Maximum Tolerated Volume in Nutrient Drinking Test for Diagnosis of Functional Dyspepsia

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ABSTRAK

Latar belakang. Metode untuk mengevaluasi patofisiologi dari dispepsia fungsional, barostat misalnya, bersifat invasif, mahal dan tidak tersedia di setiap layanan kesehatan. Uji minum mengandung nutrien dikembangkan sebagai metode noninvasif, aman, murah dan mudah dilakukan untuk menilai adanya gangguan akomodasi gaster. Tujuan studi ini adalah untuk mengevaluasi apakah uji minum dapat dimanfaatkan sebagai alat bantu diagnosis pasien dengan dispepsia fungsional.
Metode. Studi potong lintang dilakukan mulai bulan Juli 2014 sampai dengan Desember 2014, di RSUP Dr. Sardjito, Yogyakarta, Indonesia. Dua puluh pasien dispepsia fungsional (sesuai kriteria Rome III dengan normal gastroskopi) dan 20 kontrol sehat (usia, jenis kelamin dan indeks masa tubuh sudah disamakan) dilibatkan dalam penelitian. Semua pasien dan kontrol diminta minum susu (UltraMilk mengandung 0,6 kcal /mL) setelah menjalani puasa selama 8 jam. Kemampuan minum maksimal masing-masing subyek dicatat. Sensitivitas, spesifisitas, nilai duga positif, dan nilai duga negatif kemudian dianalisis.
Hasil. Menggunakan batas kemampuan minum maksimal ≤ 950 mL sebagai titik potong, masing masing nilai sensitivitas , spesifisitas, nilai duga positif, dan nilai duga negatif adalah 95 %, 100 %, 100 % dan 95 %.
Kesimpulan. Uji minum mengandung nutrien dapat membedakan antara pasien dispepsia fungsional dengan kontrol sehat, dengan nilai sensitivitas dan spesifisitas yang tinggi. Uji minum mengandung nutrien dapat digunakan sebagai metode yang obyektif, aman dan noninvasif sebagai alat bantu diagnosis pada pasien dengan dispepsia fungsional.

Kata kunci : *uji minum mengandung nutrien, gangguan akomodasi gaster, dispepsia fungsional, uji diagnostik*

ABSTRACT

Background. Methods to evaluate pathophysiology of functional dyspepsia (FD) such as barostat are invasive, expensive and not readily available. Nutrient drink test was developed as noninvasive, safe and low cost means to assess impaired gastric accommodation in FD patients. The aim of this study is to evaluate whether this test could be used for diagnostic tool for FD patients.
Method. A cross sectional study was conducted from July 2014 to December 2014, at Sardjito General Hospital, Yogyakarta, Indonesia. Twenty FD patients (according Rome III criteria with normal gastroscopy) were matched by age, gender and body mass index with 20 healthy controls. All of FD patient and healthy controls ingested nutrient drink tests (UltraMilk contain 0.6 kcal /mL). Maximum tolerated volume (MTV) of each subject was recorded. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were analyzed.

Results. Using ≤ 950 mL of maximum tolerated volume as cut off point, sensitivity, specificity, PPV and NPV were 95%, 100%, 100% and 95%.
Conclusions. A nutrient drinking test can discriminate between FD patients and healthy controls with high sensitivity and specificity. This test could be used as objective, safe and non-invasive diagnostic tool for FD patients.--

Keywords: *nutrient drink test, impaired gastric accommodation, functional dyspepsia, diagnostic test*

INTRODUCTION

Functional dyspepsia (FD) is a highly prevalent gastrointestinal disorders characterized by symptoms originating from the gastroduodenal region in the absence of underlying organic disease that readily explains the symptoms. [1] In up to half of patients seen in gastroenterologists, a standard work-up, which may include endoscopy, laboratory testing, and radiological evaluation, fails to provide an explanation for the patient's symptoms.[2] Several pathophysiology were proposed as underlying of FD such as impaired gastric accommodation, delayed gastric emptying, visceral hypersensitivity, acid exposure, Helicobacter pylori, post infections, food intolerance, central nervous system-stimulus processing, and immune system involvement.[1,3]

Impaired gastric accommodation is identified as a major pathophysiological mechanism of FD. [4] Assessment of gastric sensation and accommodation is measured using a barastat-balloon study, as a gold standard. This method is invasive, expensive and not readily available. To overcome these shortcomings, drink tests were developed as well tolerated, inexpensive, easy to perform and noninvasive methods to assess gastric sensation and accommodation. [5] The aim of this study is to evaluate whether nutrient drink test could be used for diagnostic tool for FD patients.

METHOD

A cross sectional study was conducted from July 2014 to December 2014, at Sardjito General Hospital, Yogyakarta, Indonesia. Twenty adults (> 18 years of age) FD patients that diagnosed according to the Rome III criteria were included in the study. The exclusion criteria were evidence of organic systemic diseases and structural diseases (such as esophagitis, erosive gastroduodenal lesions or ulcers), calcium blockers, anti-depressives, opioids analgetics, nonsteroidal anti-inflammatory drugs or iron supplements and milk intolerance. The patients suspended all ant secretory medications including H2 blockers and proton pump inhibitors, antacid, prokinetics or visceral analgesics, 1 weeks prior to the protocol. Patients were matched by gender, age and body mass index (BMI) with 20 healthy controls, recruited from volunteers in Sardjito hospital environment, without any digestive symptoms and not fulfilling the Rome III criteria for FD, nor past history of systemic diseases, gastrointestinal surgeries, erosion or ulcers seen on previous upper endoscopic examination, who were not taking any medications and did not have milk intolerance. All subjects signed an informed consent and the protocol was approved by the Institutional Committee for Human Research. After fasting periode of 8 hours, all the subject was asked to ingest a nutrient drink (Ultramilk, 0.6 kcal/mL) at a constant rate of 100 mL/min. At 5 - minutes intervals, participants

Table 1. Demographic characteristics of functional dyspepsia patients and healthy controls

Variabel	Patients (N=20)	Healthy controls (N=20)	p
Age (years)	32.35 ± 9.48	31.60 ± 6.60	0.773*
Body weights (kg)	55.45 ± 9.98	60.55 ± 10.63	0.126*
Body height (cm)	161.90 ± 7.59	165.55 ± 9.41	0.185*
Body mass index	21.09 ± 0.9	22.00 ± 2.68	0.312*
Sex			
· Male	12	12	1.000
· Female	8	8	

*t test

scored theirs fullness using a scale graded 0 – 5 (0 = no symptoms; 1 = first sensation of fullness; 2 = mild; 3 = moderate; 4 = severe; 5 = maximum). The subjects were told to stop intake when a score of 5 was obtained.[6,7] Maximum tolerated volume (MTV) was defined as total ingested volume that the test had to be stopped because the FD patients or healthy controls could not tolerate more volume. MTW was set based on a scale grade 5. The results of the different groups were compared using student's t test or Mann-Whitney test for the quantitative variables, according to normal or non-parametric distribution, respectively. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were analyzed. Statistical significance was considered when there was a $p < 0.05$.

RESULTS

The demographic characteristics (age, sex, and body mass index) between dyspepsia patients and healthy subjects were comparable (table 1). Patients with functional dyspepsia had maximum tolerated volume 600 (350–1000) mL and healthy subjects ingested 1375 (1000–1900) mL ($p < 0.001$). Table 2 showed the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) according several cut off point of maximum tolerated volume. Using ≤ 950 mL of maximum tolerated volume as cut off point, sensitivity, specificity, PPV and NPV were 95%, 100%, 100 % and 95%, respectively (table 3).

Table 2. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) according several cut off point of maximum tolerated volume

	Maximum tolerated volume (mL)			
	≤ 650	≤ 750	≤ 850	≤ 950
Sensitivity (%)	55	70	90	95
Specificity (%)	100	100	100	100
PPV (%)	100	100	100	100
NPV (%)	70	77	91	95

Table 3. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) using ≤ 950 mL as the cutoff point

Cut off point	Functional dyspepsia		Total
	Positive	Negative	
≤ 950 mL	19	0	19
≥ 950 mL	1	20	21
Total	20	20	40

Sensitivity: 95%; Specificity: 100%; PPV: 100% ; NPV: 95%

DISCUSSION

Accomodation of the stomach to a meal consists of a relaxation of the proximal stomach, providing the meal with a reservoir and enabling an increase in volume without an increase pressure. Impaired gastric accommodation was present in 40% of the patients.[1] Impaired accommodation of the proximal stomach will lead to an abnormal meal distribution, as observed in the earlier scintigraphic and ultrasound studies, with increased filling of the distal stomach. Especially as the antrum of patients with FD is hypersensitive to distension, impaired accommodation may significantly contribute to the development of meal-induced symptoms. [4] Intragastric barostat method is regarded as the gold standard to which all other techniques need to be compared for validation. Due to patient discomfort and special expertise required, this method never impacted clinical practice except in a few academic, tertiary centers. [8] Recently, a drink test was suggested as a noninvasive alternative to the barostat to detect impaired accommodation.[1,2]

Drink tests are performed using water, *nutridrink* or meat soup. Loza et al. [9] reported that a drinking load test with water or a nutritional beverage can discriminate FD patients from controls. Hjelland et al [10] conducted study to compare three different test meals (water, *nutridrink* and meat soup). They concluded that for non-invasive diagnosis of functional dyspepsia by a rapid drink test in combination with ultrasonography, a meat soup meal is preferable compared to nutridrink or water. In our study, we used nutrient drink (Ultramilk) for detected impaired gastric accommodation, because it was containing fat. Fat ingestion may aggravate dyspeptic symptoms. [1,11] The ideal drinking rate is not known. There is no standard way of performing a drink test rate. [10] We used 100 mL/min, as did Boeckxstaens et al.[12] Others used at a rate 15 mL/min or a water load test where the subjects drank tap water ad libitum over a 5 minutes' period until reaching fullness.[11]

Boeckxstaens et al[12] have reported normal values for nutridrink, which contains 1.5 kcal/mL with 39 % of fat, administered at 100 mL/min. Male significantly consumed more nutridrink (1.405± 81 mL vs 946 ±74 mL) that females in this rapid caloric drinking test. Using the 10th percentile as the lower limit of the normal range, nutridrink volume of < 800 mL for men and < 600 mL for women were considered abnormal. Loza et al [9] reported that the maximal tolerated volume for nutrient drinking test (Nutren) were significantly lower in FD patients compared controls (652 ±168 mL vs 1278 ± 286 mL; p = 0.001). With the volume tolerated by the controls, the percentile 10 was determined as the lower limit for tolerance. Sensitivity and specificity were 0.95 and 0.95. Our study showed that the highest sensitivity and specificity value were reached when the cutoff point of nutrient drink volume was set at < 950 mL. Not all FD patients may tolerate with milk. In the next future, trial may be designed to compare between water and nutrient drinking tests, because water was more tolerated than milk by both patients and controls.

CONCLUSION

A nutrient drinking test at 100 mL/min, can discriminate between FD patients from healthy controls in simple, non-invasive, safe, available manner with high sensitivity and specificity.

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