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A novel approach to the dual sugar test for the assessment of intestinal epithelium permeability in response to exertional heat stress and nutritional intervention

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An acute increase in intestinal epithelium permeability is induced by prolonged exertion in the heat, resulting in the translocation of pathogenic bacteria and endotoxins from the lumen into the circulation, causing a systemic inflammatory response and debilitating symptoms[1]. Acute exercise-induced gastrointestinal syndrome mimics chronic health conditions with which an impaired intestinal barrier function is associated, including coeliac disease, inflammatory bowel disease, diabetes, Alzheimer's and liver diseases[2]. Intestinal epithelium permeability is typically assessed using a dual sugar absorption test, by administering a drink containing non-metabolisable sugars (e.g. lactulose [L] and L-rhamnose [R]) that can enter the circulation by paracellular translocation when the epithelium is compromised, and are subsequently excreted and measured cumulatively in the urine[3]. We aimed to demonstrate that our recently developed ion chromatography protocol[4] can be used to accurately quantify L/R ratio in the plasma of participants exercising in hot ambient conditions and to determine the impact of nutritional intervention on intestinal epithelium permeability. Further, we hypothesised that measuring L/R in plasma collected at intervals during the post-exercise recovery period would reveal more information about intestinal permeability compared to previously published cumulative urine L/R data[3]. Endurance-trained participants completed a set of randomised crossover studies, consisting of 2 h running at 60% $\dot{V}O_{2max}$ in temperate, warm and hot ambient conditions (n = 8) and/or in the heat while consuming water, carbohydrate or protein (n = 9). The dual sugar solution was ingested at 90 min of exercise and blood was sampled at 0, 1, 2 and 4 h post-exercise. Plasma sugars were quantified by high-performance anion exchange chromatography with pulsed amperometric detection (HPAEC-PAD) and L/R ratios were compared by two-way repeated measures ANOVA with Tukey's multiple comparisons. Plasma L/R increased immediately post-exercise in the heat (0.15 ± 0.11) compared with temperate (0.06 ± 0.04, $p<0.001$) and warm (0.09 ± 0.08, $p<0.01$) conditions, while consuming glucose before and during exercise alleviated this (0.02 ± 0.02, $p<0.001$), and this novel information was otherwise missed when measuring urine L/R. Consuming glucose or whey protein hydrolysate during exercise attenuated intestinal permeability from exertional heat stress throughout recovery, with the mean plasma L/R over 4 h reduced from 0.11 ± 0.05 to 0.04 ± 0.03 ($p<0.001$) and 0.06 ± 0.04 ($p<0.01$) with glucose and protein, respectively. We recommend using the dual sugar test with quantification of plasma sugars at intervals by HPAEC-PAD to maximise intestinal permeability data collection in exercise gastroenterology research and beyond, as this gives additional acute response information compared to urinary measurements. Our approach can be employed to investigate and develop personalised nutrition strategies that prevent intestinal hyperpermeability during exertional heat stress. This has implications for athlete performance and safety, and can also build upon occupational health and safety practices and inform chronic disease management.

Keywords: leaky gut; gastroenterology; exercise; HPAEC-PAD

Ethics Declaration

Yes

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