Commentary

Caudwell Xtreme Everest: a field study of human adaptation to hypoxia

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Abstract

Caudwell Xtreme Everest (CXE) is a large healthy volunteer field study investigating human adaptation to environmental hypoxia. More than 200 individuals were studied at sea-level and in four laboratories on the trek to Everest Base Camp (5,300 m). Fifteen physicians climbed high on Everest and continued the studies as they ascended; eight of these individuals reached the summit of Everest and succeeded in sampling arterial blood at 8,400 m on their descent. Core measurements included cardiopulmonary exercise testing, neuropsychological assessment, near infra-red spectroscopy of brain and exercising muscle, blood markers and daily recording of simple physiological variables. The goal of CXE is to further our understanding of human adaptation to cellular hypoxia, a fundamental mechanism of injury in critical illness, with the aim of improving the care of critically ill patients.

Caudwell Xtreme Everest (CXE) is a large, healthy volunteer field study investigating human adaptation to environmental hypoxia [1]. The project is organised by the Centre for Altitude Space and Extreme Environment Medicine (CASE Medicine) at University College London. During April and May 2007 more than 200 individuals were studied as they were progressively exposed to hypobaric hypoxia on the trek to Everest Base Camp at 5,300 m. Most of these individuals were volunteers who gave up their holidays to be participants in the study. The remainder was comprised of doctors and scientists, 15 of whom continued the studies as they ascended up to 8,000 m. Eight of these investigators reached the summit of Everest and on their descent took the first measurement of arterial oxygen levels above 8,000 m. So what is the relevance of CXE to intensive care medicine?

Cellular hypoxia is a fundamental mechanism of injury in the critically ill [2,3]. Indeed, it is hard to think of a critically ill patient in whom cellular hypoxia, either local or generalized, is not present. Hypoxia may occur as either a cause of or as a consequence of a variety of critical illnesses. Hypoxia mediated cell death may lead to the generation of an inflammatory response. Systemic inflammation is associated with the development of cellular hypoxia caused by decreased tissue oxygen delivery associated with microcirculatory dysfunction. Cellular hypoxia may also be caused by alterations in cellular energy pathways and mitochondrial function, resulting in decreased ability to utilize available oxygen [2,3]. Although our dominant treatment paradigm revolves around maintenance of oxygen delivery to the cells, there are few data to guide the optimal level of inspired oxygen. Moreover, in some circumstances increasing oxygen delivery confers no benefit or may even cause harm; for example, elevating haemoglobin levels or 'optimization' of oxygen delivery to specific goals in established critical illness [4-6]. Might it be that variations in the cellular efficiency of oxygen metabolism account for some of the observed differences in outcome following critical illness?

The high altitude physiology literature gives us an elegant general description of adaptation to environmental hypoxia built around the idea that maintenance of oxygen delivery to the tissues will allow normal cellular function [7]. However, to date none of these adaptations explain observed (and dramatic) differences in performance between individuals at altitude. Again, the possibility that observed differences are not accounted for by variations in elements of the dominant paradigm raises the possibility that an unmeasured factor or factors may be important. The core hypothesis that CXE is addressing is that variations in metabolic efficiency (relationship between oxygen uptake and work rate) may explain, at least in part, observed differences in individuals' abilities to adapt to hypoxia. If this is true, then it may be

CXE = Caudwell Xtreme Everest.

possible - by examining the genotype and phenotype of the 'rapid adaptors' - to identify mechanisms and thereby develop treatments to benefit the 'slow adaptors' [8-10].

The studies conducted in CXE involve a variety of techniques, including cardiopulmonary exercise testing on cycle ergometers using breath-by-breath expired gas analysis, neuropsychological assessment, near infrared spectroscopy of brain and exercising muscle, blood markers (inflammatory and neuroendocrine) and daily recording of simple physiological variables [1]. These measurements and many more were taken in London before departure, in four laboratories in Nepal on the ascent to Everest Base Camp, and in two laboratories high on Mount Everest. The next few years will see whether this new approach to investigating the pathogenesis of critical illness bears fruit.

Competing interests

The authors are all investigators in the CXE research group.

Authors' contributions

AR, MM, HM and MG were all involved in either (or all) of original drafting, review and redrafting of the mansucript.

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