Nutrient-induced hyperosmosis evokes vasorelaxation via TRPV1-mediated endothelium-dependent hyperpolarization in normal and colitis mice

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May 14, 2020

Abstract

Background and Purpose: Although human blood flows are redistributed into the mesenteric circulation after meals, it is not well understood how postprandial nutrients induces vasorelaxation of mesenteric micro-arterioles and whether this process is involved in the pathogenesis of colitis. Experimental Approach: We used an auto dual wire myograph system, fluorescence imaging system and DSS-induced colitis mouse model to investigate the roles and mechanisms of nutrient-induced mesenteric relaxation in health and disease. Key Results: We found that acute application of glucose and sodium induced endothelium-dependent relaxation of human and mouse mesenteric micro-arterioles via a hyperosmotic action, which also stimulated Ca2+ influx through endothelial TRPV1 channels. The nutrient-induced vasorelaxation was almost abolished by selective blockers for TRPV1, IKCa and SKCa channels, but marginally altered by inhibition of nitric oxide production. The nutrient-induced hyperosmosis also activated functional activities of Na+/K+-ATPase and Na+/Ca2+-exchanger to further reduce [Ca2+]i in vascular smooth muscle cells. Moreover, hyperosmosis-induced endothelium-dependent hyperpolarization was significantly impaired in colitis mouse model. Conclusion and Implications: Our study provides the first evidence that nutrient-induced hyperosmosis stimulates endothelial TRPV1/Ca2+/EDH signaling pathway to eventually evoke vasorelaxation of mesenteric micro-arterioles, which may contribute to the pathogenesis of colitis as well.

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