**Alcohol-mediated Gut Dysbiosis Leads to Reduced Nitric Oxide Bioavailability and Vascular Dysfunction**

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**Introduction**

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 and alteration in gut derived metabolites. However, it is unknown if alcohol mediated gut dysbiosis has effects on vascular endothelial function and subsequent development of CVD.

**Study Experimental Protocol**

- **Pair-fed** (n=20) (completed)
- **Binge-on-chronic** (n=21) (completed n=21)
- **Binge-on-chronic + Probiotics** (n=28) (completed n=8)

**Results**

- **Circulating Nitrite Levels.** Plasma nitrite levels were measured using high performance liquid chromatography (HPLC). Samples were acquired at the 20-day time point. Alcohol controls and a significant reduction in the circulating nitrite levels compared to pair-fed controls. This reduction in the alcohol-fed controls was significantly attenuated in the presence of probiotic administration. Pair-fed control and Alcohol control (n=18). Alcohol + probiotics (n=8).

**Results**

- **Aortic Vascular Reactivity.** Thoracic aorta was isolated and dissected into rings for vasorelaxation experiments. (A) Aortic % relaxation with increasing doses of acetylcholine (ach). (B) Concentration of Ach at 50% the maximal relaxation. (C) Aortic % relaxation with increasing doses of sodium nitropusrate (SNP). (D) Concentration of SNP at 50% the maximal relaxation. Vasorelaxation was significantly blunted in the alcohol control animals. This loss of endothelial dependent vasorelaxation was significantly restored in the presence of probiotic treatment. There was no change in endothelial independent vasorelaxation with SNP. Pair-fed control (n=8). Alcohol control (n=7). Alcohol + probiotics (n=8).

**Conclusions**

Binge-on-chronic alcohol induced reduced nitric oxide bioavailability, impaired endothelial-based vascular dysfunction and increase oxidative stress (data not shown). Daily probiotic administration was able to attenuate these findings. The adaptive 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 is sufficient to reduce nitric oxide bioavailability and potentiate vascular dysfunction.