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Applied nutritional investigation

Hydrogen-rich water upregulates fecal propionic acid levels in overweight adults

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The intricate relationship between the gut microbiota, its metabolites, and human health has garnered significant attention in recent years because of its potential role in the development of many diseases [1]. Among the various metabolites produced by the microbiota, a group of organic acids, known as short-chain fatty acids (SCFAs), has emerged as key regulators of host energy metabolism. These saturated aliphatic organic acids are produced through the bacterial fermentation of dietary fibers, with acetic acid, propionic acid, and butyric acid comprising 95% of the SCFA pool [2]. Interestingly, different SCFAs can elicit distinct local and systemic metabolic responses throughout the body [3]. Extensive scientific evidence has underscored the potential significance of increasing SCFA levels in the prevention and treatment of various conditions, leading to research exploring dietary interventions to enhance SCFA production. Preclinical and clinical studies have found that hydrogen gas has emerged as a promising agent for influencing gut microbial biology, among other interventions. The consumption of hydrogen-rich water (HRW) has been found to modulate colonocyte metabolism in mouse models [4], promote the growth of beneficial bacteria in rats [5], and elevate total serum levels of SCFAs in overweight individuals [6]. However, it remains unclear whether hydrogen intake has any effect on the specific stool profiles of individual SCFAs. In this study, we conducted a secondary analysis of a previously completed, medium-term, randomized controlled trial involving HRW, using an advanced method to assess fecal levels of acetic acid, propionic acid, and butyric acid in overweight adults.

This report includes a total of 10 middle-aged overweight individuals (five women), with an average age of 44.5 ± 13.2 y and a body mass index of 28.3 ± 2.1 kg/m^2. These participants were randomly assigned to receive either HRW 0.5 L/d, containing 3 mg of hydrogen (two men and three women), or placebo (tap water: three men and two women) for a duration of 12 wk. The levels of individual SCFAs were assessed using gas chromatography–mass spectrometry. Specifically, fecal concentrations of acetic acid, propionic acid, and butyric acid (expressed as milligrams per gram of stool) were measured using a sensitive detection method for analyzing the microbial metabolites, SCFAs, in fecal samples. The analysis was performed using a 7890B GC system coupled to a 5997A MSD mass detector on an HP-5ms column (Agilent Technologies, Waldbronn, Germany), as previously described [7]. Further information on the methodology, participant characteristics, and ethical considerations can be found elsewhere [6].

The changes in fecal concentrations of three SCFAs after the interventions of HRW and placebo are depicted in Figure 1. After a

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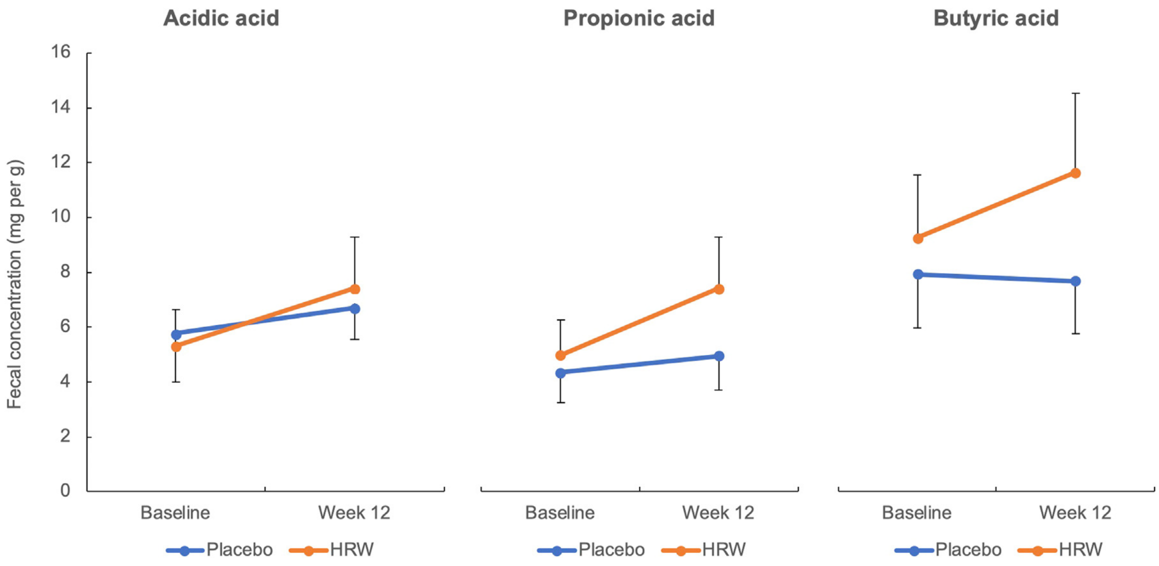

Fig. 1. The changes in fecal levels of acidic, propionic and butyric acid after a 12-wk intervention with hydrogen-rich water (HRW) and placebo. The values are presented as the mean, and the error bars represent SE.

12-wk consumption of HRW, there was an average increase of 2.10 mg/g for acetic acid (95% CI, −2.1 to 6.3), 2.44 mg for propionic acid (95% CI, −1.9 to 6.8), and 2.98 mg for butyric acid (95% CI, −6.9 to 12.9). The analysis of the area under the curve using the C statistic indicated a significant difference between HRW and placebo for propionic acid (P = 0.046), with HRW exhibiting a significantly higher area under the curve (74.6 ± 31.9 mg · w · g) compared with placebo (55.8 ± 22.1 mg · w · g). There was a notable trend of increased fecal butyric acid levels after area under the curve intervention (156.6 ± 94.4 mg · w · g versus 117.1 ± 48.1 mg · w · g; P = 0.21), but no significant difference in AUC was observed between the interventions for acetic acid (P = 0.46).

This secondary analysis of previously collected data suggests that fecal SCFAs are responsive to dietary hydrogen in overweight adults, with a significant increase observed in propionic acid levels in participants who consumed HRW for 12 wk compared with those who consumed tap water. This finding holds potential significance in addressing metabolic dysregulation, as propionic acid has been linked to appetite control and weight management in populations with metabolic conditions [8]. Our findings partially align with previous animal studies where HRW was found to promote the production of butyric acid and acetic acid in models of colitis in mice [4] and piglets fed a diet contaminated with fusarium toxin [9]. Variations in the specific SCFAs upregulated by HRW across studies may be attributed to differences in the mammalian species analyzed (e.g., rodents, piglets, and humans), disease models used (e.g., overweight, colitis, and mycotoxin), and variations in the duration and dosage of hydrogen exposure. We have reported, for the first time, that drinking HRW can stimulate the upregulation of propionic acid in the colon; however, the extent of propionic acid uptake by the systemic circulation and its effects on target organs (including the brain and liver) remain unaddressed at this time. A recent report found beneficial effects of altering SCFA profiles in irritable bowel syndrome, with propionic acid levels increased after fecal transfer [10]. A possible HRW-driven rise in fecal propionic acid thus could be clinically relevant to irritable bowel syndrome; whether HRW facilitates SCFA levels in this common condition remains unknown. The increased production of propionic acid by the gut microbiota is considered beneficial in several metabolic diseases, including obesity and type 2 diabetes mellitus. It appears that propionic acid lowers fatty acid content in liver and plasma, reduces food intake, exerts immunosuppressive actions, and probably improves tissue insulin sensitivity [11]. Yet, only limited information has been available regarding the possible side effects of propionic acid. Propionic acidemia is a rare genetic metabolic disorder characterized by accumulation of propionic acid and its metabolites, leading to a variety of complications, including life-threatening cardiac diseases [12]. Therefore, possible use of propionic acid and/or any propionic acid−producing agents requires careful monitoring and dose-specific pharmacovigilance studies. Nevertheless, the upregulation of propionic acid adds to the growing list of potential metabolic pathways influenced by exogenous hydrogen [13]. Further large-scale, long-term trials are necessary to validate HRW as an innovative functional beverage for enhancing SCFA levels and supporting metabolic health in experimental and clinical nutrition.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

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