GASTROINTESTINAL BARRIER PERMEABILITY AND ASSOCIATED INFLAMMATORY RESPONSE DURING EXERCISE AT SIMULATED ALTITUDE

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ABSTRACT

PURPOSE: Intense exercise at altitude can reduce blood flow to the gut by >70%. This study tested whether ischemic stress during exercise at altitude also promotes gastrointestinal barrier permeability and a pro-inflammatory response. METHODS: Subjects (N=5) completed two 60min treadmill runs at a workload equivalent to 60%VO₂max. One was performed at sea level (F2O2 21%) and the other at 13,250 ft of simulated altitude (F2O2 14%). Blood samples were collected before (PRE), after (POST), 1hr (1-POST), and 4hrs after (4-POST) exercise. From these samples the circulating concentration of IL-6 was measured with ELISA. Data were analyzed with Two-Way RM-ANOVA. Data were analyzed with Two-Way RM-ANOVA. RESULTS: Gut damage and leukocyte activation were increased at simulated altitude. CONCLUSION: Preliminary data suggest that exercise at altitude increases gastrointestinal barrier permeability. It may contribute to greater leukocyte activation, which acts as an anti-inflammatory myokine when produced by muscle and as a pro-inflammatory myokine when secreted by macrophages/monocytes. As IL-6 increases, it can lead to a reciprocal increase in IL-10 and TNF. Higher levels of these cytokines suggest increased inflammation and endotoxemia risk [3].

INTRODUCTION

• Intense exercise increases gastrointestinal barrier damage and endotoxemia risk [1]. It is unknown whether performing exercise at altitude, which reduces perfusion of the gastrointestinal (GI) tract, further increases these factors.

• Gastrointestinal (GI) barrier damage causes an increased concentration of IL-6 in circulation [2]. GI damage also stimulates macrophages to secrete IL-8, which activates neutrophils and causes them to home to sites of inflammation [3]. IL-8, along with CD14, ICAM-1, MCP-1, and MPO serve as markers of leukocyte activation in response to inflammation [4]. Both IL-1β and TNF can cause ICAM-1 to be upregulated. IL-6 can be produced by both muscle contraction and secreted by macrophages and monocytes; it acts as an anti-inflammatory myokine when produced by muscle and as a pro-inflammatory myokine when secreted by macrophages/monocytes. As IL-6 increases, it can lead to a reciprocal increase in IL-10 and TNFs. Higher levels of these cytokines suggest increased inflammation and endotoxemia risk [5].

• This single-blind, normoxia-controlled research protocol investigated the effect of exercise in a hypoxic environment on human subjects’ responses to exercise at 13,250 ft of simulated altitude. Systems-level physiological responses were assessed. Enzyme linked immunosorbent assays were used to assess circulating markers of gut permeability, leukocyte activation, and inflammation.

METHODS

RESULTS

Gut Damage

Leukocyte Activation

Cytokine Responses

CONCLUSIONS

• Intestinal permeability (as shown by FABP) increased significantly from PRE to POST exercise in HYPOXIA, but not NORMOXIA (Figure 1).

• Increased IL-6 and IL-10 levels in HYPOXIA suggest that both inflammatory as well as anti-inflammatory cascades are increased during exercise at simulated altitude (Figure 3).

• Collectively, these data suggest that compared to moderate intensity exercise at sea level, exercise at altitude may increase gut damage, leukocyte activation, and pro/anti-inflammatory cytokine secretion. It is possible that these factors could contribute to acute mountain sickness-associated symptoms.

REFERENCES


