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ORIGINAL RESEARCH

Cerebral Hemodynamics at Altitude: Effects of Hyperventilation and Acclimatization on Cerebral Blood Flow and Oxygenation

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Objective.—Alterations in cerebral blood flow (CBF) and cerebral oxygenation are implicated in altitude-associated diseases. We assessed the dynamic changes in CBF and peripheral and cerebral oxygenation engendered by ascent to altitude with partial acclimatization and hyperventilation using a combination of near-infrared spectroscopy, transcranial Doppler ultrasound, and diffuse correlation spectroscopy.

Methods.—Peripheral (Spo_2) and cerebral ($Scto_2$) oxygenation, end-tidal carbon dioxide ($ETCO_2$), and cerebral hemodynamics were studied in 12 subjects using transcranial Doppler and diffuse correlation spectroscopy (DCS) at 75 m and then 2 days and 7 days after ascending to 4559 m above sea level. After obtaining baseline measurements, subjects hyperventilated to reduce baseline $ETCO_2$ by 50%, and a further set of measurements were obtained.

Results.—Cerebral oxygenation and peripheral oxygenation showed a divergent response, with cerebral oxygenation decreasing at day 2 and decreasing further at day 7 at altitude, whereas peripheral oxygenation decreased on day 2 before partially rebounding on day 7. Cerebral oxygenation decreased after hyperventilation at sea level ($Scto_2$ from 68.8% to 63.5%; $P < .001$), increased after hyperventilation after 2 days at altitude ($Scto_2$ from 65.6% to 69.9%; $P = .001$), and did not change after hyperventilation after 7 days at altitude ($Scto_2$ from 62.2% to 63.3%; $P = .35$).

Conclusions.—An intensification of the normal cerebral hypocapnic vasoconstrictive response occurred after partial acclimatization in the setting of divergent peripheral and cerebral oxygenation. This may help explain why hyperventilation fails to improve cerebral oxygenation after partial acclimatization as it does after initial ascent. The use of DCS is feasible at altitude and provides a direct measure of CBF indices with high temporal resolution.

Key words: hypoxia, cerebral oxygenation, altitude

Introduction

Acute exposure to high altitude hypoxia can cause pathophysiological changes that manifest as a spectrum of disorders ranging from the relatively benign high altitude headache to life-threatening high altitude cerebral edema. Although these changes seem to be related to cerebral hypoxemia,[1] the underlying pathophysiology remains elusive with the cerebrovascular response to altitude incompletely characterized. Cerebral oxygenation is determined by arterial oxygen content, oxygen consumption, and cerebral blood flow (CBF). In turn, CBF is subject to different regulatory mechanisms than peripheral blood flow and is known to be particularly reactive to changes in arterial carbon dioxide.

Studies of cerebral hemodynamics at altitude have been hampered by the lack of an effective method to monitor intracranial blood flow. Diffuse correlation

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spectroscopy (DCS) is a novel technology that provides a noninvasive, portable estimation of changes in cortical blood flow. It measures the optical phase shifts caused by moving blood cells using near-infrared light. Importantly, it does not rely on the principles of tracer clearance.[2] Currently, this technology is able to measure relative changes in cerebral blood flow (rCBF) in response to an intervention in the acute setting, but not absolute changes over long periods.

Using this new technology in conjunction with near-infrared spectroscopy (NIRS) to measure cerebral oxygenation and transcranial Doppler (TCD) measurements of blood flow velocity in the middle cerebral artery, we sought to elucidate the effects of acclimatization and hyperventilation on a cohort of climbers ascending to 4559 m and to study the relationship between peripheral oxygenation (Spo_2), cerebral oxygenation ($Scto_2$), end-tidal CO_2 ($ETCO_2$), and CBF.

Methods

SUBJECTS AND SETTING

Approval for this study was obtained from the ethics committees of the University of Turin and University College London. All participants underwent medical screening, and written informed consent was obtained after the possible risks of the study were explained.

Twelve subjects ranging in age from 22 to 80 years, with varying degrees of experience at altitude and residing at or below 75 m above sea level, were recruited from the 2010 Xtreme Alps Medical Research Expedition. None had traveled to altitude during the previous 3 months. Subjects were studied at 75 m above sea level before the expedition. Subjects then ascended by cable car and foot to 3611 m where they acclimatized for 2 days before ascending by foot to the Capanna Regina Margherita at 4559 m. Two further sets of measurements were taken 2 days and 7 days after arriving at the Capanna Regina Margherita.

EXCLUSIONS

Subjects with symptoms of acute mountain sickness (AMS) severe enough to require treatment with dexamethasone or acetazolamide were excluded from further participation in the study after they began treatment.

MEASUREMENTS

Each subject was positioned supine and allowed to rest for 5 minutes. Baseline measurements of CBF were obtained using both DCS and TCD ultrasound (Table). Subjects were then instructed to hyperventilate while undergoing $ETCO_2$ monitoring with a tight-fitting facemask with in-line capnometry (EMMA Capnometer, Phasein Medical Technologies, Danderyd, Sweden) and given feedback regarding depth and rate of respiration needed to reach the target $ETCO_2$ of 50% of baseline.

After achieving and maintaining this target $ETCO_2$ for 3 minutes, an additional set of measurements were obtained and averaged. Peripheral arterial oxygen saturation was recorded by a near-infrared pulse oximetry probe (Onyx model 9500, Nonin Medical, Plymouth, MN).

NEAR-INFRARED SPECTROSCOPY

The Fore-Sight Absolute Cerebral Oximeter (CAS Medical Systems, Inc, Branford, CT) was used to measure the oxygen saturation of cerebral tissue. This is an "absolute cerebral oximeter" using fiberoptic laser light

Table. Resting physiology at sea level and on study days at 4559 m[a]

Altitude	*150 m*	*Day 2 at 4559 m*	*Day 7 at 4559 m*
Spo_2 (%)	98 ± 0.42	81.2 ± 1.42	85.9 ± 1.47
$Scto_2$ (%)	68.8 ± 1.21	65.4 ± 2.01	62.4 ± 1.75
DCS, % with HV	20.9 ± 3.8	24.5 ± 5.9	37.4 ± 8.2
TCD, % with HV	33 ± 3.7	31.7 ± 7.3	31.5 ± 3.1
HR (beats/min)	64 ± 4.1	81 ± 6.4	80 ± 6.25
RR (breaths/min)	14 ± 1.3	16 ± 1.7	14 ± 1.1
SBP (mm Hg)	110 ± 3.4	118 ± 4.4	127 ± 7.1
DBP (mm Hg)	70 ± 2.0	77 ± 2.9	83 ± 4.6
Resting $ETCO_2$ (kPa)	4.5 ± 0.2	3.39 ± 0.14	3.09 ± 0.15
Lake Louise Score	0.7 ± 0.2	3.7 ± 1.5	0.7 ± 0.4

[a] Values are reported as mean ± SEM.

DBP, diastolic blood pressure; DCS, diffuse correlation spectroscopy; $ETCO_2$, end-tidal carbon dioxide; HR, heart rate; HV, hyperventilation; RR, respiration rate; SBP, systolic blood pressure; $Scto_2$, cerebral oxygen saturation; Spo_2, peripheral oxygen saturation; TCD, transcranial Doppler.