Point: Counterpoint: Hypobaric hypoxia induces/does not induce different responses from normobaric hypoxia

**POINT: HYPOBARIC HYPOXIA INDUCES DIFFERENT PHYSIOLOGICAL RESPONSES FROM NORMOBARIC HYPOXIA**

Hypoxia is defined as any combination of reduced barometric pressure (PB) and/or a reduced inspired fraction of oxygen (FiO2), which ultimately results in an inspired partial pressure of oxygen (PiO2) less than 150 mmHg (6). Pathophysiological responses to hypoxia or adaptations to hypoxic training can be investigated in two different types of exposure: hypobaric hypoxia (HH; FiO2 = 20.9%; PB < 760 mmHg) or normobaric hypoxia (NH; FiO2 < 20%; PB = 760 mmHg). Traditionally, the decrease in PiO2 was thought to be the only factor relating to the physiological responses to hypoxia. Therefore, any combination of reduced PB and FiO2 resulting in the same PiO2 would potentially produce the same physiological response. This hypothesis suggests that HH and NH can be used interchangeably, both in medicine and in sport. However, a growing body of evidence in various scientific areas such as ventilation (17, 25, 29), fluid balance (18), acute mountain sickness (AMS) (8, 20, 26), nitric oxide (NO) metabolism (12, 13), and sport performance (4) supports the notion that hypobaric hypoxia induces different physiological responses compared with normobaric hypoxia and suggests that HH is a more severe environmental condition and leads to different physiological adaptations compared with NH.

**Ventilatory responses.** The potential effect of hypobaria per se on ventilation was reported early (29) and confirmed recently (17, 25). Ventilation is lower in HH than NH, with a lower tidal volume and a higher respiratory frequency. There is a trend for reduced PETCO2 and Pedro2 values in HH. Overall, HH might induce a higher alveolar physiological dead space associated with ventilatory alkalosis and hypocapnia.

It is also known that PB can modify the fluid circulation (e.g., pulmonary lymph) and the trans-alveoli-capillary membrane flux (15). This might induce larger pulmonary vasoconstriction in HH and modify O2 diffusion by decreasing the pressure gradient. PB may also influence the N2 and O2 concentration in the cerebrospinal fluid and therefore partly change the central regulation of ventilation (6).

**Fluid balance.** Change in fluid balance has been reported to be different between HH and NH (18). Compared with HH, NH exposure results in a negative fluid balance, as indicated by a significant decrease in plasma volume. This is explained by a higher diuresis (e.g., greater urine volume) and a lower ADH level in NH. Although the underlying mechanisms of this phenomenon are still uncertain, the combination of reduced PB and Po2 is believed to favor this larger fluid retention in HH in reducing urine volume. If confirmed, these results would have large implications in terms of oxygen delivery and performance-related benefits in HH vs. NH training methods.

**AMS.** Most previous studies have shown that the severity of AMS symptoms were higher in HH than in NH (6, 18, 20). The potential direct mechanisms (density of breathing gas; N2 movement or direct influence on CNS) have been discussed (6) but other factors (e.g., hemodynamic factors) require further investigation (18).

Recently, preacclimatization in HH (i.e., 3 wk of intermittent altitude exposures, 4 h/day, 5 days/wk at 4,300 m) resulted in a marked decrease in the severity of AMS and resting PETCO2 and an increase in ventilation during the subsequent 30 h in the HH condition (4,300 m altitude equivalent; barometric pressure = 446 mmHg) (3). These authors concluded that preacclimatization in HH provides “an effective alternative to chronic altitude residence for reducing the incidence and severity of AMS.”

In contrasting methods, preacclimatization in NH was less effective in response to a subsequent HH exposure (8, 26). NH preacclimatization did not induce a change in performance, HR, SaO2, AMS severity, or exercise performance after 7 nights of NH (FiO2: 16.2–14.4%) when subjects were exposed to HH (5 days at 4,300 m), other than reduced sleep SaO2 and less severe AMS symptoms upon awakening (8). Although there is no direct comparison between HH and NH exposure relating to a preacclimatization period preceding a high-altitude ascent, the current literature supports that “NH treatment provides little useful benefit during subsequent HH residence”. Hence, “NH and HH clearly cannot be used interchangeably and are not as effective as preacclimatization strategies to reduce AMS and improve exercise performance during subsequent HH residence” (8).

**NO metabolism.** Recently, it was reported that the exhaled NO was lower in HH than in NH (12) and that the PB per se played a role in this difference (14). This reduction in exhaled NO could be induced by a higher back-diffusion to the alveoli and then to the hemoglobin (Hb) in HH compared with NH, suggesting that more NO is likely recaptured by the blood compartment in HH. We postulate that the differences in NO may be related to the different ventilatory responses reported previously between HH and NH. Nitric oxide synthase (NOS) has an excitatory influence on respiration during hypoxia, and when it is inhibited, the ventilatory responses to hypoxia are likely reduced (11). Overall, the lower minute ventilation observed in HH might be an indirect consequence of reduced NO bioavailability induced by the lower PB. However, although the importance of NO bioavailability in muscle blood flow, glucose consumption, and systemic VO2 responses is well established, it is unclear whether the observed differences in NO are related to the putative higher benefits to train in HH than in NH (13).

**Performance.** Comparing the training benefits between different hypoxic methods is difficult because changes in performance result from the combination of “hypoxic dose” and training content (19). Interestingly, most of the “living high training low (LHTL)” studies conducted in NH do not report an improvement in performance (i.e., significant difference between the experimental and control groups) (1, 2, 9, 10, 21, 24, 27). Interestingly, some of these normobaric LHTL studies induced a positive erythropoietic response (erythrocytes or Hb mass) (5, 22, 23), confirming that the red blood cell increase is likely not the only parameter involved in the performance improvement during altitude training. In contrast, most of the LHTL studies reporting benefits in both erythropoietic re-
sponses and performance were mainly conducted in HH (7, 16, 28, 30). Nevertheless, it remains to be confirmed whether the benefits of training would be greater following training in HH compared with NH as suggested by the current literature (13). This assumption is supported by the results of a meta-analysis (4) in which a “terrestrial” LHTL protocol (i.e., HH) induced additional benefits in performance (estimated by change in power output) of 4.0% and 4.2% for elite and non-elite athletes vs. 0.6% and 1.4% with “artificial” LHTL (i.e., NH).

On the basis of the existing data relating to ventilatory responses, fluid balance, AMS severity, NO metabolism, and performance improvement in HH vs. NH, there is no doubt that hypobaric hypoxia induces different physiological responses from normobaric hypoxia. However, the main mechanisms remain unclear.

REFERENCES


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COUNTERPOINT: HYPOBARIC HYPOXIA DOES NOT INDUCE DIFFERENT BENEFITS FROM NORMOBARIC HYPOXIA

Studies on hypoxia are performed by lowering ambient oxygen partial pressure (PO2) either by reducing the barometric pressure (hypobaric hypoxia) or by lowering the O2 fraction (normobaric hypoxia at the prevailing barometric pressure [P0]). Upon reflection we can see that many land-