Mechanism of Alcohol Induced Mesenteric Lymphatic Vessel Leakage

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Introduction: Lymphatic vessels are involved in the trafficking of immune cells and play a role in antigen transport and immune cell regulatory functions. Lymphatic endothelial tight junctions (TJ) form a seal between endothelial cells and help to control diffusion of molecules across the endothelium, regulating the permeability of the lymphatic barrier. Our previous studies have shown that alcohol consumption can disrupt lymphatic permeability, leading to increased leakage of molecules from the lymphatic system into perilymphatic adipose tissue (PLAT). As a consequence, metabolic dysregulation in PLAT was found, characterized by PLAT inflammation and impairment of insulin-dependent responses. Although the mechanisms underlying alcohol-induced lymphatic vessel leakage are unknown, in blood vessels, alcohol-induced barrier dysfunction involves MAP Kinases (MAPK- Erk ½ and p38) activation and TJ impairment. Thus, we hypothesized that alcohol induces lymphatic leakage via disruption of lymphatic endothelial tight junctions via MAPK activation.

Objective: To prove that alcohol may induce lymphatic leakage via disruption of lymphatic endothelial tight junctions via MAPK activation.

Material and Methods: To test our hypothesis we used commercially available lymphatic endothelial cells and investigated MAPK and TJ (Claudin-5, ZO-1, and Occludin) expressions. The cells were incubated in 0, 25, and 50 mM of alcohol-supplemented cell culture media for 48 hours. Following alcohol treatment, total protein was extracted and analyzed via western blotting or the cells were fixed for immunohistochemistry.

Results: We found that alcohol increased Erk ½ phosphorylation compared to controls but didn't change p38 phosphorylation. Alcohol also decreased TJ expression compared with controls.

Conclusions: These Overall, alcohol-induced lymphatic leakage might be due to MAPK activation, leading to TJ protein phosphorylation and lymphatic endothelial barrier loss.

Keywords: alcohol, lymphatic leakage, tight junction, MAP kinases

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