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“Alcohol-mediated Gut Dysbiosis Leads to Reduce Nitric Oxide Bioavailability and Vascular Dysfunction”

Background: Chronic and hazardous alcohol use has adverse effects on cardiovascular function and homeostasis leading to increased risk of cardiovascular disease (CVD). Hazardous alcohol use has also been linked to gut dysbiosis. However, it is unknown if alcohol mediated gut dysbiosis has effects on vascular endothelial function and subsequent development of CVD.

Hypothesis: In this study, we hypothesized that binge-on-chronic alcohol exposure, through gut dysbiosis, leads to vascular dysfunction and increased susceptibility to develop CVD.

Methods: We studied C57BL/6 mice at 10 weeks of age for these studies. Mice underwent binge-on-chronic alcohol feeding (n=18), pair-fed (n=18) or binge-on-chronic alcohol + probiotics (daily) (n=8) for 20-days. Vascular reactivity, plasma nitrite, measured by HPLC, and oxidative stress were measured. Another cohort of mice (n=11-12 per group) received broad-spectrum antibiotics for 10 days followed by a cecal microbiota transplant from either pair-fed or binge-on-chronic fed mice. Plasma nitrite levels were measured to assess nitric oxide bioavailability and vascular function.

Results: Binge-on-chronic alcohol consumption resulted in a significant reduction in plasma nitrite levels compared to the pair-fed animals. Moreover, probiotics were able to significantly increase plasma nitrite levels. Endothelial vasorelaxation was significantly attenuated in the binge-on-chronic group compared to pair-fed controls and was partially restored through probiotic administration. Furthermore, mice in the adoptive transfer study who received microbiota from binge-on-chronic fed mice had a reduced plasma nitrite level versus pair-fed controls.

Conclusion: Binge-on-chronic alcohol induced reduce nitic oxide bioavailability, impaired endothelial-based vascular dysfunction and increase oxidative stress. Daily probiotic administration was able to attenuate these findings. The adoptive transfer of microbiota content from binge-on-chronic alcohol mice reduced plasma nitrite levels demonstrating that the alterations to the gut microbiome due to alcohol are sufficient to reduce nitric oxide bioavailability.