Biomedicine & Pharmacotherapy 138 (2021) 111509

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

Original article

Health properties of the Italian *San Martino*® mineral-rich water: A self-controlled pilot study

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ARTICLE INFO

Keywords:
Mineral water
Mineral-rich water
Health properties
Diuresis
Choleretic effect

ABSTRACT

The effect of hyper-mineral waters on human health has long been debated. This pilot study evaluated the influence of *San Martino*® water (Sardinia, Italy), on clinical and biological parameters, following the treatment of 10 hospitalized patients. Crenotherapy consisted of 1–2 L of the water daily for 10 days. A complete blood count, serum electrolytes, liver and kidney function tests, fasting lipid profile and plasma glucose, and abdominal ultrasound imaging were assessed before and at the end of treatment. In addition, body weight, dyspeptic symptoms, bowel movements, diuresis, uricuria and blood pressure were evaluated daily. According to its physico-chemical properties, the water is hyper-mineral (TDS 2808 mg/L) with a high content of bicarbonate and iron. At the end of the study, diuresis increased by 60% (850 vs 1295 ml/24 h, P = 0.009) and uricuria by 41% (362 vs 490 mg/24 h, P = 0.022) respectively, whereas plasma uric acid level decreased by 7% (4.7 vs 4.3 mg/dL, P = 0.043). Compared to the basal values, serum gamma-glutamyl transferase, alkaline phosphatase and total bilirubin levels, showed a reduction of 65% (31 vs 18 U/L, P = 0.022), 15% (96 vs 90 U/L, P = 0.041), and 11% (0.53 vs 0.45 g/dL, P = 0.041), respectively. Bowel movements improved in 62.5% of patients with constipation, and 80% of dyspeptic patients experienced symptoms relief. Compliance to the treatment reached 100%. Mild differences were observed in body weight and blood pressure, although not in ultrasound imaging during crenotherapy. These findings suggest that the *San Martino*® hyper-mineral water may have some benefits to human health. Additional studies with a larger-sized cohort and for a longer period are needed to confirm these preliminary results.

1. Introduction

Water is a fundamental component of the diet of human beings as it plays an important role in nutrition requirements and health outcomes. Although tap water is easily available in developed countries, the global consumption rate of bottled water has consistently increased in the last decade [1]. In a qualitative study conducted by Ward et al. at the Munrow Sports Centre, University of Birmingham campus, using semi-structured interviews, the majority of participants perceived bottled water as a "healthy option" compared with tap water, although the putative "health benefits" were not supported by the scientific evidence in all cases [2]. In fact, studies evaluating the effect of regular consumption of mineral waters on human health are still scarce.

Under Directive EU 2009/54/EC, natural mineral water is microbiologically wholesome, originating from an underground source and emerging from a spring, tapped at one or more natural exits to prevent contamination, containing a specific and constant chemical composition, and must be bottled at the source [3]. Based on their specific chemical and physical properties, mineral waters may have different beneficial health effects [4,5], although hyper-mineral spring waters have been often accused of being harmful to human health. For example, following the consumption of salt-rich mineral waters some studies have reported increased blood pressure [6] due to sodium and possible chloride retention [7]. Moreover, earlier studies have suggested a pathogenic role of hard water in the nephrolithiasis process given the hypercalciuria caused by exposure to water with high calcium content [8–10].

However, there are several studies reporting a positive association between the regular intake of hyper-mineral water and health benefits [11]. For instance, treatment using mineral water with a high content of

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https://doi.org/10.1016/j.biopha.2021.111509
Received 2 February 2021; Received in revised form 11 March 2021; Accepted 11 March 2021
Available online 31 March 2021

bicarbonate, calcium, and magnesium may enhance bowel movements [12], gastric emptying [13], and amelioration of dyspeptic symptoms, especially those of dysmotility like dyspepsia [14]. In addition, a positive impact on gallbladder kinetics has been detected in association with mineral water consumption [15]. Furthermore, changes in the lipid profile [16], in renal [17] and hepatic function [18] were observed in subjects exposed to prolonged crenotherapy. Interestingly, an inverse relationship between water intake and cardiovascular risk factors [19], and, particularly, a reduction of blood pressure in normotensive [20] and mildly hypertensive [21] individuals was observed in different surveys. According to these findings, in a rodent model of metabolic syndrome, an eight-week consumption of mineral-rich water prevented the increase in heart rate and plasma triacylglycerols and delayed the increase in systolic blood pressure induced by fructose [22].

In a recent meta-analysis including a total of 5868 patients, the authors concluded that hard water (>180 mg/L $CaCO_3$, according to the World Health Organization) might be useful for patients complaining nephrolithiasis [23]. More specifically, water that is high in calcium was recommended by five interventional studies and one observational study. Besides, the habit of drinking hard water is common among certain populations, such as the one living in the Nicoya peninsula, Costa Rica, characterized by exceptional longevity [24,25].

In Italy, natural hyper-mineral waters were subjected to epidemiological and clinical investigations that reported generally positive effects [4,5]. Among Italian hyper-mineral waters one labelled *San Martino*® is sparkling water that originates spontaneously in the north-western part of the island of Sardinia, from the springs of the volcanic Coros Plateau belonging to the Osilo andesitic massif at an altitude of 243 mt a.s.l. in the municipality of Codrongianos [26]. This spring mineral water is very rich in bicarbonate, sulphate and iron. Evidence dating back to the 11th century BC attests that pre-Nuragic populations already venerated the deities of water and the spring, attributing them with extraordinary properties [27]. Later, around the 2nd century BC, the quality of the water was also recognized by the Romans, who built a 22 miles pipeline to supply it to Porto Torres (at the time *Turris Libyssonis*) [28]. In the 16th century the source was documented by the historian G.F. Fara [29]. However, the first chemical analyses of the water were carried out by G. G. Paglietti only in 1776 [30], which were reiterated in the mid-19th century [31–34]. In 1843 the British writer J.W.W. Tyndale during his trip across Sardinia visited the source of San Martino and wrote: "*The mineral spring of San Martino is covered with an artificial dome about five feet high, and contains, according to the analysis of M. Majon, of Genoa, hydrochlorate of soda, carbonate of lime, and sulphate of magnesia. The water in passing off leaves a deposition of a red-ochrous color, composed of peroxyde of iron, carbonate of iron, carbonate of magnesia, and carbonate of lime*" [35]. In 1902 the bottling plant came into operation [30]. Although the *San Martino*® water has been known since ancient times, scientific evidence for its health benefit for humans is still lacking.

The aim of this pilot study was to investigate, for the first time, the effect of a 10-day treatment using the bottled mineral-rich water of *San Martino*® upon several physiologic and metabolic markers in hospitalized patients.

2. Methods and patients

2.1. Study design

This was a pilot intervention study with a paired samples design to test the functional properties of the mineral-rich, naturally sparkling *San Martino*® water, by assigning volunteer patients to the treatment. Clinical parameters, laboratory tests and ultrasound imaging were collected at the baseline and after 10 days of active treatment with *San Martino*® water and compared.

2.2. Water samples collection and analysis

San Martino® water samples were directly collected from the source in the Codrongianos area (Sardinia, Italy) by trained operators following the guidelines specified by the Italian law [36]. The sampling procedure was performed by using sterile 1000 ml polypropylene bottles, after measuring the water temperature and pH.

Total dissolved solids (TDS) were determined by the gravimetric method [37]. As for single ions, bicarbonate was determined using a coupled ion selective electrode [38] while sodium, calcium, magnesium, iron, and halogens were identified by flame atomic absorption spectrometric procedures [39]. Chloride concentration was measured by titration with silver nitrate ($AgNO_3$) as the titrant [40]. The sulphate level was assessed by selective ion chromatography [41], and the pH was determined by a pH-meter [41]. All chemical physical analyses of the tested water were performed at the Hygiene and Preventive Medicine Institute, University of Sassari [42].

2.3. Patients eligibility

Patients admitted to the section of Internal Medicine, University of Sassari, Italy, judged to be compliant for the study protocol by the physician, were invited to participate. Patients with acute or chronic renal failure, haematuria and/or proteinuria due to renal or extrarenal causes, heart failure, severe arterial hypertension, uncompensated liver cirrhosis, presence of oedema, peritoneal/pleural effusions, severe gastrointestinal disease including peptic ulcer, malabsorption, diarrhea, and intestinal bleeding, severe acute or chronic infectious processes, uncompensated diabetes mellitus, septic or persistent fever, dyspnoea or relapsing or persistent chest pain and malignancy were considered ineligible for the study. The presence of stones in the upper and lower urinary tract in the ultrasound imaging, or crystals in the urine sediment, were considered as additional exclusion criteria.

2.4. Study protocol

Water samples were kept in sterile glass bottles, sealed with sterilized seal caps, and stored in a refrigerator for a few days until used. Mineral water was made available to study participants daily with a total amount ranging from a minimum of 1 liter to a maximum of 2 liters for a period of 10 days. Except *San Martino*®, patients were not allowed to drink additional liquids, including normal water, and were advised to maintain the usual dietary habits.

At baseline, a complete clinical history and information about bowel habits, urinary functions and diuresis, blood pressure, heart pulse rate and respiratory rate were collected. Afterward, body weight and height were measured with a stadiometer and an electronic scale, respectively. Each patient also underwent a physical examination and an abdominal ultrasound testing. Blood sample was drawn by venepuncture from each participant after an overnight fasting. Standard laboratory tests, including complete blood count, plasma glucose, kidney and liver functional tests, electrolytes, and lipid profile, were performed and assessed using standard methods in the same referral laboratory.

Patients were evaluated daily for compliance and possible side effects or complaints by a physician, both by questioning and physical examination. Compliance was scored according to the number of bottles of water consumption daily for the entire study duration. Compliance was considered good if at least 90% of the total liters (10−20) of *San Martino*® water was consumed. Urine output, bowel movements and body weight were recorded daily. Moreover, systolic and diastolic blood pressure were measured every eight hours in a triple fashion and the mean value was calculated. The same clinical and laboratory parameters were re-evaluated on the 10th day, except for uric acid in the serum and in the urine that were earlier determined on the 5th day of the study.

Subsequently, abdominal ultrasound examination was performed in each participant before and after the *San Martino*® water treatment. The

presence of hyperechogenic spots in the kidney and urinary tract defined nephrolithiasis. To avoid interobserver variation the ultrasound scan was performed by the same operator.

2.5. Ethical issues

Verbal and written informed consent for participation in the study was requested and obtained from all patients, and the protocol was approved by the ethics committee of the School of Medicine, University of Sassari.

2.6. Statistical analysis

In order to achieve a statistical power of 80% and a two sided significance level of 5% for detecting a 50% variation in the variables, a minimum of 10 patients were required.

The average daily diuresis was calculated as the average of the urine excretion during the 10 days of crenotherapy. For all the variables considered, the mean and standard deviation of the values of the baseline and at the 10th day of intake of *San Martino*® mineral water were calculated. In addition, mean and standard deviation of the uric acid in the serum and the urine were also calculated on the 5th day. Statistical significance was then evaluated by the two-sided Wilcoxon test for paired data assuming a P value less than 0.05 to be statistically significant. All statistical analyses were performed using SPSS statistical software (version 22.0, Chicago, IL, USA).

3. Results

3.1. Physical and chemical properties of tested water

The physico-chemical properties of the *San Martino*® water are summarized in Table 1. According to the analysis, the water under investigation is classified as "acidulous, chlorinated, sulphated, and containing sodium, bicarbonate and iron". The amount of TDSs at 110 °C, was 2808 mg/L, which largely exceeded the threshold of 1500 mg/L that, according to the Italian law, enables a spring water to be labelled as "hyper-mineral" [43]. More specifically, the bicarbonate content in the *San Martino*® mineral water was 2288.14 mg/L, which was much higher compared with other Italian hyper-mineral spring waters [44]. The analysis also detected that the chloride-to-bicarbonate ratio, and the sodium content, were low (0.26 and 550 mg/L, respectively). In addition, the concentration of iron was 2900 μg/L, which was superior to that of most hyper-mineral waters [44] and comparable to that of sea water.

Table 1
Physico-chemical characteristics of *San Martino*® mineral water [42].

Parameter	San Martino® water
Outlet temperature (°C)	22.6
Total dissolved solids (mg/L)	2808.2
Electrical conductivity (μS/cm 20 °C)	2730
Chemical Oxygen Demand	1.68 at mg/L O_2
pH	6.23
Bicarbonate (mg/L)	1305.7
Sulphate (mg/L)	295
Calcium (mg/L)	145
Magnesium (mg/L)	48
Chloride (mg/L)	339.3
Sodium (mg/L)	550
Potassium (mg/L)	87.5
Lithium (mg/L)	0.71
Iron (mg/L)	2.9
Nitrates (mg/L)	3.12
Silicates (mg/L)	11.83
Fluoride (mg/L)	0.89
Bromide (mg/L)	4.75
Iodide (mg/L)	0.01

3.2. Study patient features

The main complaints at the baseline of patients admitted to the hospital and included in the study are reported in Table 2.

3.3. Clinical outcomes

Overall, study participants found the *San Martino*® mineral water tasty, and it was consequently well accepted during the entire study period. A compliance of 100% was recorded in each participant. No adverse effects were reported. Minimal variations in body weight, ranging from 0.2 to 0.4 kg, were observed in each participant between the baseline and the end of the study (Fig. 1a), underlying the absence of water retention. More importantly, a significant inverse relationship was detected between the urinary output and percent change in body weight during the intervention period (Fig. 2). Systolic and diastolic blood pressures remained unchanged over the study period (126 vs 132 mm Hg, and 72 vs 74 mm Hg, respectively) (Fig. 1c and d).

Bowel habits reverted to normal during the active treatment period in five out of eight patients (62.5%) suffering from chronic constipation. Among patients complaining dyspeptic symptoms of variable degree, mainly characterized by postprandial epigastric tension, belching, bloating and slow digestion, 80% (4 out of 5) experienced normalization of digestive function at the end of the active treatment. No patient experienced diarrhea during the crenotherapy.

Table 3 shows the clinical parameters and blood chemistry in study participants at the baseline and after 10 days of *San Martino*® water consumption. Interestingly, a statistically significant increase of urine output (60% on average) was recorded at the end of the study compared with the baseline diuresis (Fig. 1b). In particular, the average daily urine output, calculated over the entire period of mineral water intake, was 23% higher than the basal level, and this difference was significant ($P = 0.009$). It was observed that metabolic indicators such as fasting blood glucose and renal functionality tests of study participants remained unchanged as indicated by the absence of significant differences of blood urea nitrogen and serum creatinine between the mean basal values and those at the end of the treatment.

However, serum uric acid levels decreased by up to 1.5% on the fifth day and up to 7% at the end of the experiment (4.7 vs 4.3 mg/dL), with a borderline significant difference ($P = 0.043$). In accordance with the uricaemia trend, the 24-hour urinary excretion of uric acid also increased by 10% between baseline values and those on the 5th day, and by 41% on the 10th day, with the pairwise difference reaching statistical significance ($P = 0.022$). Moreover, markers of liver function displayed relevant changes following the intake of *San Martino*® water; namely, total serum bilirubin showed a statistically significant average reduction of 11% (0.53 vs 0.45 g/dL, $P = 0.041$); the alkaline phosphatase showed a reduction of 15% (96 vs 90 U/L, $P = 0.041$) and the gamma-glutamyl transferase decreased even more significantly, nearly 65%, (31 vs 18 U/L, $P = 0.022$), compared with the basal values, whereas no differences were detected in the transaminases levels. Finally, with regard to the haematological parameters and lipid profile (total cholesterol and

Table 2
Diseases of study participants at the time of admission to the hospital.

Patient	Sex	Disease
1	F	Iron-deficiency anemia
2	M	Severe influenza
3	M	Stroke and anal fissures
4	F	Cryoglobulinaemia
5	M	Subaortic stenosis
6	M	Transient ischaemic attack and cardiovascular disease
7	F	Systemic Lupus Erythematosus
8	M	Atherosclerosis and diabetes mellitus
9	F	Chronic atrial fibrillation
10	F	Atrial flutter and diabetes mellitus

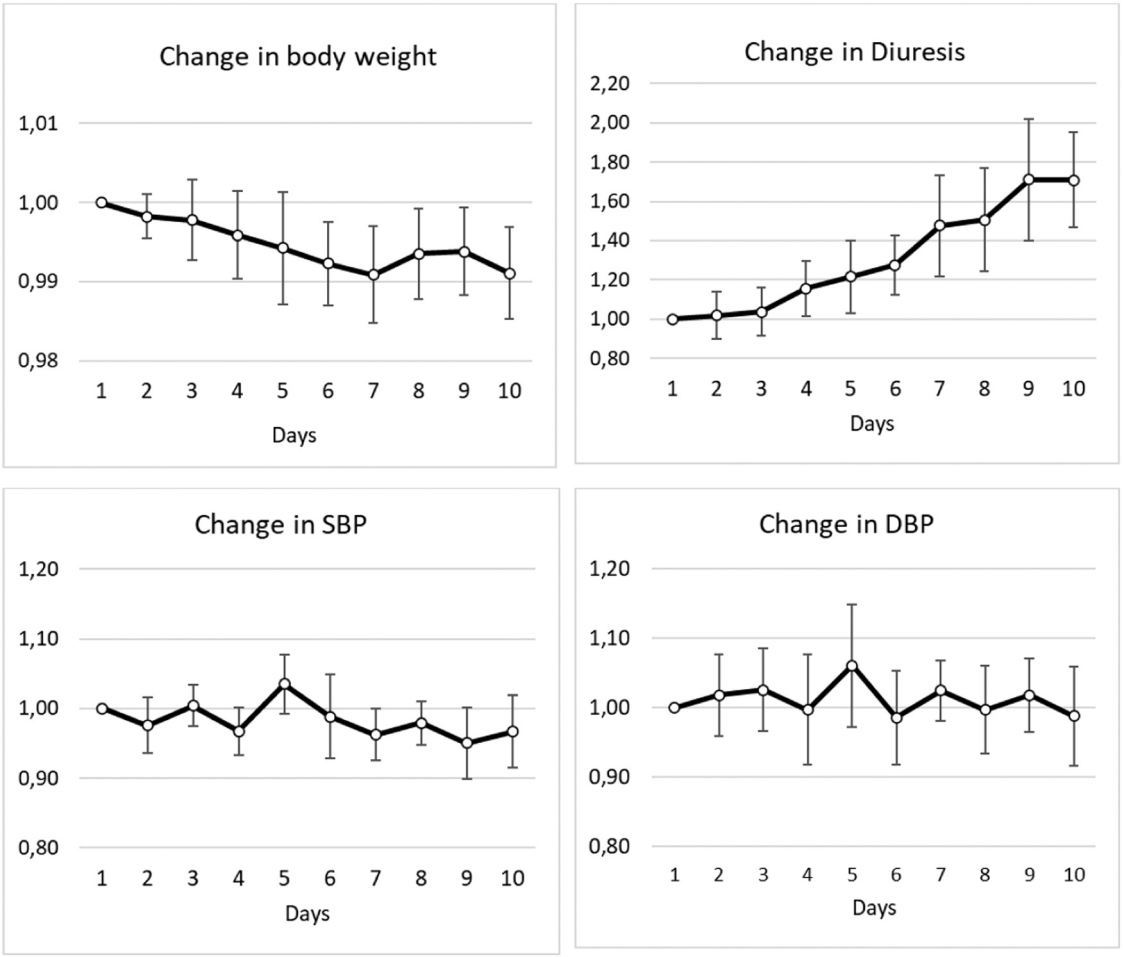

Fig. 1. Daily variation of body weight (a), urine output (b), systolic blood pressure (SBP) (c), and diastolic blood pressure (DBP) (d) (each curve point represents the percent difference from the basal value).

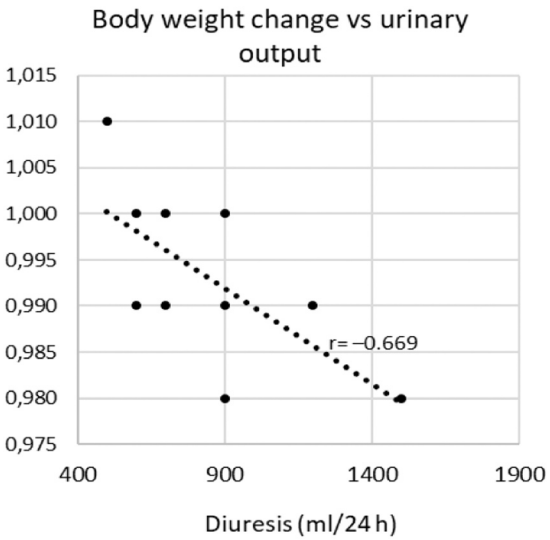

Fig. 2. Relationship between percent body weight change and urinary output during the intervention period.

triglyceride levels), no statistically significant differences were observed between the basal values and those measured at the end of the study (Table 3).

Kidney and ureteral stones were not detected in any patient by the abdominal ultrasound, nor were crystals detected in the urine sediment, at the end of crenotherapy.

4. Discussion

In the present study, the administration of *San Martino*® water to humans highlighted significant metabolic effects detectable already after a short administration period of 10 days. These effects concern:

- the significant increase in the total urine output and average diuresis;
- the rise in uric acid excretion, detectable already on the 5th day of administration and reaching statistical significance on the 10th day of experimentation;
- the significant reduction in plasma uric acid levels, evident at the end of the study when compared to baseline values; and finally
- a significant reduction of cholestasis biochemical markers. More specifically, these results indicate that the mineral water analyzed has a relevant choleretic effect, confirmed by the evidence of improvements in digestive functions and the regularization of bowel movements observed in some patients.

It seems likely that a more prolonged administration of *San Martino*® mineral water can help to promote the normalization of intestinal functions in other patients as well. A choleretic effect, i.e. the stimulation of biliary excretion, following the use of mineral waters, was reported by different authors [15,45] and could, in turn, contribute to ensuring a better regulation of lipid metabolism as previously observed

Table 3
Blood chemistry parameters before and after drinking San Martino® mineral water.

Parameter	Baseline	At 10th day	P-value[a]
Blood urea nitrogen (mg/dL)	31.7 ± 13.2	32.2 ± 9.8	0.799
Fasting blood glucose (mg/dL)	101.7 ± 64.9	91.7 ± 42.4	0.374
Serum creatinine (mg/dL)	0.86 ± 0.17	0.84 ± 0.13	0.307
Serum uric acid (mg/dL)	4.7 ± 1.3	4.3 ± 1.0	0.043
Diuresis (ml/24 h)	850 ± 306	1295 ± 423	0.009*
Urine uric acid (mg/24 h)	362 ± 119	490 ± 192	0.022*
Na^+ (mmol/L)	137.8 ± 12.7	136.6 ± 13.5	0.258
K^+ (mmo/L)	3.9 ± 0.4	4.1 ± 0.3	0.134
Ca^{2+} (mg/dL)	9.1 ± 0.4	9.3 ± 0.5	0.125
PO_4^{3-} (mg/dL)	3.1 ± 0.4	3.0 ± 0.5	0.538
Cl^- (mmol/L)	105.0 ± 1.9	104.6 ± 2.4	0.506
Serum proteins (g/dL)	6.4 ± 0.6	6.4 ± 0.4	0.546
Total serum bilirubin (mg/dL)	0.53 ± 0.15	0.45 ± 0.12	0.041*
Triglycerides (mg/dL)	69 ± 26	72 ± 22	0.220
Cholesterol (mg/dL)	158 ± 33	157 ± 34	0.507
RBC (10^3/μL)	4727 ± 755	4705 ± 656	0.838
Hemoglobin (g/dL)	13.1 ± 2.4	13.0 ± 2.2	0.607
Hematocrit (%)	41.3 ± 6.8	41.1 ± 5.6	0.959
WBC (10^3/L)	6619 ± 2958	6745 ± 2803	0.415
MCV (fL)	87.0 ± 10.4	87.7 ± 8.3	0.959
MCH (pg)	27.9 ± 3.7	27.7 ± 3.3	0.721
MCHC (g/dL)	31.7 ± 1.2	31.6 ± 1.6	0.574
PLT (10^3/μL)	212,400 ± 144,600	243,600 ± 132,800	0.799
Aspartate aminotransferase (U/L)	27 ± 7	26 ± 7	0.256
Alanine aminotransferase (U/L)	21 ± 7	19 ± 6	0.442
Gamma-glutamyl transferase (U/L)	31 ± 30	18 ± 6	0.022*
Alkaline phosphatase (U/L)	96 ± 28	90 ± 28	0.041*

[a] Wilcoxon test for paired data.
* P statistically significant.

[16,46]. Notably, no one patient experienced diarrhea, suggesting that the amount of magnesium and sulphate in *San Martino*® water did not induce an osmotic effect.

According to the most relevant studies in the field [19–21], blood pressure did not increase in enrolled participants undergoing the hyper-mineral water treatment. It could therefore be argued that the short treatment period may have biased the blood pressure results masking a potential hypertensive effect of the *San Martino*® water. However, many clinical observations indicate that blood pressure is not increased in humans by high dietary Na^+ and/or bicarbonate intake in the absence of Cl^- [47,48]. Accordingly, in the *San Martino*® water, unlike other Italian waters [44], bicarbonate -not chloride- is the most represented anion. Among several studies, bottled water is perceived by consumers as a healthier choice compared with tap water [2,49]; however, additional factors, including taste, have been reported to influence the choice for the preference for bottled water [2]. In our study, all participants found the *San Martino*® water tasty. This is not surprising as this spring water was the first mineral water in Italy to receive the Superior Taste Award in 2016 [50].

The prevalence of nephrolithiasis is increasing across the world [51] and the role of mineral water in preventing it is well known. Earlier studies in the field recommended drinking water low in minerals for patients prone to nephrolithiasis [8–10], based on the high calcium content observed in the urine of subjects consuming hyper-mineral waters. However, a recent meta-analysis that included studies from the last three decades concluded that nephrolithiasis may be prevented by drinking hard water [23]. Similarly, in our study participants, we were not able to detect any stones in the kidney and/or urinary tract by the ultrasound examination at the end of crenotherapy, nor were crystals found in the urine sediment. This may be explained by the fact that a high content of magnesium and bicarbonate, present in *San Martino*® water, may reduce the risk of calcium stones formation [23,52].

In our study we did not observe the cholesterol-lowering effect documented in other studies involving hyper-mineral waters [46]; this could be attributed to the low baseline level of this analyte, although the effect of crenotherapy over the short duration could not be excluded entirely.

The clinical and haematological results of the hospitalized patients obtained in our study, largely confirmed the previously reported data obtained on animals [42]. Experiments carried out in rats did not show any toxicity following the *San Martino*® water exposure. The treatment resulted in not significant increase in urinary output and there was a mild rise in uric acid excretion. In addition, a significant increment in bile flow was detected in the animal cases compared to controls treated with distilled water. In rats made hyperuricaemic, the load with *San Martino*® water did not increase the diuresis, although the excretion of uric acid was significantly higher. Moreover, an increased intestinal motility was observed in treated rats, reaching statistical significance in male rats.

The major limitation of our study may appear to be the small sample size of the studied cohort. However, as previously explained, the enrolment of 10 patients allowed to obtain a sufficient statistical power for the pre-set significance level. Moreover, the small number of participants enabled us to strictly follow up on them using objective clinical and biochemical parameters. It could be argued that the short period of treatment may be an additional limitation, but it may also be considered a strength of the study. Although the *San Martino*® water benefits on bowel habits and dyspeptic symptoms they might have been affected by a placebo effect; the objective modifications on blood chemistry and clinical parameters before and after crenotherapy observed during a relatively short period, potentially suggest additional benefits in a long-term treatment. Finally, in the present study only the inorganic components of water were analyzed, although the organic components were reported to be important in other settings [53].

5. Conclusions

In conclusion, the preliminary results of this pilot study show that a short-term treatment with a hyper-mineral water significantly increased diuresis and urinary excretion of uric acid, and reduced uric acid in the blood, albeit mildly, without affecting blood pressure. Furthermore, the active treatment with this water positively modified some markers of cholestasis, suggesting that crenotherapy using a hyper-mineral water could be considered as a valid treatment in patients with dyspepsia, including patients with a prevalent cholestatic component. Moreover, the water was considered tasty by all participants and it was devoid of side effects. However, additional studies are needed to evaluate the potential health benefits of *San Martino*® water in a larger-sized cohort and for a longer period.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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