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**BENEFICIAL EFFECTS OF BICARBONATE-RICH
MINERAL WATER PLUS *L. REUTERI*
ON GASTROINTESTINAL DISORDERS**



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Effect of treatment with a mineral water rich in calcium bicarbonate plus *L. reuteri* on gastric emptying in dyspepsia

G. MERRA ¹, V. GERARDI ², F. MANGIOLA ², A. CAPACCI ², M. CANDELLI ¹, F. FRANCESCHI ¹
A. GASBARRINI ², G. GASBARRINI ^{2,3}

Aim. Dyspeptic syndrome has always been a health problem of great interest due to the fact that it is so widespread. This interest has then become even greater in recent years, due to an increase in pharmaceutical expenditure. In a significant percentage of dyspeptics, slowed gastric emptying is the main symptom. Treatments based on acid secretion inhibitors and prokinetics are often inefficient in eliminating or reducing symptoms. Treatments based on mineral water are often recommended and prescribed for this type of pathology. This study aims to assess the effect of the administration of a mineral water rich in calcium bicarbonate (Uliveto) plus *L. reuteri* on the gastric emptying of solids and on symptoms reported by a group of patients suffering from functional (non-organic) dyspepsia.

Methods. Twenty patients suffering from primary dyspepsia and 10 healthy (non-dyspeptic) controls were studied. All subjects were supplemented with 1.5 L/day of bicarbonate-rich mineral water (Uliveto; fixed residue at 180 °C = 860 mg/L, bicarbonate HCO₃⁻ = 650 mg/L, calcium Ca⁺⁺ = 169 mg/L) and *L. reuteri* (in form of tablets, at a dose of 10⁸ CFU, twice daily) for 10 days. Before and after the supplementation period, each subject involved in the study was subjected to a gastric emptying assessment by means of a ¹³C octanoic acid breath test. A clinical score was also used to assess changes seen in symptoms.

Results. In terms of mean ± standard deviation results, dyspeptic subjects showed a clear improvement in emptying parameters (T_{1/2} and T_{lag}) after treatment, in addition to a reduction of average symptom scores.

Conclusions. Treatment based on oligomineral water plus probiotic *L. reuteri* would appear to improve emptying of solids in dyspeptic patients. Medium-long term longitudinal studies are required to verify the persistence of this effect.

KEY WORDS: Dyspepsia – Gastric emptying – Breath test – Mineral water – Calcium bicarbonate.

Dyspepsia is one of the main indications for specialist appointments and blood-chemical and instrumental

¹Emergency Department
"A. Gemelli" General Hospital
"Sacro Cuore" Catholic University
Rome, Italy

²Department of Gastroenterology
"A. Gemelli" General Hospital
"Sacro Cuore" Catholic University
Rome, Italy

³"Ricerca in Medicina" Nonprofit Foundation
Rome, Italy

examinations in the Western world.¹ The main problem in clinical terms concerns the treatment of the functional or non-organic form, which is defined as a disturbance affecting the upper quadrants of the abdomen only, with no specific pathology that can be detected by endoscopy.² Prevalence of dyspepsia in the general population is estimated as ranging from 14% to 41%.³⁻⁵

In Italy, almost 50% of dyspeptic subjects consulting specialised gastroenterology or endoscopy centres suffer from functional (idiopathic) dyspepsia.⁶

In a certain percentage of these cases, the clinical picture is linked to slowed emptying^{7,8} and an alteration of gastroduodenal motor activity.^{9,10} The link between functional dyspepsia and *Helicobacter pylori* infection is not yet clear⁶ and the elimination of this infection does not always result in an improvement of the symptoms.^{11,12}

Treatment of functional dyspepsia is generally based on the cyclical use of gastric acid secretion inhibitors and drugs acting on gastroduodenal transit. However, the therapeutic effect of these treatments is often unsatisfactory and transitory. Also, a prolonged use of these drugs has the potential to cause side effects. Very often dyspeptic patients are asked to follow specific dietary regimens. However, as of today, there is no evidence that any particular diet can efficiently improve the symptoms of dyspepsia.

Corresponding author: G. Merra, Emergency Department, "A. Gemelli" General Hospital, "Sacro Cuore" Catholic University, Largo Gemelli 8, 00168 Rome, Italy. E-mail: merra@libero.it

One issue that is currently a matter of intense debate in Italy is whether treatment with mineral water, so widespread throughout our country, as indeed also in France and Germany, may play a role in treating functional problems involving the gastrointestinal tract as dyspepsia. There is a significant quantity of existing literature on the topic²³ but unfortunately it is almost all from publications that do not go beyond the national boundaries of a single country. Furthermore, there is a lack of longitudinal observational studies that can acknowledge treatments with thermal water to have the characteristics of social health 'investment', thereby allowing for their recommendation and prescription by medical providers. It is only in recent times that data on this matter has been reported, such that it would lead us to believe that this kind of treatment may play a role in health strategies in the gastrointestinal field.¹³ In drinking water treatment it is assumed that the therapeutic effect is influenced by the specific ion and mineral content of the water administered.

This study therefore aimed to assess the effect of the administration of calcium bicarbonate-rich mineral water (Uliveto) plus *L. reuteri* on the gastric emptying of solids and on symptoms reported by a group of patients suffering from functional (non-organic) dyspepsia.

Materials and methods

Fifteen patients suffering from idiopathic dyspepsia were recruited. An organic cause (digestive or bilious) of the symptoms was first excluded for all patients by means of esophago-gastro-duodenoscopy and abdominal ultrasound. Dyspeptic patients with markedly slowed gastroduodenal transit assessed by means of an octanoic acid test were selected. This choice was made because our previous experience had shown us that the action of mineral waters with various concentrations of saline content was mainly seen in dyspeptic subjects with slowed gastric emptying. All subjects suffering from alterations of gastric and duodenal motility (neuromyopathies, scleroderma, diabetes) were excluded, as were those suffering from organic or functional diseases of the intestine (pyloric stenosis, peptic ulcer, gastroparesis, pseudo-obstruction) and those who had previously undergone surgery of the gastrointestinal tract. All subjects who regularly took drugs that could affect gastrointestinal function (proton pump inhibitors, H₂-antagonists, octreotide, prokinetics, anticholinergics) and those infected by *H. pylori* were also excluded.

Symptoms were assessed by assigning a score from 1 to

3 (minor, moderate and severe, respectively) to each of the following symptoms: epigastric pain, epigastric weight, slow digestion, sense of early satiety, nausea, vomiting. Each patient was therefore assigned a total score, calculated by adding up the individual scores. The subjective assessment on the part of each patient of their own state of wellbeing was then performed by means of an analogue scale from 1 to 10, where 10 represented maximum wellbeing, and 1 the minimum.

The study participants were supplemented with 1.5 L/day of calcium bicarbonate-rich mineral water (Uliveto; fixed residue at 180 °C = 860 mg/L, bicarbonate HCO₃⁻ = 650 mg/L, calcium Ca⁺⁺ = 169 mg/L) and *L. reuteri* (in form of tablets, at a dose of 10⁸ CFU, twice daily) for 10 days. The water was contained in 1 L plastic bottles. Administration of water continued for 10 days for each patient.

Before treatment and immediately afterwards, each patient's gastric emptying of solids was assessed by means of the ¹³C octanoic acid breath test. For the test 91 mg of ¹³C octanoic acid (¹³C = 99%) were dissolved in an egg yolk. An omelette was therefore prepared and served to the patient along with 50 g cured ham, 150 mL fruit juice and two slices of white bread (60 g). The meal was consumed in 10 minutes. Air samples were collected at time 0 (T₀, before eating) and every 15 minutes thereafter for the next 4 hours. Marked CO₂ (¹³C/¹²C) was separated from the other respiratory gases using a mass spectrometer (Finningan™ MAT, Thermo Electron Corp., Waltham, MA, USA). A ¹³C excretion curve was drawn for each patient. The non-linear regression analysis and the method of least squares were used to analyse the following parameters for each patient's breath tests: T_{1/2}, *i.e.* the time required for the stomach to empty 50% of the standard meal administered, and T_{lag}, *i.e.* the time needed to cause the first propulsive waves and therefore the emission of the bolus into the duodenum.

During the treatment period, each patient was subjected to a standard dietary regimen and consumed 5 meals a day with restricted calorie content.¹⁴

Compliance with mineral water drinking was verified on the basis of the patients' daily diary and of the returned (full or empty) bottles. Compliance with the diet was checked by means of a 'two-day record' system (a questionnaire concerning the consumption of food and drinks on a weekday and on one day of the weekend at the patient's choice).¹⁴ The patients were assessed before starting the treatment (T₀), on day 8 (T₈), and then 30 days after completion of the treatment (T₃₀) to assess the clinical effects at a later stage.

	PRE-TREATMENT	POST-TREATMENT	p
T _{1/2}	119.7 ± 9.9*	91.0 ± 8.7*	<0.05
T-lag	82.4 ± 14.7*	60.4 ± 5.9*	<0.001

*Student's t-Test for paired data

Table I.—¹³C octanoic acid breath test in dyspeptic patients before and after treatment.

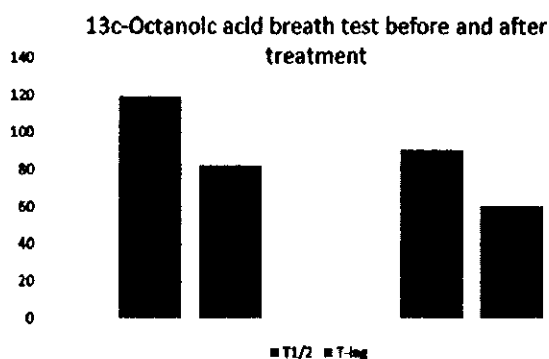


Figure 1.—¹³C octanoic acid breath test in dyspeptic patients before and after treatment.

Ten control subjects (non-dyspeptic, absolutely symptom-free, from the medical staff) were subjected to the same supplementation with assessment of gastric emptying.

The results in relation to the octanoic acid test and clinical scores were expressed as a mean ± standard deviation and subjected to statistical analysis by means of the Student's t-test for paired data. A difference of $p < 0.05$ was considered significant.

Results

The analysis concerned 30 subjects: 20 dyspeptic patients and 10 controls.

All of the 30 subjects analysed showed good compliance levels both with regard to water consumption and to the dietary regimen. All dyspeptic patients had a slowed gastroduodenal transit at the baseline, expressed by a T_{1/2} above 98 (119.7±9.9) and a mean T_{lag} of 82.4±14.7.

An associated reduction of T_{1/2} and T_{lag} was observed in 8 dyspeptic patients after 8 days of treatment (T_{1/2} = 91.0±8.7; T_{lag} = 61.4±5.9). The difference between the mean values was found to be statistically significant (Student's t-test for paired data) (Table I, Figure 1).

	PRE-TREATMENT	POST-TREATMENT	p
T _{1/2}	80.1 ± 8.2	78.6*	ns
T-lag	44.3 ± 17.8	39.7 ± 114.4*	ns

*Student's t-Test for paired data

Table II.—¹³C octanoic acid breath test in controls before and after treatment.

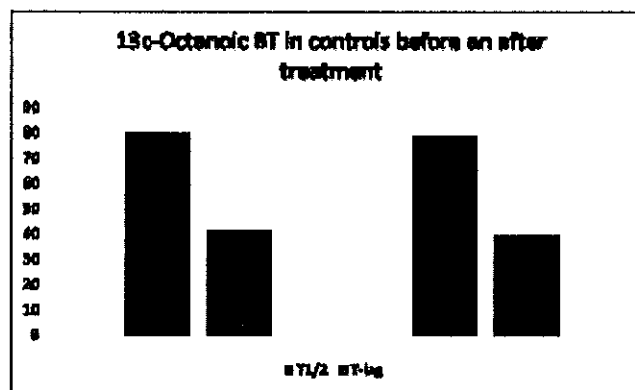


Figure 2.—¹³C octanoic acid breath test in controls before and after treatment.

No differences were seen in the control group (Table II, Figure 2).

Before treatment, the dyspeptic patients had a mean total score of 14.9±4.2. After 8 days of treatment, the mean total score was 9.8±5.6. This improvement continued 30 days later, with a mean total score of 10.5±5.1 (Table III, Figure 3). Assessment by means of the analogue scale also showed an approximate 30% reduction on the initial value at the end of the treatment. This reduction persisted at 30-day follow-up.

Four dyspeptic patients and all subjects of the control group reported a slight increase in the frequency of defecation during the week of treatment. In three subjects (two dyspeptics and one control), this phenomenon continued for approximately 10 days after treatment completion. Three dyspeptic patients and one control reported occasional widespread abdominal pain during the period of treatment; reportedly, this phenomenon persisted for a few days after treatment completion. In no case was it necessary to interrupt or delay treatment. No changes in blood pressure, heart rate, serum levels of Na, Cl, K, Ca and Mg and urine specific gravity were recorded for any of the subjects involved in the study.

	T0	T8	T30
TOTAL SCORE (mean ± SD)	14.9 ± 4.2*	9.8 ± 5.6*	10.5 ± 5.1*

* $p < 0.05$ for T0 vs T8 and for T0 vs T30

Table III.—Changes in dyspepsia score at T₀, T₈ and T₃₀.

Discussion

The ¹³C octanoic acid breath test is a definitely valid test of the solid emptying function.¹⁵ This test meets the requirements for measuring gastric emptying time: octanoic acid is a medium-chain fatty acid which, because of its lipophilic nature, can be easily dissolved in egg yolk and thus absorbed by the intestinal wall, reaching the liver unaltered through the portal blood. In the liver, it undergoes mitochondrial oxidation, which is not affected by cytochrome P450, nor by the presence of carnitine. The carbon dioxide thus produced, marked with ¹³C, is exchanged at a pulmonary level and then eliminated through exhalation. The appearance of ¹³C in the breath after the oral administration of ¹³C octanoic acid therefore depends exclusively on the speed at which the egg yolk in the duodenum is gastrically emptied. The other metabolic stages (absorption, oxidation) do not affect the respiratory excretion rate of ¹³C.¹⁵

The results of this study have shown that a daily consumption of calcium bicarbonate-rich mineral water (Uliveto) and *L. reuteri* improves gastric emptying in patients suffering from primary dyspepsia associated with a slowed gastroduodenal transit and improves the typical symptoms of this syndrome for a period of time that extends beyond treatment period. The mechanisms underlying this phenomenon are not clear. We can, however, speculate on the basis of some evidence presented in the literature and concerning the role of supplementing fluids with a greater or lesser ion and/or mineral content in functional disorders of the gastrointestinal tract. Fluid administration would appear to have significant and long-lasting effects on gastrointestinal transit in both healthy subjects and patients suffering from constipation,^{16, 17} although there is not complete agreement with regard to non-constipated subjects.¹⁸ It has been hypothesised that the different effects reported by control and constipated subjects may be due to specific physico-pathological characteristics involving the intestinal motor function in constipated subjects and it may be also influenced by the chemical composition of the supplemented fluid.^{16 A}

similar situation may be observed in dyspepsia which, in many etiopathological aspects, is similar to constipation. The specific ion and mineral content of the water used in this study may be responsible for the activation of chemoreceptors able to stimulate gastroduodenal tract motility in response to the meal, or to active complex interdigestive motors. The efficacy of this treatment in dyspeptic patients would also explain the slowed gastric emptying typical of this condition.

To date, studies in the literature on this topic only cover the pediatric population. One study¹⁹ shows that the administration of *L. reuteri* DSM 17938 significantly accelerates gastric emptying and reduces regurgitation in infants affected by non-complicated gastroesophageal reflux when supplemented for 28 days with a daily dose of 1×10^8 (CFU). The authors also collected the gastric emptying parameter in normal infants matched for age and sex with the study group and the comparison with the normal value of gastric emptying in this age range allowed to define the effect of probiotic on gastric motility. The children treated with *L. reuteri* had an acceleration of gastric emptying time. The addition of prebiotics and probiotics to a formula induces a gastrointestinal motility pattern similar to that induced by breast milk. The gastric emptying parameters showed a similar profile in all the three study groups, showing a significant difference from the placebo.²⁰

A pilot study demonstrated the potential beneficial effects of probiotics on clinical and physiological variables related to gut function. In particular, it showed that oral supplementation with *L. reuteri* improves feeding tolerance and bowel habits and reduces crying time in pre-

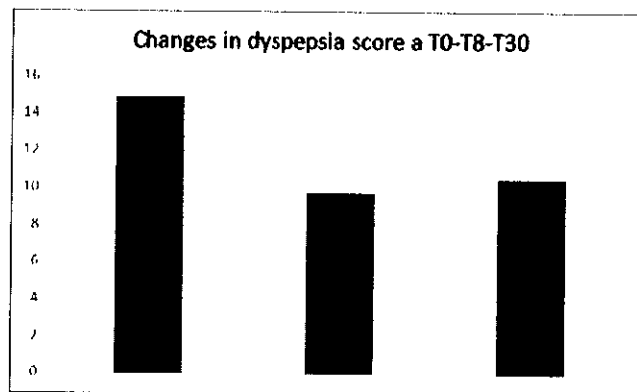


Figure 3.—Changes in dyspepsia score at T₀, T₈ and T₃₀.

term newborns. Gastric motility was improved in infants supplemented with *L. reuteri* as shown by the increased gastric emptying rate and the reduced fasting antral area. These findings were similar to those observed in newborns fed with breast milk.²¹

None of the newborns receiving *L. reuteri* had adverse events, consistently with the earlier demonstration of the safety and tolerance of this probiotic in full-term infants.²²

An increased gastric emptying rate and a reduced fasting antral areas were seen in formula-fed preterms supplemented with *L. reuteri* and in babies fed with breast milk. The clinical counterpart of such a reduction in gastric antral area may be a reduction in episodes of regurgitation. In adult functional dyspeptic patients, gastrointestinal symptoms have been related to impaired accommodation and antral dysfunction. In conclusion, our results suggest that *L. reuteri* supplementation plays a role in improving feeding tolerance and gut function in newborns. The physiological mechanisms underlying these effects involve changes in gastrointestinal motility, which is improved in both the upper and lower gut.²¹

Conclusions

The results of this study have highlighted a possible role of supplementation with Uliveto mineral water and *L. reuteri* in the treatment of function dyspepsia, supported by slowed gastric emptying. These results must be considered in terms of 'social investment' and this kind of therapy can thus be included in the scope of our country's therapeutic strategies.

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