Paper II

ORIGINAL ARTICLE

Taylor & Francis healthsciences

Drink Tests in Functional Dyspepsia: Which Drink is Best?

I. E. Hjelland, A. P. Ofstad, J. K. Narvestad, A. Berstad & T. Hausken
Division of Gastroenterology, Institute of Medicine, Haukeland University Hospital, Bergen, Norway

Hjelland IE, Ofstad AP, Narvestad JK, Berstad A, Hausken T. Drink tests in functional dyspepsia: which drink is best? Scand J Gastroenterol 2004;39:933–937.

Background: Drinking capacity is often reduced in functional dyspepsia. Drink tests may therefore have diagnostic potential. A simple drink test in combination with ultrasonography was applied in this study, the aim being to find the best drink for this test. **Methods:** On separate days, 10 patients with functional dyspepsia (FD) and 10 healthy controls (C) drank three different test meals (Nutridrink® 150 kcal/100 mL, meat soup 4 kcal/100 mL and water) at a rate of 100 mL/min until maximal drinking capacity. Intragastric volume at maximal drinking capacity was determined using 3-dimensional ultrasonography. **Results:** Drinking capacity ($P < 0.05$) and intragastric volume ($P < 0.01$) were significantly lower in patients than in the controls with the meat soup meal, but not with Nutridrink or water. Gastric emptying distinguished significantly ($P < 0.05$) between patients and controls only with Nutridrink. Gastric emptying of Nutridrink was significantly correlated to the rate by which nausea was induced ($P = 0.02$), while gastric emptying of meat soup was significantly negatively correlated to the rate by which fullness was induced ($P < 0.05$). Receiver operating characteristic (ROC) analysis indicated that optimal discrimination between patients and controls was obtained by the combined test results of symptoms per intragastric volume using meat soup as the test meal. **Conclusion:** For the 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.

Key words: Drinking; dyspepsia; functional gastrointestinal disorders; gastric emptying; stomach; ultrasonography

Ina Elen Hjelland, M.D., Institute of Medicine, Haukeland University Hospital, NO-5021 Bergen, Norway (fax. +47 5597 4973, e-mail. ina.hjelland@med.uib.no)

Patients with functional dyspepsia often experience epigastric pain or discomfort, early satiety, fullness and nausea in relation to meals. Many of these patients have indications of gastric motor or sensory dysfunctions, such as hypersensitivity to distension (1–3), impairment of accommodation to meals (3–5) or delayed emptying (6). The fact that the symptoms often begin during the meal suggests that gastric emptying and gastric distension are mechanisms by which the epigastric discomfort is provoked (7).

The gastric barostat is commonly used to study visceral sensitivity (8) and gastric accommodation (5). The procedure is invasive and unpleasant, and may itself affect gastric motility (9). A non-invasive drink test for assessment of visceral sensitivity and gastric accommodation is a much more convenient diagnostic tool. The test meals used by others have been water or high-caloric drinks. We used a low-caloric meal (Toro® clear meat soup) and combined the test with ultrasonography to study gastric volumes and emptying in addition to the meal-related symptoms (4, 10). In this study, we sought to compare the diagnostic ability of various test meals in our drink test paradigm in persons with and without functional dyspepsia.

Methods

Subjects

Ten patients with functional dyspepsia satisfying the Rome II criteria (M/F 3/7, median age 31 years, range 18–40, mean body mass index (BMI) 23.3 ± 2.8) were recruited from patients sent to our gastroenterology outpatient unit. Ten healthy persons (M/F 4/6, median age 29.5 years, range 19–37, mean BMI 21.2 ± 1.7) served as controls.

Experimental procedure

The participants were examined three times on separate days, between 0800 h and 1000 h after an overnight fast. The interval between the examinations was at least 4 days and a maximum of 1 month. The subjects ingested the test meals in a counterbalanced order, one test meal at each visit. The speed of drinking was 100 mL every minute until maximal capacity. The volume of the stomach was then assessed using 3-

 DOI 10.1080/00365520410003344

dimensional ultrasound. All investigations were done while the individuals were breathing normally, sitting in a chair, leaning slightly backwards at an angle of 120°.

Test meals

Test meals consisted of water, meat soup and Nutridrink®. The water was drawn from the tap, and ingested lukewarm. The meat soup (4 kcal/100 mL) was commercially available (Toro clear meat soup, Rieber & Søn A/S, Bergen, Norway). The soup contained 1.8 g protein, 0.9 g fat, 1.1 g carbohydrate and non-soluble seasoning (0.2 g) per 500 mL. The pH of the soup varied between 5.4 and 5.7, and the osmolarity was 350 mOsm/kgH_2O. The soup was first boiled and then cooled to 37°C. Nutridrink (Nutricia Norway A/S, Oslo, Norway), a high-caloric meal (150 kcal/100 mL) tasting of vanilla, contained 5 g protein, 18 g carbohydrate and 6.5 g fat per 100 mL. Nutridrink was ingested at room temperature. In this way, the test meals were neither too hot nor too cold to be ingested quickly.

Symptoms

Nausea, fullness and epigastric pain were assessed at maximal drinking capacity, using a visual analogue scale (VAS). Scoring was done on a 100-mm unmarked line where a mark at 0 mm expressed ‘no symptoms’ and a mark at 100 mm expressed ‘excruciating symptoms’. The sum of the scores for nausea, fullness and pain at maximal drinking capacity was denoted as the ‘pooled symptom score’. The rate by which a symptom was induced was calculated as symptom score at maximal drinking capacity divided by ingestion time.

Ultrasonography

The applied triplex scanner (System Five Ving Med A/S, Horten, Norway, with a 3.5 MHz curved array probe) allowed visualization of real-time ultrasound images. Three-dimensional (3D) ultrasound imaging was performed using previously validated methods (10, 11).

Gastric emptying is defined as the fraction of the meal emptied from the stomach during the test ((drinking capacity minus intragastric volume) × 100%/drinking capacity).

Intragastric distribution of the meal was assessed by the ratio of proximal to distal volume (12).

Ethics approval

The study was conducted in accordance with the revised Declaration of Helsinki after clearance from the Regional Ethics Committee and written, informed consent from patients and controls.

Statistical analysis

The results are expressed as means ± s (standard deviation) if not otherwise stated. Between groups, comparisons were done by two-factor analysis of variance (ANOVA), adding Bonferroni post-tests when appropriate. Within-group comparisons were performed using one-way ANOVA. Correlation between symptom scores and volumes was determined using the Spearman correlation coefficient. Receiver operating characteristic (ROC) curves were analysed to find the test that best discriminated between patients with functional dyspepsia and healthy controls. The $P \leq 0.05$ (alpha criterion) was chosen as the level of statistical significance using two-tailed tests. All statistical calculations and graphic designs were performed using commercially available software (Graph Pad Prism 3.0 and 4.0 for Windows). None of the subjects dropped out of the study, but because of technical problems, a few volume measurements are missing.

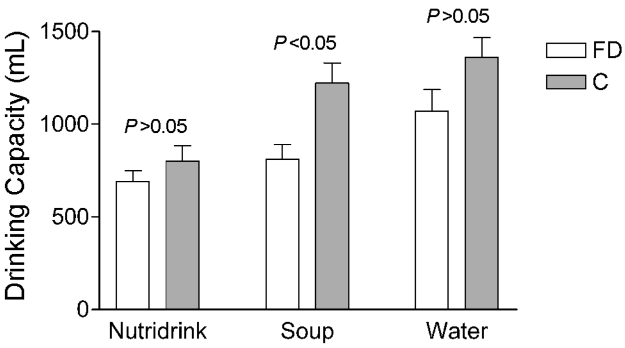

Fig. 1. Drinking capacity (mL, mean ± $s_{\bar{x}}$ (standard error of the mean)) in 10 patients with functional dyspepsia (FD) and 10 healthy controls (C).

Results

Drinking capacity

The patients had significantly lower drinking capacity (830 ± 254 mL) than the controls (1220 ± 349 mL) when they ingested meat soup ($P < 0.05$), but not when they ingested Nutridrink or water (Fig. 1). In general, drinking capacity was highest with water and lowest with Nutridrink (Fig. 1). Ingested volumes of Nutridrink, meat soup and water correlated significantly within patients, but not or barely within the controls (Table I).

Intragastric volumes

Intragastric volumes were significantly lower in patients compared with the controls when they ingested meat soup (533 ± 115 ml and 846 ± 179 mL, respectively, $P < 0.01$),

Table I. Correlation between drinking capacity within patients with functional dyspepsia ($n = 10$) and controls ($n = 10$) when drinking Nutridrink, meat soup and water

Drinking capacity	Functional dyspepsia		Controls	
	r	*P* value	*r*	*P* value
Nutridrink versus meat soup	0.9	0.007	0.7	0.04
Nutridrink versus water	0.9	0.007	0.2	0.5
Meat soup versus water	0.9	0.006	0.4	0.2

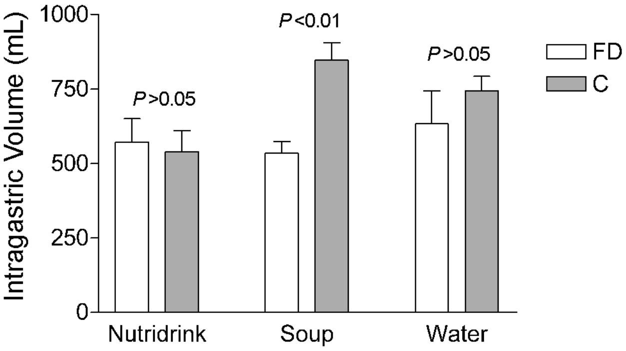

Fig. 2. Intragastric volume (mL, mean ± $s_{\bar{x}}$ (standard error of the mean)) in patients with functional dyspepsia (FD) and healthy controls (C) (FD: $n = 8$, C: Nutridrink $n = 9$, meat soup $n = 9$, water $n = 10$).

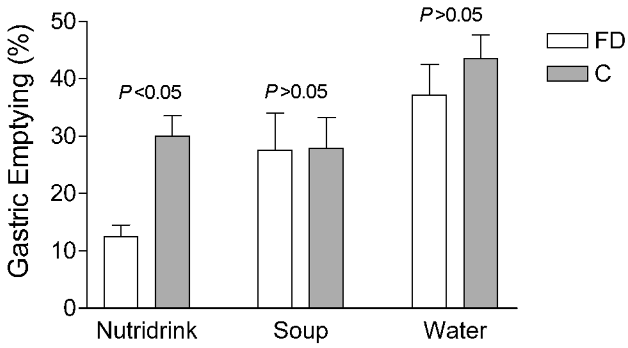

Fig. 3. Gastric emptying (%, mean ± $s_{\bar{x}}$ (standard error of the mean)) in patients with functional dyspepsia (FD) and healthy controls (C) (FD: $n = 8$, C: Nutridrink $n = 9$, meat soup $n = 9$, water $n = 10$).

not when they ingested Nutridrink or water (Fig. 2). There was a trend towards group (patients and controls) by drink (Nutridrink, meat soup and water) interaction ($F = 3.0$, $P = 0.06$), suggesting that the meat soup 'effect' is different in patients and controls.

In the patients, intragastric volumes at maximal drinking capacity were remarkably similar for all three meals ($F = 0.46$, $P = 0.6$). In the controls, however, a significantly lower intragastric volume of Nutridrink than of meat soup was seen ($P < 0.01$).

The ratio of proximal to distal volume of the stomach was not significantly different between patients and controls for any of the test meals. Volume of the distal stomach was not significantly different in patients compared to controls for any of the test meals. Volume of the proximal stomach was significantly larger in the controls than in the patients only when they ingested the meat soup ($P < 0.05$).

Gastric emptying

Gastric emptying was much slower with Nutridrink than with meat soup or water, particularly in the patient group (Fig. 3). The patients had a significantly lower emptying rate of Nutridrink than of water ($P < 0.01$). Controls had a lower gastric emptying rate of meat soup than of water ($P < 0.05$).

Table II. Areas under the ROC curves (AUCs)

Test meal	Measure	AUC	95% CI	*P* value
Meat soup	Intragastric volume	0.96	0.87 to 1.05	0.0015
Nutridrink	Gastric emptying rate	0.94	0.83 to 1.06	0.0021
Meat soup	Pooled symptom score	0.85	0.68 to 1.025	0.008
Meat soup	Ingested volume	0.84	0.65 to 1.03	0.010
Water	Ingested volume	0.73	0.50 to 0.95	0.09
Water	Intragastric volume	0.69	0.39 to 0.98	0.2
Nutridrink	Ingested volume	0.64	0.38 to 0.89	0.3
Water	Gastric emptying rate	0.60	0.31 to 0.89	0.5
Nutridrink	Intragastric volume	0.54	0.25 to 0.84	0.8
Meat soup	Gastric emptying rate	0.51	0.21 to 0.82	0.9

ROC = receiver operating characteristic.

Symptoms and gastric emptying

Pooled symptom score at maximal drinking capacity of meat soup was higher in patients than in controls (174.0 ± 44.0 in patients, 123.0 ± 26.5 in controls, $P = 0.007$). In patients, the rate by which fullness was induced was negatively correlated to gastric emptying of meat soup ($r = -0.73$, $P = 0.046$), while the rate by which nausea was induced was positively correlated to gastric emptying of Nutridrink ($r = 0.81$, $P = 0.02$). In the controls, the rate by which fullness was induced was significantly negatively correlated to gastric emptying of water ($r = -0.85$, $P = 0.006$). The rate by which pain was induced was unrelated to gastric emptying in both patients and controls (results not shown).

ROC analyses

Of all single variables analysed, intragastric volume with the meat soup yielded the highest value for the area under the ROC curve (AUC: 0.96), closely followed by gastric emptying rate with Nutridrink, pooled symptom score with meat soup, and drinking capacity with meat soup (Table II). None of the other tests discriminated significantly between patients and controls.

A combined score calculated for pooled symptoms divided by intragastric volume at maximal drinking capacity with meat soup yielded the highest AUC value (AUC: 0.99, $P = 0.0008$). Neither Nutridrink ($P = 0.6$) nor water ($P = 0.09$) distinguished significantly between patients and controls using this variable (Fig. 4). The results suggest that optimal discrimination between patients and controls by our test paradigm is obtained with meat soup using pooled symptom score per gastric volume unit at maximal drinking capacity as the discriminatory variable.

Discussion

With our meat soup drink test, patients with functional dyspepsia had significantly lower drinking capacity, intragastric volume and more abdominal discomfort than healthy

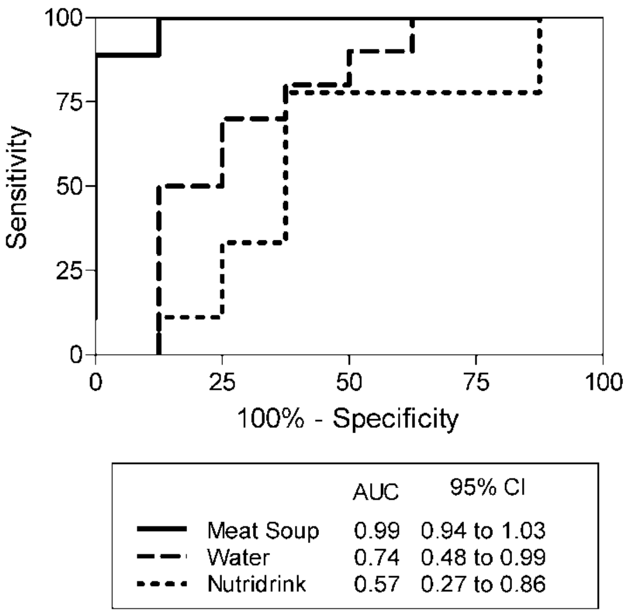

Fig. 4. Receiver operating characteristic (ROC) curves comparing three drink tests (meat soup, water and Nutridrink) using pooled symptom score (mm) per intragastric volume (mL) as the discriminatory variable. The meat soup test reached the highest AUC (area under the curve) value, i.e. this test discriminated best between patients with functional dyspepsia and healthy controls. An AUC of 0.5 indicates that the discriminatory power of the test equals the random draw.

persons. These differences between patients and healthy persons were not significant with either Nutridrink or water as test meals. Gastric emptying was slowest with Nutridrink, particularly in patients. ROC analysis indicated that drinking capacity, intragastric volume and pooled symptom score after drinking meat soup and gastric emptying of Nutridrink discriminated significantly between patients and healthy persons. Drink tests with water had poor discriminatory power regardless of the variable analysed. Pooled symptom score divided by intragastric volume at maximal drinking capacity turned out to be the best variable for distinguishing patients from controls.

Fat ingestion may aggravate dyspeptic symptoms (13). Consistently, Nutridrink, which is rich in fat, generated much more discomfort than meat soup or water in both patients and healthy subjects. In fact, none of the participants was able to drink large amounts of Nutridrink at a rate of 100 mL per minute, and the discriminatory power of the test was poor. In a recent study Tack et al. (14) used the same type of meal, but an ingestion rate of only 15 mL per minute. With this slower drinking rate, the tested persons were able to drink much more than in our test. Hence, a calorie-dense drink like Nutridrink may be useful in a slow drinking test, but not in the rapid drinking paradigm we applied.

We found that the perception of nausea was related to the rate of gastric emptying of Nutridrink, so that the more Nutridrink that emptied into the duodenum, the more nausea that occurred. Gastric emptying is inhibited by long chain fatty acids acting on duodenal chemoreceptors after hydrolysis of triacylglycerols (15). Teleologically, the slow gastric emptying of Nutridrink could be a consequence of enteric reflexes aiming to obviate nausea. With meat soup, the perception of fullness was significantly negatively correlated to gastric emptying, i.e. the less meat soup emptied into the duodenum, the more fullness. The results suggest that fullness is related to distension of the stomach, as also indicated in earlier studies using the gastric barostat (16). Water was well tolerated by both patients and controls, but its fast emptying from the stomach made intragastric volume assessment difficult, contributing to the poor discriminatory power of the test. It thus appears that the ideal test meal should be something between water and Nutridrink. Our meat soup meal seems to satisfy this requirement. Despite its low caloric density (40 kcal/L), meat soup induces fed state motility and empties from the stomach at a rate slow enough to allow accurate ultrasonographic assessment of intragastric volumes. Furthermore, even at a high drinking rate, it seldom provokes nausea.

The gastric accommodation reflex is elicited both by distension of the stomach and by nutrients in the duodenum. Slow drinking of Nutridrink predicted impaired nutrient-induced accommodation fairly well in the study by Tack et al. (14). Our meat soup meal is a weak stimulus of nutrient-induced accommodation (17). Hence, our drink test might primarily be a test of sensitivity to gastric distension and of distension-induced accommodation, and not of nutrient-induced gastric accommodation.

In our patients with functional dyspepsia, intragastric volumes at maximal drinking capacity were remarkably similar regardless of the drink applied. Tack et al. also found that subjects ingested similar volumes of 1.5 and 3 kcal/mL of their test meals (14). Intragastric volume might therefore be an important determinant of drinking capacity. When we applied a score for pooled symptoms per intragastric volume unit at maximal drinking capacity, the meat soup meal was the only test meal that significantly distinguished between patients and controls. Hence, following a meat soup meal, the relationship between intragastric volume and symptoms appears to be abnormal in functional dyspepsia.

There is no standard way of performing a drink test. We used 100 mL/min, as did Boeckxstaens et al. (18). Others, e.g. Jones et al., used a water load test where the subjects drank tap water ad libitum over a 5-min period until reaching fullness (19). Increasing the speed of drinking may provoke more symptoms (20). The ideal drinking rate is not known. For a proper comparison of the various test paradigms, head-to-head comparisons need to be made.

Because we had a small number of patients in our study, there is a risk of type 2 errors. However, the results that did reach statistical significance are interesting, and all the important results received a statistical significance level of $P < 0.01$.

For non-invasive diagnosis of functional dyspepsia by a rapid drink test combined with ultrasonography, the meat soup meal clearly performed better than Nutridrink or water. In the present explorative study, a score relating symptoms to intragastric volume at maximal drinking capacity distinguished excellently between patients and controls. The diagnostic value of this test warrants further testing in prospective clinical studies.

Acknowledgements

This study was funded by a grant from The Norwegian Research Council.

References

1. Coffin B, Azpiroz F, Guarner F, Malagelada J-R. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. Gastroenterology 1994;107:1345–51.
2. Lemann M, Dederding JP, Flourie B, Franchisseur C, Rambaud J C, Jian R. Abnormal perception of visceral pain in response to gastric distension in chronic idiopatic dyspepsia. The irritable stomach syndrome. Dig Dis Sci 1991;36:1249–54.
3. Caldarella MP, Azpiroz F, Malagelada J-R. Antro-fundic dysfunctions in functional dyspepsia. Gastroenterology 2003;124:1220–9.
4. Gilja OH, Hausken T, Wilhelmsen I, Berstad A. Impaired accommodation of proximal stomach to a meal in functional dyspepsia. Dig Dis Sci 1996;41:689–96.
5. Tack J, Piessevaux H, Coulie B, Caenepeel P, Janssens J. Role of impaired gastric accommodation to a meal in functional dyspepsia. Gastroenterology 1998;115:1346–52.
6. Stanghellini V, Tosetti C, Paternico A, Barbra G, Morselli-Labate AM, Monetti N, et al. Risk indicators of delayed gastric emptying of solids in patients with functional dyspepsia. Gastroenterology 1996;110:1036–42.
7. Hausken T, Gilja OH, Undeland KA, Berstad A. Timing of postprandial dyspeptic symptoms and transpyloric passage of gastric contents. Scand J Gastroenterol 1998;33:822–7.
8. Kim DY, Myung SJ, Camilleri M. Novel testing of human gastric motor and sensory functions: rationale, methods, and potential applications in clinical practice. Am J Gastroenterol 2000;95:3365–73.
9. Mundt MW, Hausken T, Samsom M. Effect of intragastric barostat bag on proximal and distal gastric accommodation in response to liquid meal. Am J Physiol Gastrointest Liver Physiol 2002;283:G681–G6.
10. Tefera S, Gilja OH, Olafsdottir E, Hausken T, Hatlebakk JG, Berstad A. Intragastric maldistribution of a liquid meal in patients with reflux oesophagitis assessed by three-dimensional ultrasonography. Gut 2002;50:153–8.
11. Gilja OH, Hausken T, Odegaard S, Berstad A. Monitoring postprandial size of the proximal stomach by ultrasonography. J Ultrasound Med 1995;14:81–9.
12. Gilja OH, Detmer PR, Jong JM, Leotta DF, Li XN, Beach KW, et al. Intragastric distribution and gastric emptying assessed by three-dimensional ultrasonography. Gastroenterology 1997;113:38–49.
13. Feinle C, Rades T, Otto B, Fried M. Fat digestion modulates gastrointestinal sensations induced by gastric distension and duodenal lipid in humans. Gastroenterology 2001;120:1100–7.
14. Tack J, Caenepeel P, Piessevaux H, Cuomo R, Janssens J. Assessment of meal induced gastric accommodation by a satiety drinking test in health and in severe functional dyspepsia. Gut 2003;52:1271–7.
15. Feinle C, O'Donovan D, Doran S, Andrews JM, Wishart J, Chapman I, et al. Effects of fat digestion on appetite, APD motility, and gut hormones in response to duodenal fat infusion in humans. Am J Physiol Gastrointest Liver Physiol 2003;284:G798–G807.
16. Rossi P, Andriesse GI, Oey PL, Wieneke GH, Roelofs JMM, Akkermans LMA. Stomach distension increases efferent muscle sympathetic nerve activity and blood pressure in healthy humans. J Neurol Sci 1998;161:148–55.
17. Undeland KA, Hausken T, Gilja OH, Ropert R, Galmiche JP, Berstad A. Gastric relaxation in response to a soup meal in healthy subjects. Scand J Gastroenterol 1995;30:1069–76.
18. Boeckxstaens GE, Hirsch DP, Van Den Elzen BDJ, Heisterkamp SH, Tytgat GNJ. Impaired drinking capacity in patients with functional dyspepsia: relationship with proximal stomach function. Gastroenterology 2001;121:1054–63.
19. Jones MP, Hoffman S, Shah D, Patel K, Ebert CC. The water load test: observations from healthy controls and patients with functional dyspepsia. Am J Physiol Gastrointest Liver Physiol 2003;284:G896–G904.
20. Hjelland IE, Hausken T, Svebak S, Olafsson S, Berstad A. Vagal tone and meal-induced abdominal symptoms in healthy subjects. Digestion 2002;65:172–6.

Received 23 December 2003
Accepted 12 May 2004