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



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## PANMINERVA MEDICA

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# Effect of treatment with a mineral water rich in calcium bicarbonate plus *L. reuteri* on orocaecal transit in patients suffering from chronic constipation

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Aim. Constipation is a common ailment in clinical practice, and whilst it can sometimes be a clinical symptom of different organic diseases, but it often presents as a stand-alone problem that is not associated with any other pathology. Our study aims to evaluate intestinal transit time in patients suffering from chronic constipation after the administration of calcium bicarbonate water (Uliveto) associated to *L. reuteri*.

Methods. Fifteen patients suffering from chronic constipation (average age:  $41\pm5$ , 5 female and 5 male) and 15 healthy controls (average age:  $40\pm7$ , 5 females and 5 males) were enrolled and were subjected to a lactulose breath test to determine orocae-cal transit time. The study participants therefore began to take a supplementation with 1.5 L/day of calcium bicarbonate-rich mineral water (Uliveto; fixed residue at 180 °C = 860 mg/L, bicarbonate HCO<sub>3</sub>-= 650 mg/L, calcium Ca<sup>++</sup> = 169 mg/L) and L. reuteri (in form of tablets, at a dose of  $10^8$  CFU, twice daily) for 15 days. At the end of the therapy, the patients were re-assessed by repeating the lactulose breath test and once again completing the questionnaire on gastrointestinal symptoms.

Results. Intestinal transit time was statistically slower in patients suffering from chronic constipation as compared with controls. All patients showed an alteration in orocaecal transit time. After 15 days of therapy with water supplementation plus *L. reuteri*, a statistically significant overall increase was seen in the orocaecal transit time in all patients.

Conclusion. Thus we may state that supplementation with Uliveto mineral water and *L. reuteri* resulted in improved intestinal transit time in patients suffering from chronic constipation. Further studies are needed to established if this effect is linked to the supplementation with Uliveto mineral water, to *L. reuteri*, or to the combination of both.

**KEY WORDS:** Constipation – Transit time – Breath test – Mineral water – Calcium bicarbonate.

Constipation is a common ailment in clinical practice and generally indicates a persistent condition marked

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by difficulty in defecating, infrequent defecation or defecation that often gives the impression of being 'incomplete'. Constipation can sometimes be a clinical symptom of different organic diseases, but it often presents as a stand-alone problem that is not associated with any other pathology. As such, it is, in itself considered a disease, more correctly defined as "idiopathic constipation".<sup>1-5</sup>

Given the wide variability of 'normal' intestinal habits, constipation is difficult both to describe and to quantify. Frequency of defecation alone is not a sufficient criterion for diagnosis, although the majority of individuals have at least 3-4 defecations per week. Form and consistency of faeces are closely linked to the amount of time that has passed since the previous defecation: hard, small faeces are indicative of slowed intestinal transit, while soft, watery faeces are associated with rapid transit. Some psychological factors or certain social habits can also cause the onset of constipation.

From a clinical-descriptive viewpoint, constipation can be classified as:

a) recent-onset constipation, usually caused by some form of colon obstruction (neoplasia, ischemic or diverticular type of constipation), spasm of the anal sphincter (for example in the case of anal fissures, painful haemorrhoids) or drugs; or b) chronic constipation, sometimes seen in various different pathological conditions, such as inflammatory intestinal diseases, megacolon (Hirschprung, Chagas), pelvic floor dysfunctions, rectocele, endocrinopathies (hypothyroidism, hypocalcaemia), psychiatric problems or neurological diseases, but also often associated with insufficient fibre or water intake. This latter aspect should not be underestimated. It has been observed that 90% of chronic constipation cases have no apparent underlying cause, and constipation tends to go into remission with regular physical exercise, supplementary dietary fibre (from 15 to 25 grams/day) and the consumption of plenty of water.<sup>6-8</sup> Very often, these simple steps can help avoid the chronic resort to laxatives.

Our study aims to evaluate intestinal transit time in patients suffering from chronic constipation after the administration of a mineral water rich in calcium bicarbonate (Uliveto) associated to *L. reuteri*.

### Materials and methods

Fifteen patients suffering from chronic constipation (average age: 41±5, 5 female and 5 male) and 15 healthy controls (average age: 40±7, 5 females and 5 males) were enrolled at the Gastroenterology Unit of the "A. Gemelli" General Hospital of Rome, Italy (Tables I, II). All subjects (patients and healthy controls) were subjected to a lactulose breath test to determine orocaecal transit time. They all also filled in a questionnaire evaluating gastrointestinal symptoms (meteorism, abdominal pain, number of defectations/week).

The participants then started a supplementation with 1.5 L/day of a bicarbonate-rich mineral water (Uliveto; fixed residue at 180 °C = 860 mg/L, bicarbonate HCO<sub>3</sub><sup>-</sup> = 650 mg/L, calcium Ca<sup>++</sup> = 169 mg/L) and *L. reuteri* (in form of tablets, at a dose of 108 CFU, twice daily) for 15 days. During this period, the patients followed a calorie-restricted diet with standard fiber content. No patients with known alterations to intestinal transit following organic pathologies (abdominal surgery, diabetes mellitus, sclero-derma, hypothyroidism, etc.) were included in the study. At the end of the treatment, patients were re-assessed by repeating the lactulose breath test and filling in once more the questionnaire on gastrointestinal symptoms.

The lactulose breath test 9 was performed by administering 20 g lactulose dissolved in 100 cc water to the subjects. Breath samples were obtained by asking the patients to blow into suitable containers at time 0 (before ingesting the lactulose) and then every 15 minutes thereafter for 4

hours following lactulose administration. Gas chromatography was used to assess the presence and quantity of hydrogen in the breath (QuinTron, Milwaukee, WI, USA). Orocaecal transit time was calculated for each patient by drawing the curves of breath hydrogen over time. This showed the time needed for the bolus to reach the caecum. Each patient was subjected to a standard dietary regimen during the period for which mineral water was administered, and consumed 5 meals a day with restricted calorie content.

Actual consumption of water was verified on the basis of the full and empty bottles returned. The patients were assessed prior to starting the treatment and at the end of the treatment period (15 days later).

Fifteen control subjects (not suffering from constipation and absolutely free from symptoms, from the medical staff) were subjected to the same supplementation with Uliveto mineral water, and relevant orocaecal transit time assessment.

The results in relation to the lactulose test were expressed as a mean  $\pm$  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. Where applicable, the  $\chi^2$  or Student's t-test were used to assess symptoms.

### Results

Intestinal transit time was statistically slower in patients suffering from chronic constipation as compared with controls (Figures 1, 2). All patients showed an alteration of the orocaecal transit time. After 15 days of therapy with water supplementation plus *L. reuteri*, a statistically significant overall increase was seen in the orocaecal transit time of all patients (Figures 3, 4). An increase in the number of weekly defecations and a reduction of meteorism was also recorded in patients affected by constipation. After the treatment, a moderate increase in the orocaecal transit time was observed in controls as well (Figure 5).

### Discussion

The mechanism by which the lactulose breath test can assess orocaecal transit time has now been internationally validated 9 and is based on the non-absorbance of this sugar by the digestive tract mucosa. Hence the lactulose passes the stomach and small intestine intact and reaches the caecum, where the bacteria (normally present in the

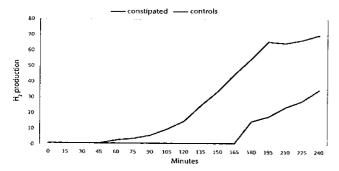
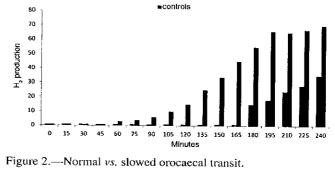


Figure 1.—Normal vs. slowed orocaecal transit



■ constipated

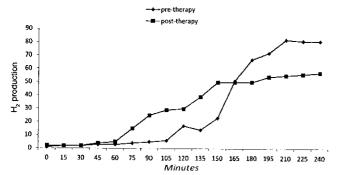


Figure 3.—Orocaecal transit pre- and post-therapy.

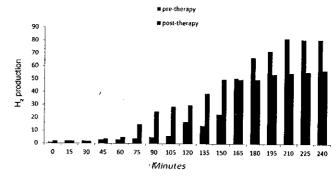


Figure 4.—Orocaecal transit pre- and post-therapy.

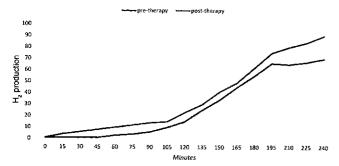


Figure 5.—Controls pre- and post-therapy.

colon flora) break it down, leading to the production of hydrogen. Part of this hydrogen is absorbed by the intestinal mucosa and therefore enters the bloodstream before being released at the pulmonary alveoli and expired. By evaluating the time at which hydrogen appears in the breath, we are therefore able indirectly to determine orocaecal transit time.

Idiopathic constipation is a very widespread pathology throughout the general population, and particularly

among the elderly. It can be eased by many pharmacological and non-pharmacological therapies.

Unfortunately, a growing tendency by the general population to medicalize this kind of disorders and the easy accessibility of drugs which sometimes do not even require medical prescription has resulted in laxatives being amongst the most commonly purchased drugs. This means that, in strictly economic terms, the cost of drugs for constipation is ever-increasing. Furthermore, the use of laxatives very often produces benefits in the short term only, as their continued use can cause the intestine to physiologically adapt, developing an addiction that results in the drug's loss of efficiency. Hence the reason why we wanted to determine if a fibre-rich diet associated with an increased fluid intake can constitute a valid, inexpensive, harmless alternative to therapy with laxatives. <sup>10, 11</sup>

The results of our study have shown that a supplementation of at least 1.5 litres of Uliveto mineral water per day, for 15 days, leads to a significant improvement in orocaecal transit time in patients suffering from chronic constipation. 12-15 Furthermore, the symptoms of these patients also improved considerably, with excellent patient com-

pliance with the therapy. The physiological mechanisms underlying the improved intestinal transit have not been entirely clarified. The water probably acts in several ways: firstly, by the simple fact of being a fluid (and therefore softening the intestinal content); secondly, by joining the intestinal content and forming a mass that urges the wall baroreceptors to contract; and thirdly through its mineral salt content: it has been shown that bicarbonate ions are able to stimulate intestinal motility.6 The ions present in mineral waters, and particularly in the water chosen for this study (Uliveto), may also stimulate intestinal motility by activating the intestinal neuroendocrine system by directly stimulating the wall chemoreceptors.3 Stimulation of these receptors can induce the onset of giant peristaltic waves (motor migrant complexes) underlying the transit of the bolus in the intestine on the one hand, and encourage gastric emptying through a reflex both during the interdigestive period and at mealtime, on the other. All this results in a reduced intestinal transit time and, therefore, an increased number of weekly defecations and reduced symptoms. Lesser contact time of the intestinal content with bacterial flora results in a reduction of the metabolisation of food residues by bacteria, and a reduced gas formation with an improvement of meteorism.

The intestinal microbiota <sup>24</sup> may play a role in the etiology of functional constipation. Imbalance in microbiota composition has been described in the stools of patients with constipation. <sup>16, 17</sup> However, up to now, trials in constipated patients receiving probiotics, prebiotics and synbiotics showed conflicting results. <sup>18-23</sup>

Another study has evaluated the evidence on the effectiveness of Lactobacillus reuteri DSM 17938 for treating and preventing diseases in infants and children arguing that the use of *L. reuteri* may be considered in the management of acute gastroenteritis as an adjunct to rehydration and in reducing the incidence of diarrhea, it may be effective in the prevention of some functional gastrointestinal disorders, such as colic and regurgitation and it also provides a rationale for treating functional constipation or functional abdominal pain.<sup>25</sup> Therefore, the administration of *L. reuteri* in infants with chronic constipation may have a positive effect on bowel frequency, even with no improvement in stool consistency and episodes of inconsolable crying.<sup>26</sup>

### Conclusions

In conclusion, based on the results of this study we can state that supplementation with Uliveto mineral water and L. reuteri resulted in improved intestinal transit time in patients suffering from chronic constipation. Further studies are needed to established if this effect is linked to the supplementation with Uliveto water, to L. reuteri, or to the combination of both.

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