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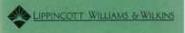
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Effects of carbonated water on functional dyspepsia and constipation

Rosario Cuomo^a, Raffella Grasso^a, Giovanni Sarnelli^a, Gaetano Capuano^a, Emanuele Nicolai^a, Gerardo Nardone^a, Domenico Pomponi^a, Gabriele Budillon^a and Enzo Ierardi^b

Objective The effects of carbonated beverages on the gastrointestinal tract have been poorly investigated. Therefore, this study aims to assess the effect of carbonated water intake in patients with functional dyspepsia and constipation.

Methods Twenty-one patients with dyspepsia and secondary constipation were randomized into two groups in a double-blind fashion. One group (10 subjects) drank carbonated water and the other (11 subjects) tap water for almost 15 days. Patients were evaluated for dyspepsia and constipation scores, and underwent a satiety test by a liquid meal, radionuclide gastric emptying, sonographic gallbladder emptying and colonic transit time, using radio-opaque markers.

Results The dyspepsia score was significantly reduced with carbonated water (before = $7.9 \pm 2.8 \ vs$ after = 5.4 ± 1.7 ; P < 0.05) and remained unmodified after tap water ($9.7 \pm 5.3 \ vs \ 9.9 \pm 4.0$). The constipation score also decreased significantly (P < 0.05) after carbonated water ($16.0 \pm 3.9 \ vs \ 12.1 \pm 4.4$; P < 0.05) and was not significantly different with tap water ($14.7 \pm 5.1 \ vs \ 13.7 \pm 4.7$). Satiety was significantly reduced with

carbonated water (before = 447 \pm 146 kcal vs after = 590 \pm 245; P < 0.01). Gallbladder emptying (delta percent contraction) was significantly improved only with carbonated water (39.9 \pm 16.1% vs 53.6 \pm 16.7%; P < 0.01).

Conclusion In patients complaining of functional dyspepsia and constipation, carbonated water decreases satiety and improves dyspepsia, constipation and gallbladder emptying. Eur J Gastroenterol Hepatol 14: 991–999 © 2002 Lippincott Williams & Wilkins

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Keywords: carbonated water, dyspepsia, constipation, satiety test, gastric emptying, gallbladder emptying, colonic transit time

^aEpatogastroenterologia, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Napoli 'Federico II', Napoli and ^bCattedra di Gastroenterologia, Università degli Studi di Foggia, Foggia, Italy

Correspondence to Dott. Rosario Cuomo, Epatogastroenterologia, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Napoli 'Federico II', Via Sergio Pansini, 5, 80131 Naples, Italy Tel: +39 81 7463892; fax: +39 81 7463892; e-mail: r.cuomo@unina.it

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Introduction

For centuries, carbonated water has been considered capable of relieving gastrointestinal symptoms, including dyspepsia [1,2]. As a consequence of this allegedly therapeutic effect, carbonated water was the only beverage included in the USA pharmacopoeia until 1830 [3]. Today, carbonated beverages are consumed widely, but despite their supposedly therapeutic effects on the gastrointestinal tract [3], the role of carbonated water on gastrointestinal functions has been poorly investigated.

Observations have been made on the use of sparkling water on healthy volunteers [4]. This study did not show any effect on total gastric emptying, but revealed a modified intragastric distribution of both the liquid and solid components of the meal. In clinical practice a low fluid intake is thought to play an important role in constipation, and patients with this problem are frequently advised to increase their daily intake of fluids

[5–8]. Several reports have described a beneficial effect of increased water intake in these patients, even if the efficacy of such treatment has never been demonstrated in controlled studies.

Moreover, patients who usually drink mineral water as self-medication or following medical advice for their gastrointestinal symptoms often suffer from both dyspepsia and constipation, the coexistence of which has led to a postulation of a common cause for both disturbances. Some studies have shown that a slow bowel transit may be responsible for dyspeptic symptoms or may influence gastric emptying; several authors have hypothesized that chronic constipation is part of a more generalized gastrointestinal motor disorder [9–15]. In addition, it has been shown that patients with slow transit constipation often have smaller fasting gallbladder volumes and impaired gallbladder responses [13,16].

The simultaneous presence of functional dyspepsia and constipation can be considered as a good model to test the efficacy of carbonated water intake, which has been suggested to improve movements of the whole gastrointestinal apparatus by acting on smooth muscles [4,8,17,18].

The aim of this study was to assess the effects of a brief period of carbonated water intake, compared to tap water, in patients suffering from functional dyspepsia and constipation.

Patients and methods

Study subjects

Twenty-one patients (15 women [median age 30 years, range 19-64 years] and six men [median age 38 years, range 21-58 years]) complaining of functional dyspepsia and constipation were investigated. Their mean weight was 64.5 ± 12.4 kg and their mean height was 164.7 ± 8.7 cm (mean \pm standard deviation). Patients had experienced either pain or discomfort located in the upper abdomen for at least 12 weeks in the 12 months prior to the study; this was defined as early satiety, postprandial fullness, bloating and nausea [19]. Patients were also evaluated for belching, vomiting and epigastric burning. All recruited patients complained also of persistently difficult, infrequent or seemingly incomplete defaecation for at least 12 weeks in the 12 months prior to the study [20]. Subjects were enrolled consecutively after a common diagnostic routine that included gastroscopy, barium enema and/or colonoscopy to rule out organic diseases such as peptic ulcer, gastric cancer, oesophagitis, inflammatory bowel diseases and colonic neoplasms. Patients with a prevalence of digestive symptoms associated with other gastrointestinal syndromes (irritable bowel or gastrooesophageal reflux) were excluded from the study.

Helicobacter pylori levels were assessed on gastric biopsies using the urease test. Ultrasonography of the upper abdomen was normal in all patients. None had undergone abdominal surgery or had evidence of any systemic disease known to affect gastrointestinal motility. Common laboratory tests were normal in all patients. All drugs potentially affecting gastrointestinal motility were discontinued at least 1 week before the study.

All subjects gave their written, informed consent before the study. An expert of the National Health Office verified the study protocol.

Study design

The study was designed as a double-blind, randomized protocol. The protocol schedule is reported in Figure 1. Subjects were randomized, in a double-blind fashion, into two groups: one given carbonated water (Uliveto water; Terme Uliveto, Pisa, Italy) and the other tap water (1.51 per day) for at least 15 days and until the end of the study. At recruitment, patients were informed that the intention of this experimental study was to compare two different mineral waters, without disclosing the characteristics of each, and particularly the fact that one was carbonated water. The patients could not exchange comments among themselves because each was studied on different days and the examiners who performed the tests were instructed not to ask the patients any information on the type of treatment being administered. Moreover, the two types of water were put in similar 1.5 l bottles and numbered with a key that was decoded only at the end of the study. To confirm the volumes ingested each day and to ensure that they were comparable between the groups, patients were instructed to use a new bottle every day and, in case of a greater need for water, to use a new bottle, appropriately coded, only until midnight. Participants were asked to return the empty bottles as well as those with any remaining water to the examiners, who had to verify the amount of water drank every day.

The observers administering the questionnaires or those performing the tests did not know which water was being used by whom; only RC and GB knew the characteristics of each water and they were not directly involved in the evaluation of the symptom scores and tests. The key list was decoded and analysed only after having collected all the data. In addition, at the end of the analysis each single patient was questioned on the taste of the water they had consumed.

The chemical composition of the two types of water was evaluated by different methods (Table 1).

At the end of the study, the subjects were divided into

Table 1 Chemical composition of the carbonated and tap waters

	Carbonated		
	water	Tap water	Analysis
Hardness (F°)	62.5	28.8	Т
Total dissolved solids (mg/l)	986	241	W
Electrical conductibility (μδ)	1388	651	EC
pH	6.00	7.37	рН
Alkalinity (ml HCl 1N/l)	11.3	4.83	Т
Free carbon dioxide (mg/l)	820	1.2	T
Li ⁺ (mg/l)	0.2	trace	LC
Na+ (mg/l)	113.7	28.7	LC
K ⁺ (mg/l)	11.6	2.2	LC
Mg ⁺⁺ (mg/l)	29.8	11.6	LC
Ca++ (mg/l)	202	97	LC
F- (mg/l)	1.40	0.39	LC
CI ⁻ (mg/l)	121.4	48.9	LC
NO ₃ - (mg/l)	5.90	11.1	LC
SO ₄ - (mg/l)	151	32	LC
SiO ₂ (mg/l)	7.0	trace	W

T, titimetric; W, weighing; EC, electrical conductibility; pH, pHmetric; LC, liquid

two groups, one assigned to drink carbonated water (10 patients; seven women; height 168 ± 11 cm; weight 66 ± 16 kg) and the other tap water (11 patients; eight women; height 162 ± 6 cm; weight 60 ± 8 kg).

Before and after the treatment period, patients underwent biochemical analyses (glucose, urea, creatinine, calcium, magnesium, sodium, potassium and chlorine levels), and were also evaluated for dyspepsia and constipation scores, satiety test, radionuclide gastric emptying, sonographic gallbladder emptying and colonic transit time with radio-opaque markers (Fig. 1).

Symptoms score questionnaires Dyspepsia score

Each patient completed a symptoms questionnaire that assessed belching, bloating, early satiety, epigastric pain and burning, nausea, postprandial fullness and vomiting [21,22]. Each symptom except vomiting was graded 0-3, according to its influence on the patients' usual activities: 0 = absent; 1 = mild (not influencing usual activities); 2 = moderate (diverting from, but not urging modifications of, usual activities); and 3 = severe (markedly influencing usual activities so as to urge modifications). Based on a method previously described, the inclusion criterion was a total symptom score of ≥ 3 , with at least one of the eight dyspeptic symptoms graded ≥ 2 [23]. Total score ranged from 3 to 24.

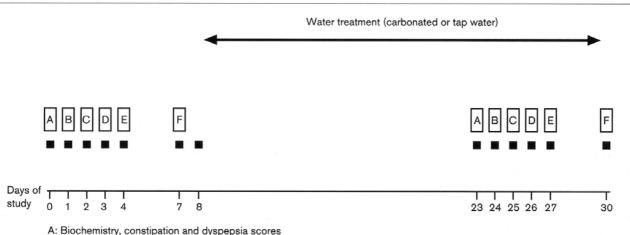
Constipation score

The standardized questionnaire addressed seven items, including frequency of bowel movement, difficulty (evacuation effort or sensation of anorectal obstruction), completeness (feeling of completion), pain (abdominal pain), straining time (minutes in lavatory per attempt), assistance (laxatives, digital or enemas) and number of unsuccessful attempts to evacuate for 24 h [24]. Patients were recruited when two or more of these symptoms, excluding bowel movement frequency, were present in more than one out of four episodes of defaecation; the inclusion criterion for frequency of bowel movements was more than three defaecations per week. Total scores ranged from 4 to 26.

Satiety testing

All subjects underwent a test to quantify the occurrence of meal-induced satiety, which was performed according to a method previously described [21,22]. Briefly, a peristaltic pump filled one of two beakers at a fixed rate of 10 ml/min with a vanilla-flavoured calorific (1.5 kcal/ml) liquid meal (Nutridrink; Nutricia N.V., Zoetermeer, Holland). The meal was kept at a constant temperature and the test was performed after an overnight fast, at the same time (approximately 11 a.m.). The subjects were asked to drink at any time, as much as they wished, maintaining intake at the filling rate, thereby alternating the beakers as they were filled and emptied. At 5-min intervals, they were asked to score their feelings of satiety using a simple rating scale that combined verbal descriptors on a scale grade of 0-5





- B: Early satiety test, radiopaque markers (colonic transit time)
- C: Radionuclide gastric emptying, radiopaque markers (colonic transit time)
- D: Sonographic gallbladder emptying, radiopaque markers (colonic transit time)
- E: X-ray (day four colonic transit time)
- F: X-ray (day seven colonic transit time)

Study design schedule for tests performed on patients in the carbonated water group and tap water group.

(1 = threshold; 5 = maximum satiety). Participants were instructed to stop drinking when a score of 5 was reached.

Gastric emptying study

After an overnight fast, all patients underwent a gastric emptying test by a single-labelled radionuclide meal. Immediately after ingestion of the meal (a whole egg labelled with 20 Mbq of Tc-99 human serum albumin micro colloid), the patients were positioned in front of a gamma camera (Siemens Orbiter, Siemens Medical Systems Inc., Hoffman Estates, Illinois, USA) fitted with a low-energy, all-purpose collimator using a $140 \text{ keV} \pm 20\%$ window. Images were collected every 30 s using 128 × 128-word matrices in anterior and posterior views every 10 min for 1 h, then every 15 min for 1 h, followed by every 30 min for 1 h. Anterior and posterior gastric counts were obtained from manually drawn regions of interest. Three parameters were measured: half-emptying time (t1/2; min), emptying rate (percentage of emptying per min) and lag phase (min). The lag phase was considered to be the time required for redistribution of food particles from the gastric fundus to maximal antrum accumulation [25-27].

Colonic transit time

Total colonic transit time was assessed as previously described [28]. Three sets of distinctive markers were ingested at the same time on three subsequent days. Abdominal X-rays were obtained on days four and seven at the same time as the pellets were ingested. Patients with markers still present on day seven underwent an additional abdominal X-ray on day 10. All subjects were asked to maintain their usual diet for the duration of the study and were prescribed a daily fibre supplement (10 g methyl cellulose). The markers were readily identified and counted on the abdominal X-ray films. Colonic transit time, expressed as the number of hours taken for the markers to pass through the entire colon, was calculated using the formula previously described [28].

Gallbladder emptying

Subjects were evaluated at 11 a.m. after an overnight fast. Ultrasound images were used to calculate gallbladder basal volume by the ellipsoid method [29]. Gallbladder diameters can be easily evaluated by real-time ultrasonography by means of two perpendicular scans. The first is made parallel to the main gallbladder axis and corresponds to the longitudinal and anteroposterior diameters. A scan made perpendicular to this plane allows measurement of the transverse diameter. These measurements were used to calculate gallbladder volume before and 30 min after the ingestion of 250 ml milk.

Data analysis

For meal-induced satiety testing, the amounts of kilocalories (kcal) ingested until the occurrence of maximum satiety (a score of 5) were calculated as previously reported [21,22].

A paired *t*-test was performed using GraphPad InStat version 3.05 for Windows 98 (GraphPad Software, San Diego, California, USA) to evaluate the differences in each group before and after water treatment.

Differences were considered significant at the 5% level. All data are given as means \pm standard deviation.

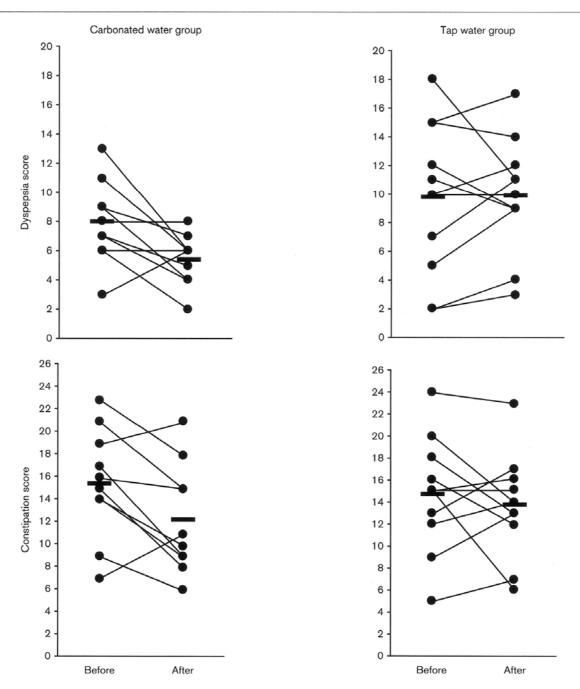
Results

The chemical composition of the waters used in this study are shown in Table 1; a higher level of mineral compounds was found in the carbonated water than in the tap water. In particular, the carbonated water contained a markedly greater amount of free carbon dioxide, five times as much sodium, potassium and sulphate, three times as much fluorine and chlorine, and twice as much magnesium and calcium.

No difference was observed between patient groups in either anthropometric characteristics or in biochemical parameters before and after water treatment (data not shown). *Helicobacter pylori* infection was present in three patients from the carbonated water group and two patients from the tap water group.

Nine patients in the carbonated water group reported that the water had a clear sparkling taste and only one said that it produced a moderate sensation. None of the patients in the tap water group reported any particular taste. The consumption of water was similar in the two groups (carbonated water: 1.6 ± 0.11 vs tap water: 1.7 ± 0.2 l; not significant).

Figure 2 shows the total dyspepsia and constipation scores before and after the water treatments. The dyspepsia score was significantly reduced in the patients who drank carbonated water (before: $7.9 \pm 2.8 \ vs$ after: 5.4 ± 1.7 ; P < 0.05). The treatment markedly improved the symptoms in seven patients, while two reported no variation and one worsened. Dyspepsia worsened in about 60% of patients who drank tap water, and the mean value of the dyspepsia score in this group remained unmodified before and after the water treatment $(9.7 \pm 5.3 \text{ vs } 9.9 \pm 4.0)$. Of all the dyspeptic symptoms, only early satiety significantly decreased after treatment with carbonated water $(1.4 \pm 0.9 \text{ vs } 0.5 \pm 0.9; P < 0.05)$, while belching increased (1.0 \pm 1.0 vs 1.4 \pm 0.8; P < 0.05). The constipation score also decreased significantly in eight patients after carbonated water treatment (16.0 \pm 3.9 vs 12.1 ± 4.4 ; P < 0.05), while it increased in six patients



Dyspepsia and constipation scores before and after each water treatment. Means are indicated by a short horizontal line in each column of data.

treated with tap water (14.7 \pm 5.1 vs 13.7 \pm 4.7). However, no substantial modification was found in colonic transit time after the water treatments in either group. A decreasing trend in gastric emptying parameters (half time, lag phase and emptying rate) was instead observed in both groups after water treatments (Table 2).

Early satiety, measured by the satiety test, was signifi-

cantly reduced after the treatment with carbonated water (before: 447 ± 146 kcal vs after: 590 ± 245 kcal; P < 0.01). In particular, eight patients (80%) clearly improved, while two had the same calorie intake as before the treatment (Fig. 3). In contrast, the patients on tap water showed a trend to reduction of ingested calories during the satiety test after the water treatment, compared with basal condition (473 \pm 220 vs

	Carbonated water group		Tap water group	
	Before	After	Before	After
Colonic transit time (total transit; h)	40.8 ± 18.0	35.6 ± 10.2	56.4 ± 38.2	53.6 ± 30.6
Gastric emptying (half time; min)	$\textbf{76.6} \pm \textbf{12.6}$	68.4 ± 16.1	$\textbf{94.8} \pm \textbf{22.4}$	78.9 ± 21.4
Rate (% per min) Lag phase (min)	$\begin{array}{c} 0.64 \pm 0.14 \\ 19.9 \pm 7.7 \end{array}$	$\begin{array}{c} 0.70 \pm 0.16 \\ 16.2 \pm 7.0 \end{array}$	$\begin{array}{c} 0.57 \pm 0.14 \\ 21.1 \pm 13.9 \end{array}$	$\begin{array}{c} 0.64 \pm 0.14 \\ 16.2 \pm 12.7 \end{array}$

Table 2 Colonic transit time and gastric emptying parameters in the two treatment groups

 432 ± 100). Six patients in this group (54%) also showed an improvement - albeit moderate - in their early satiety.

Figure 4 shows gallbladder emptying values expressed as delta percent contraction before and after a milk meal. Only the carbonated water group showed a significant improvement in mean value of gallbladder emptying efficiency (39.9 ± 16.1% vs 53.6 ± 16.7%; P < 0.01). In the tap water group, only five subjects (45%) showed an increase in delta percent contraction after a milk meal (35.7 \pm 18.7% vs 41.3 \pm 20.5%; not significant).

Discussion

The chemical and physical analyses of the two waters utilized in this study showed that the carbonated water had a higher mineral content than the tap water. The sparkling sensation reported by the patient who drank carbonated water was caused by the free carbon dioxide content. It is a matter of speculation whether the mineral and carbon dioxide content of the carbonated water explain its effect.

The absence of modifications in the serum biochemical parameters after water treatment in both the groups studied shows that neither type of water altered the patients' metabolic homeostasis.

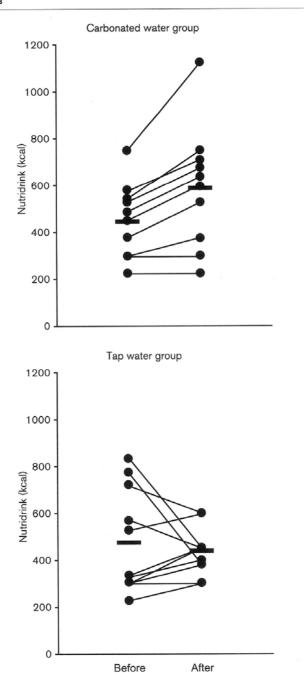
In this study we observed a trend, although not a significant one, toward an increased gastric emptying rate and a decreased colonic transit time after treatment with either carbonated or tap water. However, the patients treated with carbonated water showed significantly better dyspepsia and constipation scores than those who drank tap water. Hence, treatment with carbonated water improves dyspepsia and constipation symptoms without clearly improving gastric and intestinal function. In addition, this study shows that patients had a better gallbladder function and decreased sensation of satiety during a liquid meal test after treatment with carbonated water.

Based on experimental data from another study, the presence of carbon dioxide in the carbonated water could explain the decrease in symptom severity. The sensation

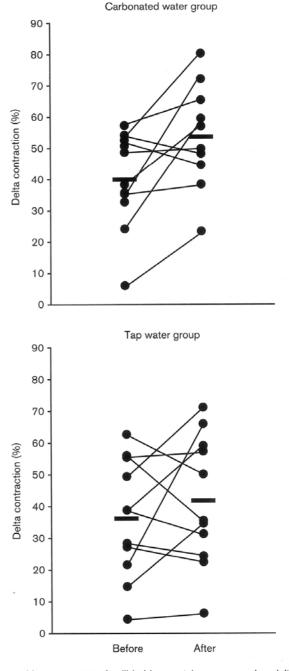
produced by carbonated beverages has been attributed to a chemical excitation of the nociceptors in the oral cavity via the conversion of carbon dioxide to carbonic acid, through a reaction catalysed by carbonic anhydrase [30]. The administration of carbonated water to animals has shown that excitation of the trigeminal neurons on the tongue occurs, which is involved in signalling oral irritation. This stimulation transmits a signal to the dorsal vagal complex in the brain stem, which is synaptically connected with visceral sensory neurons and through which it establishes extensive connections [31]. The proximity with the sensory neurons might modify visceral sensitivity. It is possible that even a small amount of carbon dioxide is able to elicit this mechanism, thus explaining the improvement in the dyspepsia and constipation scores after treatment with carbonated water. However, if such mechanisms were involved, the same effect would also be found with other types of water or beverages containing carbon dioxide.

The increased consumption of the liquid meal in the satiety test and the decrease in early satiety severity as part of an overall improvement in the dyspepsia score in patients treated with carbonated water, along with reports in the literature, suggest other possible hypotheses. Firstly, mineral water has been shown to have a stimulating effect on gastric emptying and on the interdigestive cyclic motor activity of the gastroduodenal tract in patients with functional dyspepsia and delayed gastric emptying [32]. On the other hand, Kobashi et al. [33] observed that the administration of water to rats inhibited the motility of the distal stomach, and that the degree of inhibition was negatively correlated with sodium concentration. They also found that intragastric pressure in the proximal stomach was reduced in response to the administration of water. In our study, we observed an overall decrease in gastric emptying time in both groups of patients (carbonated and tap water), but failed to find any significant difference between pre- and post-treatment levels in either group. Hence, the increased intake in nutritive liquids at the end of a satiety test could be associated with a possible decrease in pressure in the proximal stomach [22]. In addition, it is not unreasonable to hypothesize that the increased frequency of belching experienced by the patients treated with carbonated





Satiety test scores (kcal ingested) before and after each treatment, determined by administration of a standardized liquid meal. Means are indicated by a short horizontal line in each column of data.



Sonographic assessment of gallbladder emptying, expressed as delta contraction after a milk meal, measured before and after each water treatment. Means are indicated by a short horizontal line in each column of data.

water, which is triggered by the induction of transient lower oesophageal sphincter relaxations, could decrease proximal stomach pressure [34].

Pouderoux et al. used a radiolabelled meal in their study, which showed that sparkling water did not alter gastric emptying, but did induce modifications in the intragastric distribution of the meal related to gas distension of the proximal stomach [4]. This effect was transient and limited to the duration of the lag phase. In our study we did not observe any changes in lagphase parameters, but this discrepancy may depend on the study methodology adopted. Pouderoux et al. explored gastric emptying simultaneously with carbonated water intake, while we performed the test after a

period of water treatment. This suggests that the increased intake of liquid meal during the satiety test and the decrease in early satiety in the symptom score of dyspeptic patients may be related to a constant stimulus of the gastric fundus due to gas distension by carbon dioxide.

With reference to constipation, we did not observe a clear effect of water treatment on colonic transit time. This may be due to the lack of changes in the patients' dietary habits, since we only prescribed a fibre supplement during the colonic transit evaluation and not in the treatment period. Previous data showed that only the association of increased fibre and water intake can improve colonic transit time [35,36]. Hence, increasing water intake alone is not enough to ameliorate colonic transit time.

Our study showed improved gallbladder contraction with carbonated water treatment. It has been hypothesized that the presence of sulphate in mineral waters may increase osmotic pressure; this could be responsible for the stimulation of bile flow and pancreatic exocrine secretion as well as the regulation of gastrointestinal motility disorders [37]. Moreover, a direct effect of calcium has been hypothesized on gallbladder smooth muscle contraction. This is supported by the higher concentrations of sulphate and calcium (fourfold and two-fold, respectively) in the carbonated water compared to tap water. However, if an effect of calcium or sulphate is to be supposed, it is independent of any serum modifications due to these elements.

In conclusion, the major finding of this double-blind study is the efficacy of carbonated water to decrease early satiety and improve symptoms of dyspepsia and constipation. Furthermore, there was evidence of improved gallbladder emptying after almost 15 days of carbonated water intake. Whether these effects are partly due to the carbon dioxide or mineral content of this water remains to be clarified.

Acknowledgements

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Publisher Caroline Black (cblack@lww.co.uk)

Senior Production Editor Ian Burgess (iburgess@lww.co.uk)

Editorial Assistant Saila Shah

Information for contributors: Papers submitted for publication should be sent to Saila Shah, European Journal of Gastroenterology & Hepatology, Central Middlesex Hospital, Department of Gastroenterology, Acton Lane, Park Royal, London NW10 7NS, UK. Tel: +44 (0)20 8453 2777; fax: +44 (0)20 8961 1317; e-mail: sshah_ejgh@compuserve.com

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