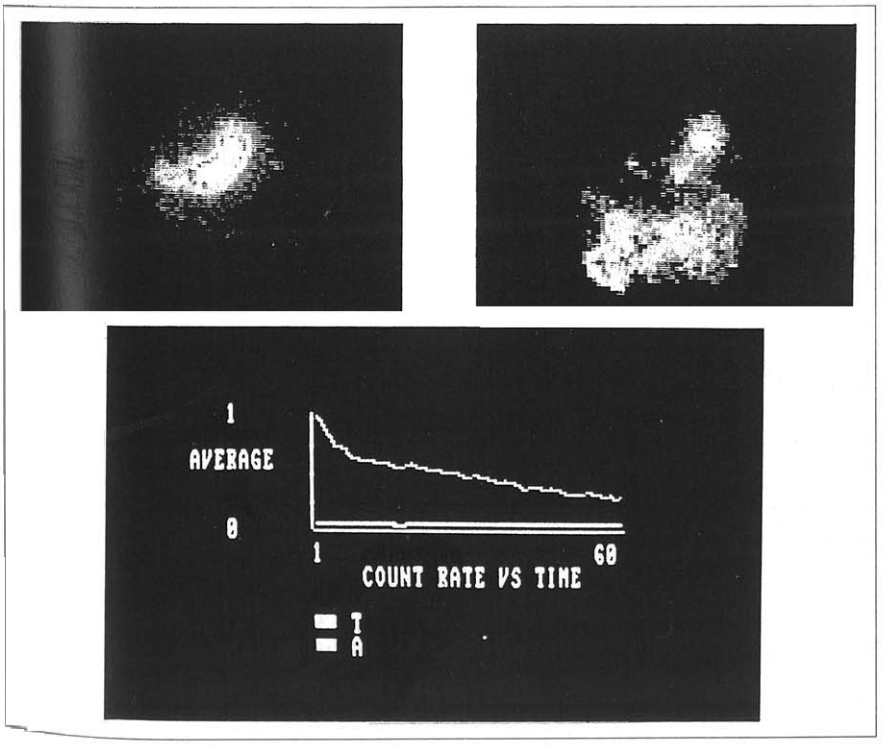

Figure 1. *Serial epigastrical images showing the decrease of gastric activity and the passage to the intestine.*

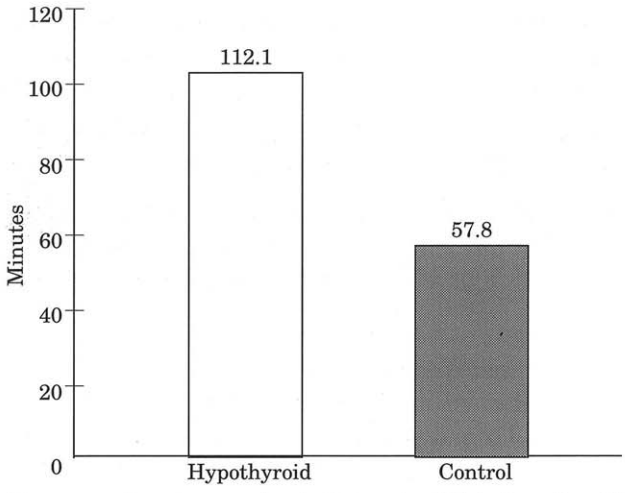

Figure 2. *Gastric emptying half-time (t 1/2) in hypothyroid patient and control groups.*

1/2) were 112.13±48.96 minutes, and 57.87±6.38 minutes in patient and control groups, respectively. GEHT in hypothyroid patients was significantly longer than in the control group ($p<0.001$) (Fig. 2). There were no significant correlation between the GEHTs and either the duration of symptoms or plasma TSH levels, as well as other laboratory data.

DISCUSSION

Hyptohyroidism causes slowing of motor activity in all regions of gastrointestinal tract, and consequently gastroparesis, constipation, fecal impaction, sigmoid volvulus and megacolon can be seen. If the disease is not treated for a long time, intestinal atony and ileus can develop (1,5,11,16-19). Rarely, hypomotility can cause diarrhea and malabsorbtion. Radiological examination of severe hypothyroid patients may reveal the dilatation of the gastrointestinal tract, especially in large intestine (17,20,21). Hypothyroidism can also cause functional gastrointestinal symptoms that are relieved by thyroid hormone replacement (22).

In hypothyroid patients, mucinous materials (mucopolysaccarides, hyaluronic acid, chondroitin sulfate) acumulate in the muscle layers and the submucosa of intestinal wall especially in the colonic region by an unknown mechanism. Pathologic examination reveals edematous, pale and thick intestinal wall with mononuclear cell infiltration (1,9,17,21,23). It has been reported that in hypothyroidism with short duration gastrointestinal system mucosa was normal, and mucopolysaccaride accumulation was not present (24).

The pathogenesis of gastric motor hypoactivity is not precisely known. Autonomic neuropathy, disturbance of conduction of impulse at myoneural junction, intestinal ischemia, lessening of β adrenergic receptor numbers, changing in gastrointestinal peptide hormone metabolism and intestinal myopathy are the most favorable theoretical explanations for this dysfunction (5,21,24-26). It is also claimed that hypomotility can directly result from autoimmune disease or chronic inflammatory changes of the stomach (19).

Gastric and intestinal motor activity can be evaluated by means of several diagnostic methods. Electrical, contractil and prepulsid activity of the gastrointestinal tract can be measured by electrophysiological studies, manometric calculation of the pressure and the use of radioactive markers, respectively (4,5,13,27,28). Usually, nuclear-scanning methods are used to determine the effects of various diseases to the GET, and to evaluate the results of therapeutic approaches. In our study, standard semisolid food marked with the radiopharmaceutical Tc99m-SC is used to determine the GET in patients with primary hypothyroidism. The GETs in our patients were significantly longer than the control group (Fig. 2). No previous report concerning GET determination in hypothyroid patients by this method could be found in the literature. In spite of numerous non-physiological methods (e.g. barium studies) used in previous studies, only Holdsworth and Besser (7), calculated GETs by using nonabsorbable liquid radioactive markers in hypothyroid patients and found their GETs to be longer than normals.

It is shown that gastric hypomotility is dependent on the duration of hypothyroidism and so, if the duration is short, gastric motility can be normal (8), but we couldn't find any correlation between GET and the duration of symptoms. Goto et al. (24) showed slowing of colonic motility in acutely hypothyroid rats, without any histopathologic finding. This observation may be in favor of the reason of this disorder to be functional.

Studies of the Basic Electrical Rytm (BER) have shown evidence of marked slowing of the intestinal pacemaker (slow waves) in these patients (5). It is also revealed that there was a high degree of correlation between the duodenal BER frequency and the serum thyroid hormone levels (28). Kowalewski et al (4) investigated gastric electrophysiologic changes in hypothyroid dogs and showed that 1) frequens of electrical control activity of the

stomach was decreased, 2) electrical response to stimulation (spike potential) was low, and 3) mechanical response to stimulants like food and pentagastrin was severely reduced comparing to normals. Lessening of electrical response correlates with hypomotility, but the reason of slowing of the basal electrical rhythm is not precisely known.

Some investigations showed that orocecal transit time determined by lactulose hydrogen breath test is very long in hypothyroid patients, while others found no change in transit time and no difference after thyroid hormone replacement therapy (19,20). It is claimed that slowing of the colonic motility and constipation may occur due to the accumulation of the mucinous substances predominantly in the colonic wall in spite of the normal orocecal transit time and normal stomach and small intestine (9,20).

Solid food must be broken down to small particles for gastric emptying. This function is also disturbed in hypothyroid patients due to the decreased motility. In addition to these factors, the gastro-duodenal pressure gradient that is necessary to pass the gastric content through the pyloric canal is also reduced (10,13).

In conclusion, determining gastric emptying time by using radioactive-labelled semisolid food is a more reliable and correct method in the diagnosis of hypothyroid gastroparesis, because of being absolutely physiological, and though not affecting the gastric motility.

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