COMPARING ACUTE MOUNTAIN SICKNESS DEFNITIONS TO EXAMINE DIFFERENCES IN SYSTEMIC INFLAMMATION

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Introduction

The low oxygen levels that exist at high altitudes are often a difficulty for those that live, work, and travel to these extreme environments. Most people successfully adjust to the low partial pressure of oxygen, while those who do not use proper acclimatization or ascent profiles can develop acute mountain sickness (AMS). AMS occurs when individuals go too high in altitude too quickly. The pathophysiology behind AMS remains unknown, however, AMS is associated with hypoxemia (low blood oxygen) which everyone gets when going to high altitude (Loeppky et. al., 2008). Hypoxia at altitude increases inflammation and AMS is reported to be associated with systemic inflammation as measured by elevated cytokines such as interleukins (Wang, 2018). AMS was defined by the following definitions: 1) Lake Louise Questionnaire (LLQ) score ≥3 and a headache score ≥1 at the 10-hour time point, 2) maximum LLQ score ≥3 and a maximum headache score of ≥1, 3) maximum LLQ score ≥3 and a maximum Environmental Symptoms Questionnaire (ESQ) score of 0.7 or maximum LLQ ≥3, a maximum headache score ≥2, and a maximum ESQ ≥0.4, 4) maximum LLQ ≥3, 5) LLQ score ≥3 at the 10-hour time point. The purpose of this study was to determine if the AMS definition used will alter the association between AMS and inflammation.

Methodology

- 34 subjects (17 female)
- UO Evonuk Environmental chamber simulated conditions at ~15,600 ft (11.5% oxygen)
- AMS scores and plasma samples collected before entering the chamber, at 4 hours, 7 hours, 10 hours, and after breathing oxygen from outside the chamber
- AMS scores assessed using the Lake Louise Questionnaire (LLQ) and Environmental Symptoms Questionnaire (ESQ)
- Plasma samples were stored at -80°C in a freezer
- Plasma samples were assayed for 13 inflammatory markers using a 13-Plex Bead Based Assay Kit (LegendPlex, BioLegend)
- Inflammatory markers include: IL-1β, INF-α2, IFN-γ, TNF-α, MCP-1, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33, and IL-10
- Beads were divided by size and internal fluorescence intensity to determine the quantity of each cytokine in the sample

Results

Table 1. Comparing the number of AMS- and AMS+ participants for each AMS definition.

Subject ID	Definition 1	Definition 3	Definition 5	Definition 2	Definition 4
AMS-075	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-012	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-082	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-049	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-070	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-150	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-627	AMS-	AMS-	AMS-	AMS-	AMS-
AMS-001	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-808	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-021	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-092	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-376	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-120	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-404	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-017	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-061	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-273	AMS+	AMS+	AMS+	AMS+	AMS+
AMS-039	AMS-	AMS-	AMS-	AMS+	AMS+
AMS-298	AMS-	AMS-	AMS-	AMS+	AMS+
AMS-044	AMS-	AMS-	AMS+	AMS-	AMS+
AMS-101	AMS-	AMS-	AMS+	AMS+	AMS+
AMS-232	AMS-	AMS+	AMS+	AMS-	AMS+
AMS-313	AMS-	AMS+	AMS-	AMS+	AMS+
AMS-072	AMS-	AMS-	AMS+	AMS+	AMS+
AMS-653	AMS-	AMS+	AMS+	AMS-	AMS+
AMS-048	AMS+	AMS-	AMS-	AMS+	AMS+
AMS-018	AMS+	AMS-	AMS-	AMS+	AMS+
AMS-014	AMS+	AMS-	AMS-	AMS+	AMS+
AMS-052	AMS+	AMS-	AMS-	AMS+	AMS+
AMS-927	AMS-	AMS+	AMS+	AMS+	AMS+
AMS-034	AMS-	AMS+	AMS+	AMS+	AMS+
AMS-523	AMS-	AMS+	AMS+	AMS+	AMS+
AMS-045	AMS+	AMS-	AMS+	AMS+	AMS+
AMS-921	AMS+	AMS+	AMS-	AMS+	AMS+
AMS- Subjects	18	17	15	10	7
AMS+ Subjects	16	17	19	24	27

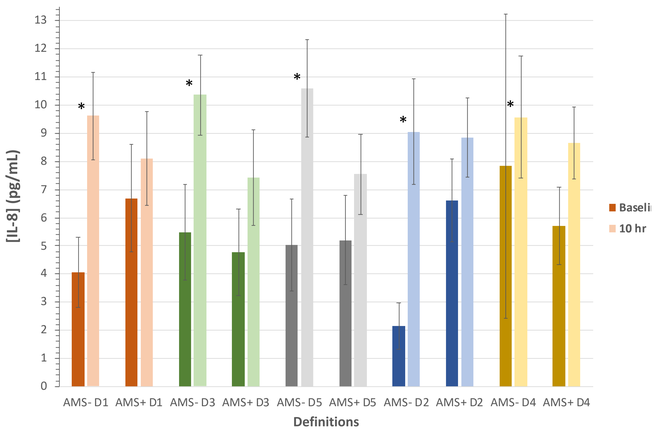

Figure 1. **Change in [IL-8] from baseline to 10 hours in AMS- and AMS+ subjects comparing AMS definitions.** Note that AMS- subjects significantly increase [IL-8] while AMS+ subjects do not. *p<0.05 paired t-test. Mean ± SEM.

Results

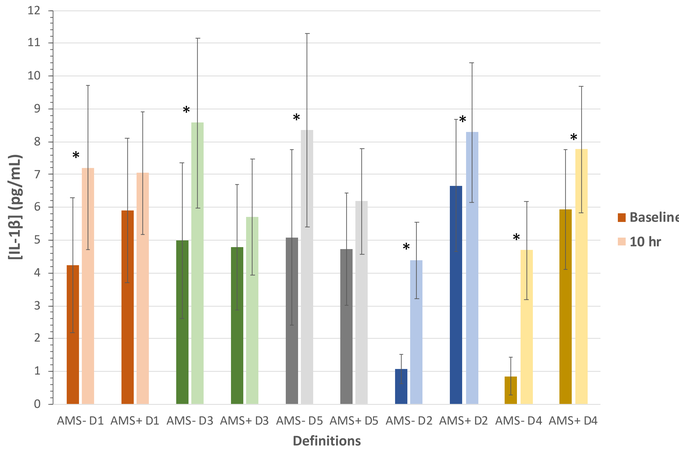

Figure 2. **Change in [IL-1β] from baseline to 10 hours in AMS- and AMS+ subjects comparing AMS definitions.** Note that there is a significant increase in [IL-1β] for all subjects except AMS+ subjects for definitions 1, 3, and 5. *p<0.05 paired t-test. Mean ± SEM.

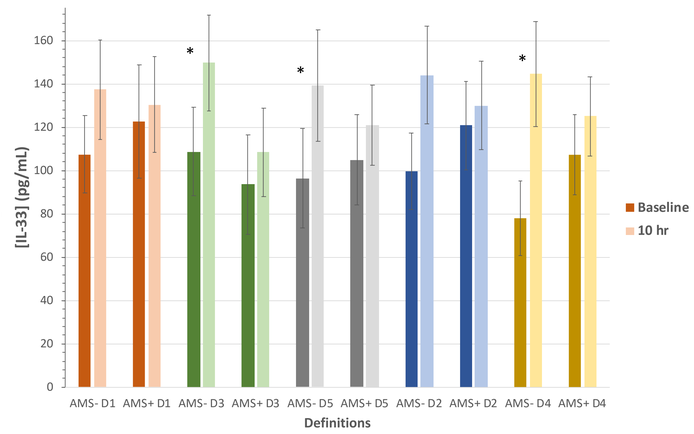

Figure 3 **Change in [IL-33] from baseline to 10 hours in AMS- and AMS+ subjects comparing AMS definitions.** Note that AMS- subjects significantly increase [IL-33] only for definitions 3, 4, and 5. *p<0.05 paired t-test. Mean ± SEM.

Summary & Conclusions

- IL-8 significantly increased in AMS- but not AMS+ participants regardless of the AMS definition. This indicates that IL-8 may be important in reducing AMS susceptibility by the activation of neutrophils that IL-8 causes (**Figure 1**)
- The change in [IL-1β] was not significant for AMS+ subjects for definition 1, 3, & 5. IL-1β helps lymphocytes fight infections, so AMS- subjects may have additional protection during hypoxia (**Figure 2**)
- AMS- subjects, not AMS+ subjects, significantly increased [IL-33] for definitions 3, 4, and 5 so IL-33 is not involved in altitude headaches (**Figure 3**)
- The AMS definition used may alter the observed relationships between AMS and systemic inflammation.

References

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