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Mild dehydration in dyspeptic athletes is able to increase gastrointestinal symptoms: Protective effects of an appropriate hydration

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Abstract

Background: Water balance influences gastrointestinal (GI) activity. Our aim was to evaluate how dehydration and rehydration with different types of water are able to affect GI activity in healthy and dyspeptic athletes.

Methods: Twenty non-competitive athletes, respectively 10 healthy and 10 dyspeptic subjects, were enrolled. All subjects underwent three test sessions (0, A, B) of 6 hours. Dehydration was achieved with a walking/jogging exercise test on a treadmill. After exercising, 500 mL of calcium-bicarbonate (Test A) or soft water (Test B) were administered, while no rehydration was provided during Test 0; thereafter, all subjects consumed a light lunch. GI symptoms were evaluated during each test and an electrocardiogram (ECG) Holter recording was performed at the end of the exercise.

Key Results: Dyspeptic subjects exhibited higher overall symptoms during Test 0 (VAS: 30.8 ± 0.8 mm) compared to Test A (18.4 ± 1.1, $P < 0.001$) and Test B (24.4 ± 1.3, $P < 0.001$). However, analyzing GI symptoms, only subjects receiving calcium-bicarbonate water (Test A) showed significantly lower symptomatic scores compared to Test 0 or Test B. Moreover, heart rate variability analyses revealed that only in Test A dyspeptic patients exhibit a trend to a decrease in the post-prandial low/high frequency (LF/HF) ratio, similarly to healthy subjects, while in Test 0 and Test B, post-prandial LF/HF ratio was increased compared to the pre-prandial phase.

Conclusions and Inferences: Our results show that mild dehydration in dyspeptic athletes is able to increase GI symptoms but an adequate rehydration, with calcium-bicarbonate water, is able to improve post-exercise disturbances restoring sympatho-vagal imbalance.

1 | INTRODUCTION

Water balance deeply influences many physiologic processes and both acute and chronic dehydration may affect body health.[1] The association between acute dehydration, whether caused by increased water loss or decreased water intake, and severe adverse health outcomes as consequence of extreme electrolyte abnormalities is well known[2,3]; in fact, there is a large body of evidence showing that acute water imbalance, exceeding 10% of body mass, is able to determine severe, or even fatal, dysfunction of both cardiovascular and

central nervous systems or renal failure.[4] Surprisingly, emerging evidences are demonstrating that even chronic mild dehydration is able to induce minimal electrolyte imbalance increasing the risk for long-term clinical disorders, such as chronic kidney disease, cardiovascular morbidity and mortality, neurological disorders, gastrointestinal (GI) symptoms, obesity, and new-onset hyperglycemia.[5,6] Although the pathophysiologic mechanism underlying the effect of chronic dehydration seems to be multifactorial, it has been hypothesized that even mild water changes may modify hormonal and autonomic balance whose activities regulate several physiologic processes.[7]

Impaired autonomic function of the nervous system seems to be involved in the onset of functional GI disorders, including irritable bowel syndrome (IBS) and functional dyspepsia (FD).[8,9] Supporting such evidences, the onset of nausea, vomiting or diarrhea, experienced by 30%-50% of healthy endurance athletes during intense physical activity, is considered an effect of decreased intestinal blood flow as consequence of parasympathetic tone reduction in favor of the sympathetic one. Although classified as chronic disorders, functional GI symptoms exhibit typically a fluctuating trend and may be precipitated by several factors including the dietary regimen and the lifestyle.

Hence, the aim of our study was to evaluate how a controlled mild dehydration is able to influence sympathovagal balance, inducing GI symptoms both in healthy and dyspeptic non-competitive athletes, and to evaluate how rehydration with two different types of water is able to prevent GI disorders and restore sympathovagal balance.[10]

Key Points

- Functional dyspepsia exhibits a multifactorial pathogenesis including impaired autonomic nervous activity and it has been hypothesized that mild chronic dehydration, caused by an inadequate water intake, may increase the severity of dyspeptic symptoms.
- This paper shows that a correct hydration improves gastrointestinal (GI) symptoms, induced by physical activity, in dyspeptic athletes.
- An adequate water intake, in particular with electrolyte-enriched water, is able to restore imbalance of autonomic nervous system in dyspeptic patients and improves GI symptoms.

2 | MATERIALS AND METHODS

2.1 | Subjects

The study was performed in Campania, a region of Southern Italy, from October 2013 to February 2014. Ten non-competitive healthy athletes, as control group, (CNT; mean age: 26.5 ± 1.4 years, mean body mass index: 21.8 ± 0.6 kg) and 10 non-competitive athletes (mean age range: 28.4 ± 0.9 years, mean body mass index: 23.2 ± 0.8 kg) with dyspeptic symptoms (FD) were enrolled in the study.[11,12] According to the Rome III criteria for FD,[14] all symptomatic subject had recently (<1 year) performed EGDS and H. Pylori testing in order to rule out organic cause of dyspepsia. The trial was conducted as double blind, limited to the type of water they received during Test A (calcium-bicarbonate) or Test B (soft water). All subjects were studied on three different days at 2-week intervals between each session.

2.2 | Protocol

All subjects underwent a three-session test (0, A, B) each lasting 6 hours, beginning at 9.00 AM after a light breakfast (Figure 1). Thereafter, in random order, after a 60-minute rest (from T0 to T60) they performed a 90-minute exercise session (from T60 to T150) to achieve a 1% dehydration, measured as a decrease in total body weight. After physical activity, during the 60-minute post-stress resting phase (from T150 to T210), rehydration was achieved in both

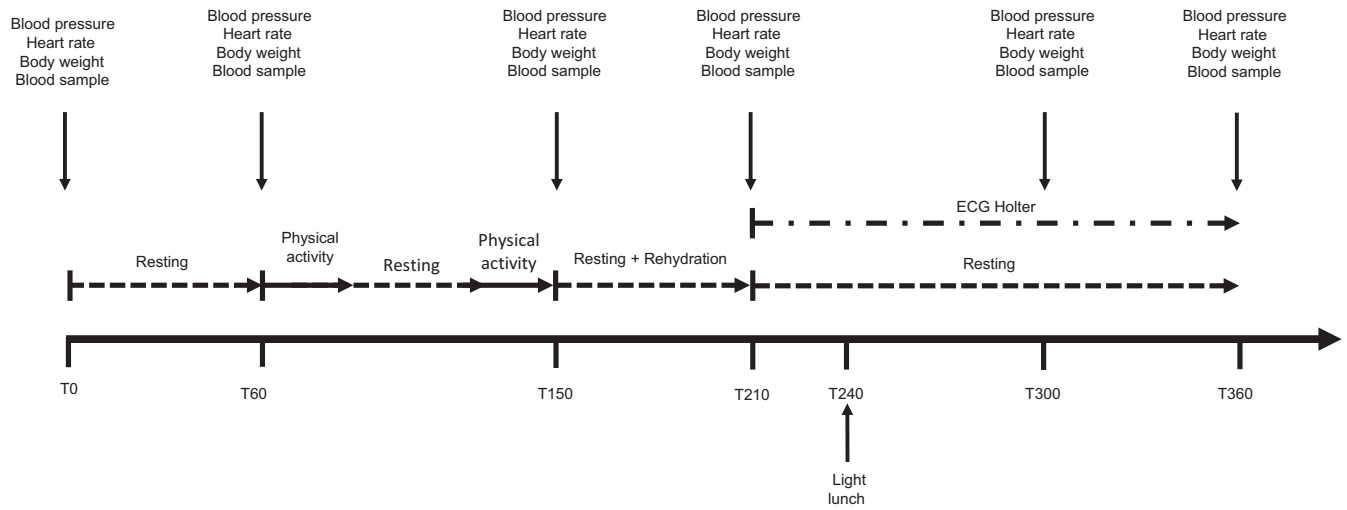

FIGURE 1 Study protocol

Test A and Test B (see rehydration paragraph). All non-competitive athletes were evaluated for blood pressure, heart rate, body weight, and dyspeptic symptoms at basal condition (T0), at the end of physical exercise (T150) and at the end of the rehydration phase (T210); a blood sample was taken to assess changes in plasmatic osmolarity. Thirty minutes after the end resting/hydration phase (T240), every participant was given a light meal. GI symptoms were investigated at 60 (T300) and 120 (T360) minutes after lunch. Holter electrocardiogram (ECG) recordings were obtained from each participant for 150 minutes after the end of the rehydration phase. Each test was performed in an air-conditioned room.

2.3 | Pre-test phase

All subjects were asked to restrain from consuming alcohol, caffeine-containing foods or drinks, drugs, or from performing intense physical exercise the day before each session. During the 7 days before Test A and B (pre-test phase), all subjects received, respectively, five 500 mL bottles/d containing calcium-bicarbonate or soft water and they were encouraged to drink almost 2 L/d of water. Neither bottles nor advices regarding water consumption were administered to subjects undergoing Test 0. Moreover, in order to evaluate the exact amount of water consumed, all participants had to register daily water intake, expressed as number of water glasses (125 mL), on a weekly diary and only subjects undergoing Test A and B had to return all bottles of water.

2.4 | Dehydration test

Dehydration was achieved through a walking/jogging test on a treadmill in two 30-minute stress experiments. Initial speed was set at 5 km/h and constantly increased by 1 km/h every 5 minutes up to 10 km/h. A 30-minute resting phase was allowed between the two sessions. All experiments were performed in a room with a controlled environmental temperature set at 30°C. The study protocol was approved by the Ethics committee of the "Federico II" University of Naples, and all participants received a complete written description of the experiment before giving their informed consent.

2.5 | Rehydration phase

After the dehydration test, during the 60-minute resting phase, rehydration was achieved by administering 500 mL of calcium-bicarbonate (Test A) or soft (Test B) water (see Tables S1 and S2 for water characteristics) No rehydration was performed during Test 0. Athletes were requested to drink the entire amount of water administered during the resting phase, but they were able to choose the speed of rehydration.

2.6 | GI symptoms

At baseline, at the end of both stress and rehydration (when applied) phases, and 60 and 120 minutes after the meal, all participants were asked to report the presence and intensity of GI symptoms using a 100 mm visual analogue scale ranging from 0 (absence) to 100 (severe). Upper GI symptoms investigated were as follows: belching, epigastric pain, epigastric burning, post-prandial fullness, abdominal pain, abdominal bloating, nausea, early satiety, and flatulence. Overall dyspeptic symptom score was calculated in every test as mean of all symptoms for each time (Figure 2). All patients were advised to discontinue any upper GI/motility drugs (prokinetics, proton pump inhibitors) a month before the start of the first test and to avoid the intake of these compounds until they had completed the study protocol.

2.7 | Meal composition and gastric emptying

All subjects were asked to consume a test meal consisting of 60 g white bread, 10 g butter, 50 g ham, an omelet made from one egg with egg yolk doped with 74 kBq 13C-octanoic acid (Eurisotop, Saint Aubin, France) and 500 mL of water (Test A and B). The test meal contained 480 kcal (19% protein, 50% carbohydrate, 31% fat). Subjects were encouraged to eat the meal within 60 minutes. Breath samples were collected into 1.3 L aluminum bags before ingestion of the meal, and samples were obtained at lunch and 30, 60, 90, 120, 150, 180, 210, 240, and 270 minutes following the meal. CO_2 excretion in breath was subsequently analyzed using isotope-selective infrared spectroscopy to derive gastric emptying half-time. A light breakfast at 8.00 AM and mouthwashing with 40 ml of 1% chlorhexidine solution were admitted. Smoking was not allowed 24 hours before and throughout the test. Sampling of expired air, following a deep inspiration, was analyzed by means of a commercial device (SerCon ABCA 13C Breath Analyser) which allowed the detection of CO_2 concentration with an accuracy of ±1 ppm (part per million). After each test, the expired CO_2 concentration of all air samples from each subject was analyzed using a software in order to obtain a final score expressing if gastric emptying was impaired. Delayed gastric emptying was diagnosed when final result was higher than 120.[15]

2.8 | ECG Holter

All subjects underwent a 150-minute ECG Holter recording. Seven electrodes were applied to the anterior chest surface

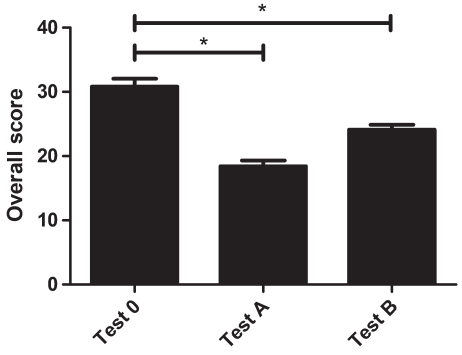

FIGURE 2 Overall symptomatic score in dyspeptic athletes in Test 0, A and B. *$P < 0.001$ vs Test 0

after preparation of the electrode sites with an abrasive paste and electroconductive gel. Electrodes were connected to a three-channel data logger (Syneflash v 1.01F; ELA Medical, Arvada, CO, USA) with a signal amplifier. Patients' data and recording start time were reported on a data logger. The analog ECG signals were converted and stored in digital form to be transferred to a computer. Data were analyzed by a specific software (Synetech v 1.2; ELA Medical) to identify the R-R peaks and interpolate the R-R intervals. Overall, tack analysis was applied to the heart rate variability (HRV) signal to extract two sympathovagal parameters: power in low frequency (LF) and power in high frequency (HF). LF represents mainly sympathetic activity while HF represents parasympathetic or vagal activity. The LF/HF ratio represents the participant's sympathovagal balance and has been calculated in both pre-prandial and post-prandial phases. The LF/HF ratio trend during the meal was calculated in both healthy and dyspeptic non-competitive athletes, as difference between LF/HF ratio before and after the meal ($\Delta LF/HF_{pre\text{-}post}$).

2.9 | Statistical methods

Significant differences in terms of GI symptoms, body weight or plasmatic osmolarity changes, HRV variations, and gastric emptying rate in the three sessions of the study within CNT and FD groups and between CNT and FD were evaluated using paired and unpaired *t* test, respectively. The statistical analysis was performed by the statistical software package SPSS for Windows Version 20.0 (SPSS, Chicago, IL, USA). The results are reported as mean ± SEM. Differences were considered statistically significant when *P* value was <0.05.

A preliminary evaluation of published data variability was performed to calculate sample size. We assumed alpha level at 0.05 and statistical power at 80%. Based on the published data on prevalence of GI symptoms in athletes, we extrapolated sample sizes for 10 patients and for 10 controls.[11,13,15]

3 | RESULTS

3.1 | Pre-test water intake

The amount of water consumed in the 7 days before each session was higher in subject undergoing both Test A and B (1.90 L ± 0.06 and 1.95 L ± 0.05, respectively) if compared to Test 0 (1.60 L ± 0.20). Calcium-bicarbonate water is slightly sparkling compared to soft water (CO_2 1404 mg/L vs 8.2 mg/L). Seventeen subjects (nine dyspeptic and eight healthy subjects) reported that water A had a moderate sparkling taste and only three (one dyspeptic and two healthy subjects) reported no taste perception. None of patients during Test B reported any relevant taste perception.

3.2 | Body mass weight

All subjects completed the two 30-minute walking/jogging sessions for each test. Significant dehydration (paired *t* test), measured as body weight variation after physical exercise (T0 vs T150), was observed in both dyspeptic (Test 0:73.4 ± 3.6 kg vs 72.7 ± 3.5 kg, $P < 0.001$; Test A: 73.0 ± 3.7 vs 72.4 ± 3.6, $P < 0.001$; Test B: 73.1 ± 3.6 kg vs 72.5 ± 3.5 kg, $P < 0.001$) and healthy athletes (Test 0:67.1 ± 2.9 kg vs 66.3 ± 2.9 kg, $P < 0.001$; Test A: 66.6 ± 2.9 vs 66.0 ± 2.9, $P < 0.001$; Test B: 66.8 ± 2.8 kg vs 66.2 ± 2.8 kg, $P < 0.001$). Moreover, the administration of a water load after physical activity (T210) resulted in complete rehydration in both FD (Test A: 73.0 ± 3.6; Test B: 73.0 ± 3.7) and healthy subjects (Test A: 66.7 ± 2.9; Test B: 66.8 ± 2.8). No significant differences, in terms of dehydration or rehydration, were observed in either FD or healthy subjects between Tests A and B.

3.3 | Plasmatic osmolarity

Dehydration was associated with a significant increase in plasma osmolarity during each test in both CNT and FD. In Tests A and B, after rehydration, a significant decrease in osmolarity was observed in both FD and CNT, with no difference between the two tests. No differences were noticed when FD was compared with CNT (see Table 1).

3.4 | GI symptoms

In dyspeptic athletes, dehydration was associated with a significant increase in GI symptomatic score. The total score was significantly increased at the end of Test 0 (VAS: 30.8 ± 0.8 mm) compared to Test A (18.4 ± 1.1, $P < 0.001$) and Test B (24.4 ± 1.3, $P < 0.001$; Figure 2). Very slight symptom increase was recorded in healthy subjects without significant differences between the tests.

TABLE 1 Plasma osmolarity of both controls and dyspeptic patients in each test session

	CNT			FD		
	Baseline Osm	Osm T150	Osm T210	Baseline Osm	Osm T150	Osm T210
Test 0	292.5 ± 2.6	296.5 ± 2.3*	297.9 ± 2.0	291.7 ± 2.4	295.0 ± 2.0*	294.3 ± 2.1
Test A	290.6 ± 2.3	292.8 ± 2.4*	289.7 ± 1.9**	290.1 ± 2.1	293.6 ± 2.7*	287.9 ± 2.9**
Test B	293.7 ± 2.9	296.2 ± 2.6*	291.5 ± 2.8**	294.4 ± 2.4	297.9 ± 3.0*	289.8 ± 2.5**

All data are expressed as milliosmole plus standard deviation.
*$P < 0.01$ vs baseline.
**$P < 0.01$ vs T150.

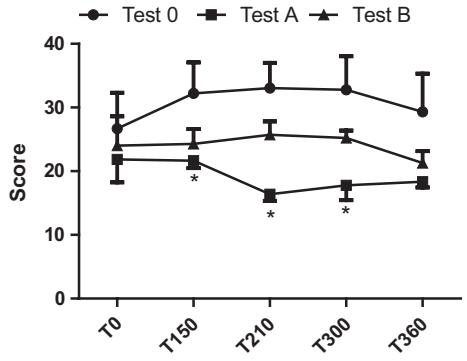

FIGURE 3 Dyspeptic symptoms during Test 0, A and B. *$P < 0.05$ vs Test 0

Moreover, the analyses of dyspeptic symptoms at different time (T0, T150, T210, T 300, and T360, respectively) of each test (Test 0, Test A, and Test B) showed a similar clinical score at baseline when Test 0 was compared to Test A or Test B (Test 0: 26.7 ± 5.6; Test A: 21.8 ± 3.6; Test B: 24.0 ± 4.6). Only subjects undergoing Test 0 experienced a significant worsening of dyspeptic symptoms between T0 and T150 (26.7 ± 5.6 vs 32.2 ± 4.9, $P < 0.01$) while no differences were observed between the same times during both Test A and B. On the contrary, after dehydration, dyspeptic symptoms increased in each session of Test 0 compared to Tests A and B, but significant difference was reached only comparing Test 0 vs Test A for T150, T210, and T300 (T150: 32.2 ± 4.9 vs 21.6 ± 1.2, $P < 0.05$; T210: 33.1 ± 3.9 vs 16.4 ± 1.0, $P < 0.01$; T300: 32.8 ± 5.3 vs 17.8 ± 2.3, $P < 0.05$; Figure 3). No significant differences were observed between Tests A and B, and between Tests 0 and B.

3.5 | Gastric emptying

No differences were observed between dyspeptic and healthy subjects when all tests were compared. Likewise, no statistical differences were observed between Tests 0, A and B in both dyspeptic patients and controls.

3.6 | HRV parameters

In healthy subjects, the comparison between pre-prandial and post-prandial LF/HF ratio in each test showed a decrease in LF/HF ratio after the consumption of the standard meal, albeit not to a statistically significant extent. Moreover, while no significant differences were observed among pre-prandial LF/HF after the three different tests, when post-prandial parameters were compared, the LF/HF ratio in Test 0 (1.7 ± 0.2) was significantly lower than both Test A (2.6 ± 0.4, $P < 0.05$) and Test B (3.1 ± 0.5, $P < 0.05$).

In dyspeptic patients, only during Test A post-prandial LF/HF ratio exhibits a trend to a decrease after the meal, as observed in healthy subjects; in both Test 0 and Test B, instead, there was an increase in post-prandial ratio. The post-prandial ratio (1.5 ± 0.3) after Test A was significantly lower compared to Test 0 (2.3 ± 0.5, $P < 0.05$), while no differences were observed when compared to Test B. No differences were observed among the pre-prandial parameters of each test.

When dyspeptic patients were compared to healthy subjects, pre-prandial ratio was significantly lower in FD in both Test 0 (1.3 ± 0.2 vs 2.7 ± 0.6, $P < 0.05$) and Test B: (1.7 ± 0.3 vs 3.2 ± 0.4, $P < 0.05$), while no significant difference was observed in Test A (Figure 4).

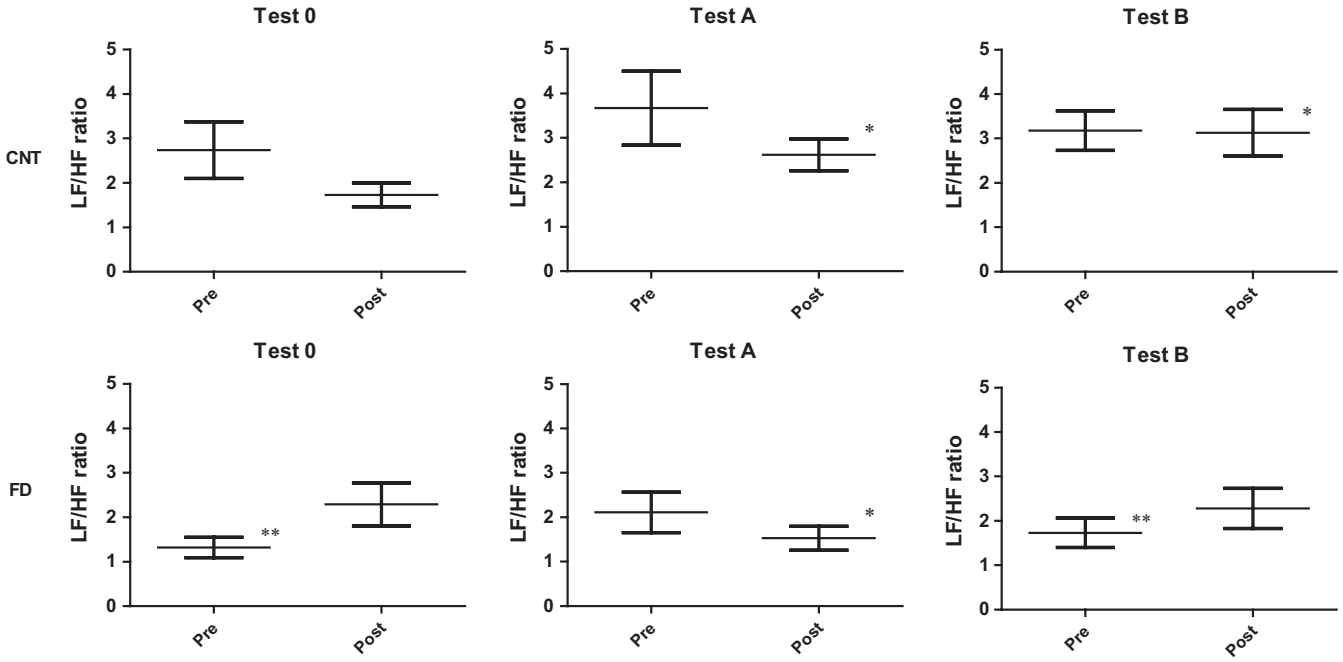

FIGURE 4 Pre-prandial and post-prandial low/high frequency (LF/HF) ratio parameters in both CNT and FD groups during Test 0, A and B. *$P < 0.05$ vs Test 0 Post-prandial LF/HF, in both CNT and FD; **$P < 0.05$ vs CNT Pre-prandial LF/HF

In the dyspeptic group, HRV analyses highlighted that, in Test A, $\Delta LF/HF_{pre\text{-}post}$ (0.6 ± 0.4) was significantly higher than Test 0 and Test B (−1.0 ± 0.5; −0.6 ± 0.5, respectively, $P < 0.05$). Moreover, when $\Delta LF/HF_{pre\text{-}post}$ between CNT and FD were compared, a significant difference was observed in Test 0 (CNT: 1.0 ± 1.6 vs FD: −1.0 ± 1.7; $P < 0.05$) but no significant differences were observed in Test A (CNT: 1.1 ± 0.8 vs FD: 0.6 ± 0.4, ns) and Test B (CNT: 0.1 ± 0.4 vs FD: −0.6 ± 0.5, ns). However, while in Test B the comparison of $\Delta LF/HF_{pre\text{-}post}$ between CNT and FD showed a trend similar to Test 0 with FD exhibiting a negative $\Delta LF/HF_{pre\text{-}post}$ as consequence of a higher postprandial LF/HF ratio, in Test A both CNT and FD displayed the same positive trend of $\Delta LF/HF_{pre\text{-}post}$ (Figure 5).

4 | DISCUSSION

Our results show that mild dehydration in dyspeptic athletes is able to increase GI symptoms and that, at the same time, an adequate rehydration, especially with a calcium-bicarbonate water, is able to improve post-exercise disturbances. Indeed, our finding provides evidence that rehydration with specific types of water may restore the sympathovagal imbalance occurring in subject with FD, leading to a decrease in post-prandial LF/HF ratio, as would be expected in healthy subjects.

In healthy subjects, postprandial LF/HF ratio compared to the fasting state decreased in all tests and was not influenced by the hydration state (dehydration, Test A or B). Only few studies have so far evaluated the sympathovagal balance in the post-prandial phase using the spectral analysis of the HRV, with quite controversial results. Ching-Liang et al. reported an increase in LF/HF ratio lasting at least 1 hour after food ingestion[16]; conversely, Vaz et al.[17] observed a different trend during the post-prandial period, with the LF component unchanged and the HF component tending to a decline . These differences remain unclear, although it has been hypothesized that the type of meal, the timing and setting of the measurement could account for these discrepancies. Moreover, before HRV analyses, our subjects underwent physical stress and mild dehydration with consequent further imbalance of the sympathovagal status.

On the contrary, dyspeptic patients experienced an increase in LF/HF ratio in the post-prandial phase either when rehydration did not occur or when soft water was administered. In these patients, the change in sympathovagal balance was mainly associated with an increase in sympathetic activity, while parasympathetic tone remained stable. Several studies have shown an increased sympathetic tone and a relative reduction of vagal activity in subjects suffering from functional GI disorders, such as FD or IBS[15,18,19]; it has thus been hypothesized that the sympathovagal imbalance may alter GI functions and induce visceral hypersensitivity, typically observed in these patients. Moreover, Iovino et al. have shown that, even in healthy subjects, the activation of the sympathetic nervous system, obtained by changing body position from supine to orthostatism, increased visceral but not somatic sensitivity, leading to the onset of GI symptoms at a lower level of gastric or duodenal distension.[20] According to these results,

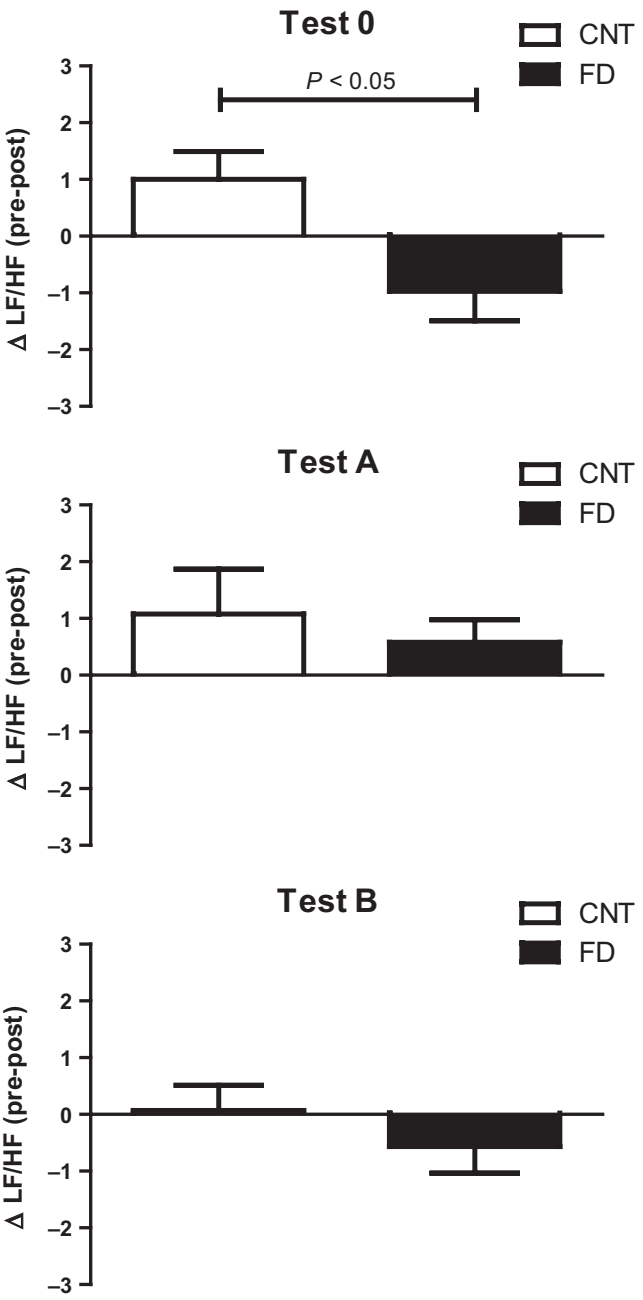

FIGURE 5 Difference between low frequency and high frequency in both control and dyspeptic patients during Test 0 (A), Test A (B), and Test B (C)

dyspeptic patients in both Test 0 and B (dehydration alone or rehydration with soft water, respectively) showed an increased sympathetic tone in the post-prandial phase, possibly explaining why these patients reported more severe symptoms than dyspeptic subject rehydrated with a calcium-bicarbonate water (Test A).

The gastric emptying test was not associated with pathological findings in the dyspeptic group, in either case of dehydration or rehydration, despite dyspeptic patients in Test 0 and B reported higher symptomatic scores than those in Test A. However, the association between delayed gastric emptying and FD is still controversial, as abnormal results have been reported in a subset of patients with FD,

ranging from 25% to 30%, with some studies surprisingly reporting even accelerated gastric emptying.[21,22] In these patients, gastro-duodenal hypersensitivity to distension and acid seems to have a pivotal role in the onset of symptoms, and the evidence that the LH component was higher in post-prandial phase support this hypothesis. In fact, Iovino et al. have shown that the activation of the sympathetic nervous system is associated with a selective increase in visceral sensitivity as a result of sympathovagal imbalance. However, they observed that, in healthy subjects, the activation of gut reflexes heightened the perception of intestinal distension without impairing somatic sensitivity.[20]

Different studies have evaluated how the hydration state may influence the sympathovagal balance and which is the effect of dehydration on the health status of athletes. Moreover, the imbalance of the autonomic nervous system in functional dyspeptic patients, and the consequent visceral hypersensitivity, has been widely demonstrated.[23,24] In our study, we evaluated for the first time how dehydration, but in particular rehydration with different types of water, may influence sympathovagal balance in dyspeptic athletes and trigger the onset GI symptoms.[25] We have also shown that an adequate rehydration, with a calcium-bicarbonate water, is able to improve post-exercise disturbances, restoring sympathovagal imbalance, as would be expected to occur in healthy subjects.

Our data show that hydration itself, whether water is enriched or not with electrolytes, is able to improve dyspeptic symptoms. However, we have also observed that calcium-bicarbonate water is able to further improve post-exercise symptoms in dyspeptic patients better than soft water. For this reason, it is possible to speculate that such beneficial effect may be associated with the higher concentration of several electrolytes observed in this type of water. In fact, during physical activity, several electrolytes are lost via sweating with consequent imbalance of body fluid homeostasis and normal physiological functions.[26,27] Several studies have shown that interstitial ions concentration appears to be as important as plasmatic electrolyte levels since cellular homeostasis may be deeply influenced by imbalance of both.[28] Sodium, calcium, and magnesium, for example, exhibit a pivotal role in both muscular and neuronal cell activity and either acute or chronic deficiency of such electrolyte is associated with severe muscular or neurologic disorders. As shown by O'Mahony et al.,[29] the homeostasis of digestive tract is ensured by several regulatory pathways which control GI motility/secretion or sensation and their dysfunctions may contribute to the symptoms that characterize functional GI disorders (FGIDs). In line with this, inadequate fluid intake may cause mild electrolytes alterations able to worsen autonomic imbalance typical of FGIDs, and it is possible to hypothesize that the administration of an appropriate amount of water enriched in electrolyte, such as calcium-bicarbonate water, may be able to improve GI symptoms restoring regular sympathetic/parasympathetic balance. The role of electrolytes to further improve dyspeptic symptoms can be matter of future studies particularly oriented to interstitial electrolytes' concentration rather than plasmatic values.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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