Chemokines in High Altitude Pulmonary Edema

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To the Editor

We read the article titled “Hypoxia-induced inflammatory chemokines in subjects with a history of high-altitude pulmonary edema” by Mishra et al. [1] with profound interest. Indeed hypoxia exposure whether, in vitro or in vivo, is associated with rise in inflammatory markers. However, in the previous studies, as also quoted in the article by the authors, the duration of hypoxia exposure varied from 16 to 72 h [2–5]. On the contrary, in the present study duration of simulated hypoxia of 4500 m was only 30 min. It remains obscure that those changes seen in the chemokines are actually the result of hypoxia induced inflammation or otherwise. The baseline values of all chemokines (MIP-1 α , MCP-1 and IL-8) in HAPE-S group were found to be higher compared to control group. It would be nice to know if any inclusion/exclusion criteria were applied for selection of subjects to control for confounders like presence of common infections or bronchial asthma which might contribute to higher levels of chemokines [6]. There was considerable variation in the values of chemokines among subjects of HAPE-S group. We would like to know if data regarding time elapsed since previous episode of HAPE was collected, which might possibly explain the variation in baseline and exposure values of chemokines in the HAPE-S group.

Authors of the present study have compared SpO₂ levels in subjects susceptible and resistant to high pulmonary edema (HAPE) but have inadvertently missed out the comparison of respiratory rate (RR) and heart rate (HR) in them. Differences in these two parameters among participants of the two groups would have clarified variations of compensatory mechanisms in response to hypoxia among the HAPE-S group compared to control group. Thus reporting of RR and HR could have elucidated further the findings of this study as tachypnoea and tachycardia are two important signs which form the diagnostic criteria for HAPE [7].

In HA medicine, HAPE is not considered a severe form of acute mountain sickness (AMS) as mentioned by the authors. HAPE and AMS are two distinguished forms of high altitude illnesses with hypoxia as a common causative agent. HAPE can also occur without any symptoms of AMS [8]. Also, HAPE is not limited to only genetically susceptible individuals as they are the ones who report their illness earlier than the general population. Essentially all healthy people are vulnerable to HAPE [9]. In fact during Operation Everest II, after a rapid ascent to 6100 m in a chamber all the seven participants developed HAPE [10]. Occurrence of overt or clinical form of HAPE is dependent on quantum of hypoxia exposure (altitude achieved), rate of ascent, duration of hypoxia exposure and amount of physical activity undertaken at that altitude by the individual [9]. Therefore, assuming that an individual resistant to HAPE at 3400 m will not suffer from it at 4500 m seems to be an anomaly. Possibly, results of the present study could have been very interesting if chemokine levels were studied in these individuals after exposure to simulated hypoxia equivalent to 3400 m for a longer duration (like 24 h) as clinical HAPE is known to occur after an exposure to hypoxia of 2 or more days after an ascent to altitudes above 3000 m [11].

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Moreover, HAPE is a rare disease with a reported incidence of 0.31 % in Northern Himalayas and incidences of HA related illnesses are known to reduce with acclimatization [12]. This has been acknowledged by the authors as well. In a disease with such a low incidence, practical use of measurement of inflammatory markers for identification of individuals at risk of HAPE remains to be seen considering the extensive interaction between hypoxia-related and inflammatory chemical pathways [13] and wide arrays of inflammatory, infectious and other conditions which are likely to cause elevation of chemokines in participants [6].

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