Carbon dioxide contributes to the beneficial effect of pressurization in a portable hyperbaric chamber at high altitude

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ABSTRACT

Regional cerebral oxygenation (rSo_2) and peripheral oxygen saturation (Spo_2) have been studied in subjects inside a portable hyperbaric chamber at altitude during pressurization. The effects of the accumulation of carbon dioxide within the chamber on rSo_2 and Spo_2 have also been investigated. Three studies of cerebral regional oxygenation were undertaken, using near-IR spectroscopy, in subjects who had ascended to 3475 m in the Alps, 4680 m in the Andes or 5005 m in the Himalayas. At 3475 m and 5005 m the effects of the removal of inspired carbon dioxide by a soda lime scavenger were also studied. On pressurization of the chamber to 19.95 kPa, inspired carbon dioxide rose within the chamber from 0.03% (0.06 kPa) ambient to over 1% (1.3 kPa). At 5005 m, Spo_2 rose from a baseline of 79.5% (S.D. 4.5%) to 95.9% (2.0%) ($P < 0.0001$), and cerebral rSo_2 rose from 64.6% (3.4%) to 69.4% (3.6%) ($P < 0.0001$). The introduction of a soda lime CO_2 scavenger into the breathing circuit resulted in a drop in Spo_2 from 95.9% (2.03%) to 93.6% (2.07%) ($P < 0.001$) and a fall in rSo_2 from 69.4% (3.64%) to 68.5% (3.5%) ($P < 0.01$). Chamber pressure was maintained throughout at 19.95 kPa. Similar changes were seen at the other altitudes. Cerebral rSo_2 increased rapidly following pressurization at all three altitudes. Scavenging of inspired carbon dioxide was associated with a significant fall in cerebral rSo_2 and Spo_2, and we estimate that the contribution of carbon dioxide may account for up to one-third of the beneficial effect of the portable hyperbaric chamber.

INTRODUCTION

Acute mountain sickness (AMS) is a common clinical problem affecting otherwise fit individuals who ascend to high altitude. The prevalence of AMS has been reported to vary from 43 to 63% in the Himalayas [1], and from 9 to 69% in the Alps [2]. The severity depends upon a number of factors, including rate of ascent, altitude achieved, recent previous acclimatization, and the susceptibility of the individual to the syndrome. Although usually relatively benign and self-limiting, the condition can deteriorate and progress to high-altitude cerebral

Key words: carbon dioxide, cerebral oxygenation, high altitude, near-infrared spectroscopy, portable hyperbaric chamber.

Abbreviations: AMS, acute mountain sickness; NIRS, near-infrared spectroscopy; rSo_2, regional oxygen saturation; Spo_2, peripheral oxygen saturation; $Pico_2$, partial pressure of inspired carbon dioxide; $Petco_2$, end-tidal partial pressure of carbon dioxide; Pio_2, partial pressure of inspired oxygen.

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oedema and pulmonary oedema, both of which are potentially fatal syndromes that have been reported in trekkers, mountaineers and military personnel.

A number of strategies have been developed to prevent AMS, including slow rate of ascent, rest days for acclimatization and drug prophylaxis with acetazolamide and dexamethasone. Mild symptoms of AMS may be treated with simple analgesics and rest while acclimatizing. Moderate AMS may require dexamethasone. The best treatment for severe AMS is rapid descent to a lower altitude, but the local terrain or weather conditions may make this difficult. Oxygen is effective, but cylinders are heavy and only a limited supply can be carried. More recently, portable hyperbaric chambers made of lightweight fabric have been developed [3], which may be taken on trekking expeditions to treat AMS. These allow rapid pressurization of a subject up to 19.95 kPa (200 mBar) above ambient pressure by use of a foot or hand pump. For example, at an altitude of 5000 m a simulated descent to 2500 m is achieved within minutes. Early symptom relief and improvement in peripheral oxygen saturation have been reported [4], but there are no data on the effects of compression on cerebral oxygenation.

The introduction of the technique of reflected near-infrared spectroscopy (NIRS) allows continuous, non-invasive monitoring of cerebral oxygenation. The technique was first described in adults in 1991 [5], and has widespread research and clinical applications [6]. Reflected cerebral NIRS uses light in the near-IR spectrum (650–1100 nm) and, like pulse oximeters and mixed-venous oximeters, uses the principles of light transmission and absorption to measure concentrations of oxygenated, deoxygenated and total haemoglobin in cerebral tissue. The cerebral regional oxygen saturation (rSO_2) is derived from the equation:

$$rSO_2 = (\text{oxygenated haemoglobin}/\text{total haemoglobin}) \times 100$$

The non-invasive NIRS technique has recently been used to assess cerebral oxygenation in healthy volunteers under laboratory conditions of normocapnic and hypercapnic hypoxia. It has been reported that cerebral oxygenation, as assessed by NIRS, precisely tracks changes in jugular bulb venous saturation within individuals [7]. The technique has also been validated in studies comparing NIRS with PET (positron-emission tomography) scanning [8], with ^{133}Xe washout techniques [9] and also with internal carotid artery stump pressures [6]. We have reported changes observed on ascent to altitude, and have found the equipment to be robust and suitably sensitive for use in the field [10,12,16].

Hitherto, the beneficial effect of pressurization has been considered to be due solely to an increase in the partial pressure of inspired oxygen (PiO_2). However, pressurization in a small hyperbaric chamber results in an increase in carbon dioxide within the chamber, resulting in an increase in the partial pressure of inspired carbon dioxide ($PiCO_2$). Efforts have been made in the design of the bag to minimize the accumulation of carbon dioxide, either using a carbon dioxide scrubber or by a pressure relief valve to ensure a flow of fresh air. Using the bag as recommended with a foot pump, carbon dioxide within the lung increases, reaching a plateau of mean 0.74% (range 0.56–0.97%) after 3 min [11]. Carbon dioxide itself will improve peripheral oxygen saturation and increase cerebral blood flow, and we have demonstrated that cerebral regional oxygenation is also increased [12]. We postulated that the accumulation of carbon dioxide in the portable hyperbaric chamber may contribute to the beneficial effect of pressurization.

The aim of the present study was to measure cerebral oxygenation and peripheral pulse oximetry in subjects inside a hyperbaric chamber, and to assess the contribution of accumulated carbon dioxide to cerebral and peripheral oxygenation.

METHODS

Subjects and methods

Experiments were performed shortly after arrival at three different altitudes, on three different expeditions. The first experiment was undertaken in 10 healthy, non-smoking subjects (seven men) aged 24–59 years, who ascended from sea level to 4680 m in a minibus over 3 days. At 3 days after arrival at 4680 m, the hyperbaric chamber study was performed. Subjects were placed in a Gamow bag (Chinook Medical Gear, CO, U.S.A.) and the cabling for the various probes (NIRS, digital pulse oximeter) was bound together with tape and led through the airtight zip of the chamber. After 2 min of baseline measurements, the bag was sealed and pressurized to 6.88 kPa (69 mBar) using a foot pump. Pressurization took 2–3 min. Although there was an audible leak of air around the cables, the predetermined pressure was readily achieved and was maintained by operating the foot pump at 20–25 pumps/min. Peripheral oxygen saturation (SpO_2) and heart rate were measured using a hand-held digital pulse oximeter (model 3770; Ohmeda, BOC Group). The end-tidal partial pressure of CO_2 ($PETCO_2$) was measured using a Hewlett Packard capnograph 78356 in two subjects.

A second experiment was performed in nine healthy, non-smoking subjects (six men) aged 24–53 years who ascended to 3475 m in a cable car, having spent one night at 700 m. The pressurization study was undertaken 3 days after ascent using a Certec compression chamber Mark 1 (69210; Sourcieu, Les Mines, France), which works on the same principle as the Gamow bag [13]. The chamber was pressurized to 19.95 kPa (200 mBar) using a

foot pump, with a good seal obtained with only one cable (for NIRS) passing through the airtight zip. Pressurization took 3–4 min. SpO_2, heart rate, $PiCO_2$ and P_{ETCO_2} were measured using a battery-powered Propac Encore (Propac Systems Inc, Beaverton, OR, U.S.A.), which was kept within the chamber; readings were made through the viewing window. Measurements were made over 5 min before a paediatric soda lime circuit (Waters 'to and fro') was inserted by the subject within the bag into the breathing circuit for 5 min. After a further 5 min of basal recordings, a piece of tubing with the same dead space as the paediatric soda lime circuit was also inserted into the breathing circuit. A steady state was achieved after each manipulation, and pressure was maintained at 19.95 kPa throughout.

A third experiment using a similar protocol to the 3475 m experiment was undertaken at 5005 m. Nine healthy, non-smoking subjects (eight men) aged 22–55 years ascended from 1345 m to 5005 m on foot over 13 days. The study was undertaken 2 days after arrival at 5005 m using a Certec compression chamber Mark 11 (69210; Sourcieu, Les Mines, France). SpO_2 and heart rate were measured using a battery-powered Propac Encore within the chamber. A steady state was achieved after each manipulation, and pressure was maintained at 19.95 kPa (200 mBar) throughout.

Six subjects were common to two studies, and three subjects were common to all three studies.

Measurement of Spo_2

SpO_2 and heart rate were measured at 1 min intervals using a hand-held digital oximeter (model 3770; Ohmeda, BOC Group) in the 4680 m study and a Propac Encore (Propac Systems Inc.) in the 3475 m and 5005 m studies. Extraneous light was excluded.

Measurement of P_{ETCO_2}

A BOC face mask was positioned on the face of the subject, with a Clausen harness ensuring a good seal. A capnograph (Hewlett Packard capnograph 78356 at 4680 m and a Propac Encore at 3475 m and 5005 m) was attached to the mask inlet in order to measure $PiCO_2$ and P_{ETCO_2}.

Measurement of cerebral rSo_2

Continuous non-invasive NIRS was performed using a Critikon 2020 monitor (Johnson and Johnson Medical Ltd). The sensor position was standardized to a point over the right fronto-parietal region, with the sensor margins 3 cm from the midline (avoiding the sagittal sinus) and 3 cm above the orbital crest. The Critikon disposable pads were unsatisfactory, and a Blue-line Tubifast bandage (Seton Healthcare Group plc, Turbiton, Oldham, Lancashire, U.K.) was used to keep the sensor in place. Data samples every 1 s were logged on to a Toshiba Satellite 200 CDS laptop computer. The interlock hold time was set at 120 s. Oxyhaemoglobin, deoxyhaemoglobin and total haemoglobin were measured.

Statistics

Results are given as means (S.D.). The statistical significance of results obtained was assessed by repeated-measures ANOVA, except where indicated in the text (paired t test). All calculations were performed using Statview for Windows software (Abacus Concepts, Berkeley, CA, U.S.A.). P values of < 0.05 were considered significant.

Ethics

Approval for the studies was given by the South Birmingham Local Research Committee, and written informed consent was obtained from all subjects.

RESULTS

Barometric pressure

Barometric pressure at 200 m was 1008–1015 mBar (100.55–101.25 kPa), at 3475 m it was 641 mBar (63.9 kPa), at 4680 m it was 582 mBar (58.05 kPa) and at 5005 m it was 547 mBar (54.56 kPa).

$Pico_2$

During pressurization at 3475 m, $PiCO_2$ rose from 0.059 (0.18) to 1.33 (0.18) kPa ($P < 0.0001$). On introducing soda lime after pressurization at 3475 m, $PiCO_2$ fell from 1.33 (0.18) to 0.05 (0.13) kPa ($P < 0.0001$), thus validating the efficacy of the Waters 'to and fro' canister (Table 1, Figure 1).

P_{ETCO_2}

P_{ETCO_2} at 3475 m rose on pressurization from a baseline of 3.8 (0.33) to 4.17 (0.52) kPa ($P < 0.0001$). On introducing soda lime after pressurization at 3475 m, P_{ETCO_2} fell from 4.17 (0.52) to 4.01 (0.41) kPa ($P < 0.0001$) (Table 1, Figure 1).

Digital pulse oximetry

Baseline SpO_2 at 3475 m was 91.0% (2.8%), that at 4860 m was 75.1% (10.3%) and that at 5005 m was 79.5% (4.5%). SpO_2 rose rapidly following pressurization at all three altitudes, reaching a plateau within 3 min. At 3475 m SpO_2 rose from 91.0% (2.8%) to 97.8% (1.4%) ($P < 0.0001$); at 4680 m SpO_2 rose from 75.1% (10.3%) to 81.7% (8.1%) ($P < 0.05$); and at 5005 m SpO_2 rose from 79.5% (4.5%) to 95.9% (2.0%) ($P < 0.0001$) (Table 2). The introduction of the soda lime

Table 1 Changes in carbon dioxide partial pressures and in Spo_2 and cerebral rSo_2 at 3475m

Values are mean (S.D.). ns, not significant.

Conditions	$Pico_2$ (kPa)	P_{ETCO_2} (kPa)	Spo_2 (%)	rSo_2 (%)
Baseline	0.059 (0.18)	3.8 (0.33)	91.0 (2.8)	63.4 (4.5)
At 19.95 kPa	1.33 (0.18)	4.17 (0.52)	97.8 (1.4)	66.9 (4.7)
P	< 0.0001	< 0.0001	< 0.0001	< 0.0001
At 19.95 kPa + soda lime	0.05 (0.13)	4.01 (0.41)	96.1 (1.4)	65.7 (5.7)
P compared with 19.95 kPa alone	< 0.0001	< 0.0001	< 0.0001	< 0.05
P compared with baseline	ns	ns	ns	ns
At 19.95 kPa + spacer	1.63 (0.17)	4.16 (0.53)	98.2 (1.5)	66.1 (5.0)
P compared with + 19.95 kPa	< 0.01	ns	ns	ns

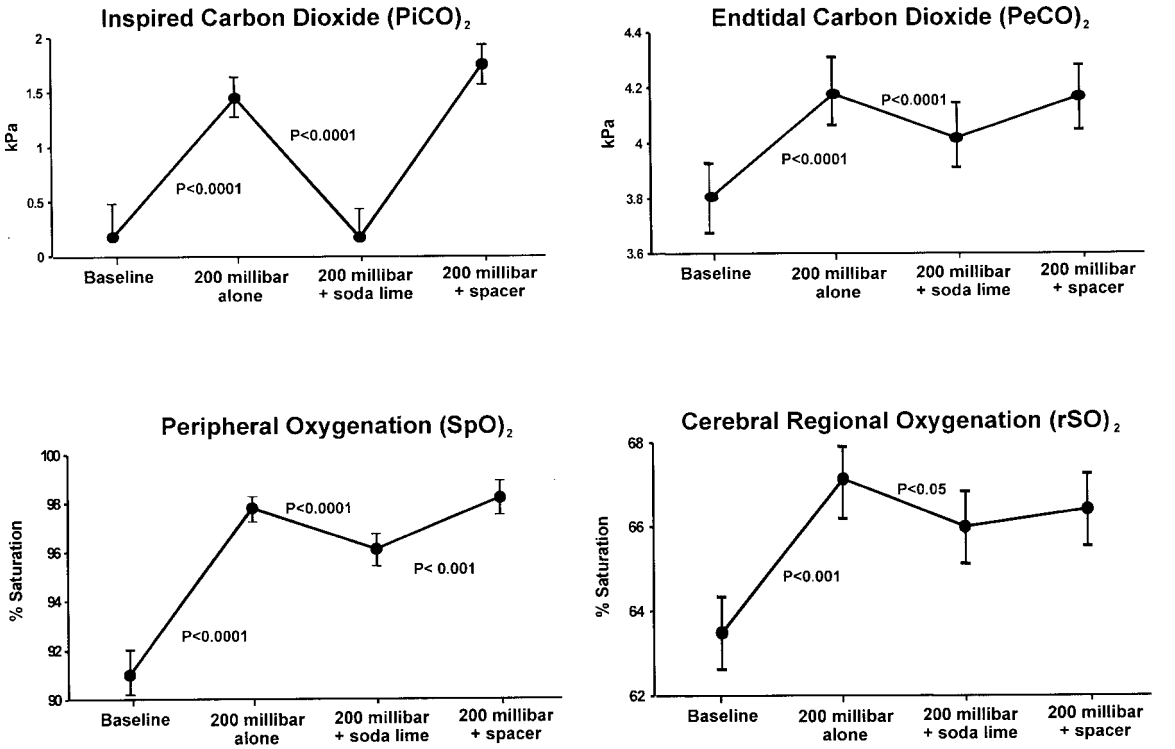

Figure 1 Portable hyperbaric chamber study at 3475 m

See the text for details. 200 mBar = 19.95 kPa.

CO_2 scavenger resulted in a fall in Spo_2 [from 97.8% (1.4%) to 96.1% (1.4%) ($P < 0.0001$) at 3475 m and from 95.9% (2.0%) to 93.6% (2.1%) ($P < 0.001$) at 5005 m].

Cerebral rSo_2

Baseline cerebral rSo_2 at 3475 m was 63.4% (4.5%), that at 4680 m was 62.5% (3.4%) and that at 5005 m was 64.6% (3.4%). Cerebral rSo_2 following pressurization showed similar rises at all three altitudes (Tables 1 and 2). At 3475 m with pressurization to 19.95 kPa, rSo_2 rose from 63.4% (4.5%) to 66.9% (4.7%) ($P < 0.0001$). The introduction of the CO_2 scavenger resulted in a decrease in rSo_2 to 65.7% (5.7%) ($P < 0.049$). At 4680 m, rSo_2 rose with pressurization to 6.88 kPa from 62.5% (3.4%) to 65.4% (3.2%) ($P < 0.0001$). At 5005 m rSo_2 rose with pressurization to 19.95 kPa from 64.6% (3.4%) to 69.4% (3.6%) ($P < 0.0001$). The introduction of the CO_2 scavenger resulted in a decrease in rSo_2 to 68.5% (3.5%) ($P < 0.001$) (Table 3).

Cerebral oxygenation is dependent in part on the haematocrit. There was no significant rise in the total cerebral haemoglobin at altitude in the 4680 m study [16], although there was a trend towards a rise at altitude [sea level, 112.3 (11.6) μmol/l of tissue; 150 m, 105.2 (11.2) μmol/l of tissue; 4680 m, 116.8 (16.6) μmol/l of

Table 2 Changes in Spo_2 and cerebral rSo_2 during pressurization

Values are mean (S.D.). *P* values (paired *t* test) refer to data at 5 min (3475 m and 5005 m) or 4 min (4680 m) compared with baseline.

	19.95 kPa at 3475 m		6.88 kPa at 4680 m		19.95 kPa at 5005 m	
Time (min)	Spo_2 (%)	rSo_2 (%)	Spo_2 (%)	rSo_2 (%)	Spo_2 (%)	rSo_2 (%)
Baseline	91.0 (2.8)	63.4 (4.5)	75.1 (10.3)	62.5 (3.4)	79.5 (4.5)	64.6 (3.4)
1	97.0 (2.2)	66.6 (4.1)	79.2 (12.7)	64.4 (3.3)	93.6 (2.3)	68.6 (3.4)
2	97.4 (1.7)	66.2 (4.4)	80.4 (10.6)	64.4 (3.1)	95.5 (2.2)	68.9 (3.4)
3	97.3 (1.7)	66.7 (4.3)	81.7 (7.6)	65.2 (3.3)	95.7 (2.1)	69.1 (3.3)
4	97.3 (1.7)	67.1 (4.1)	81.7 (8.1)	65.4 (3.2)	96.0 (2.5)	69.2 (3.5)
5	97.8 (1.4)	66.9 (4.7)	–	–	95.9 (2.0)	69.4 (3.6)
P value	< 0.005	< 0.01	< 0.05	< 0.01	< 0.0001	< 0.0001

Table 3 Changes in Spo_2 and rSo_2 at 5005 m

Values are mean (S.D.).

Conditions	Spo_2 (%)	rSo_2 (%)
Sea level	97.4 (1.0)	68.6 (3.1)
5005 m baseline	79.5 (4.5)	64.6 (3.4)
P compared with sea level	< 0.0001	< 0.0001
At 19.95 kPa	95.9 (2.0)	69.4 (3.6)
P compared with 5005 m baseline	< 0.0001	< 0.0001
At 19.95 kPa + soda lime	93.6 (2.1)	68.5 (3.5)
P compared with + 19.95 kPa	< 0.001	< 0.001
P compared with 5005 m baseline	< 0.0001	< 0.0001

tissue]. At 5005 m there was a rise in total haemoglobin from 107.5 (26.3) to 132.1 (37.4) μmol/l of tissue ($P < 0.04$; paired *t* test).

DISCUSSION

Oxygenation of the brain is likely to be critical in determining performance and illness at high altitude [12]. The first commercially successful, high-altitude bag was described by Gamow et al. in 1990 [11]. This portable hyperbaric chamber, weighing approx. 7 kg, has rapidly increased in popularity, based initially upon anecdotal reports and then upon clinical studies assessing efficacy [4,14]. Treatment of sick subjects within the very confined space of the chamber can be difficult, and prolonged treatment makes considerable demands on the individuals required to maintain pressure with the foot pump. The chambers are now carried on many high-altitude trekking and mountaineering expeditions, and are being used to treat AMS, sometimes as an alternative to descent. The chambers are designed to operate at pressures between 15.96 and 21.95 kPa, being pressurized by a foot or hand pump. In order to prevent the build-up of carbon dioxide within the chamber, air has to be pumped in at 40–50 litres/min. Even with this rapid turnover of air, the carbon dioxide levels rise to approx. 0.7% [11,15]. Soda lime has been used to prevent carbon dioxide build-up, with the aim of reducing the effort of pumping, but is not usually employed. Treatment of subjects with AMS at 4559 m in a portable compression chamber at 19.25 kPa for 1 h has been shown to improve SpO_2 during treatment and to decrease clinical AMS scores immediately after treatment, but with no benefit 12 h later [15].

NIRS is a relatively new non-invasive technique for measuring cerebral regional oxygenation. It has been used to assess cerebral regional oxygenation in healthy volunteers under laboratory conditions of normocapnic and hypercapnic hypoxia. We have reported [12] the use of NIRS techniques in field studies, making repeated measurements after physiological manipulations. Cerebral rSO_2 fell on ascent from sea level to 4680 m [16]. To date, there are no data regarding cerebral oxygenation within a portable hyperbaric chamber at altitude.

The first of our present studies (at 4680 m) was a simple observational study to determine whether the technique of cerebral NIRS could be used to measure the presumed rise in cerebral oxygenation inside a hyperbaric chamber. A pressure of only 6.88 kPa was achieved, partly due to leakage around the cabling but also because of a misunderstanding of the optimal operating pressures. However, a rise in P_{ETCO_2} was observed in two subjects. The magnitude of the rise in P_{iCO_2} was similar to that observed by others [11] and, in view of the leaks around the cabling in this experiment, the increase in the level of CO_2 is likely to have been an underestimate compared with the use of the chamber in a standard fashion.

In the second study (3475 m), a pressure of 19.95 kPa resulted in a rise in SpO_2 and a rise in cerebral rSO_2 (Figure 1). The rises in both parameters occurred within 2–3 min of achieving the desired pressure. The contribution of the rise in carbon dioxide within the closed space of the hyperbaric chamber on both peripheral and cerebral oxygenation was clearly significant, as shown by the changes that occurred when the soda lime carbon dioxide

scavenger was introduced. With the soda lime in the circuit, there was a small but significant fall in both SpO_2 and cerebral rSO_2 (Table 1). Removal of the soda lime from the circuit returned these values to the previous levels. The fall in SpO_2 on the introduction of a carbon dioxide scavenger has been recorded previously [17], but not commented on, by others. The introduction of a spacer into the circuit within the Gamow bag resulted in a return of both cerebral and peripheral oxygenation to pre-CO_2-scavenger levels, suggesting that the dead space of the soda lime canister was not as clinically significant as the soda lime itself. It should be noted that the build-up of approx. 1% CO_2 within the chamber during normal use will result in a fall of approx. 1% of O_2 in the bag removed [18].

The third experiment (5005 m) was undertaken at an altitude more representative of the altitudes at which portable compression chambers are usually used. Unfortunately, malfunctioning of the capnograph meant no data were obtained regarding $PiCO_2$ and $PETCO_2$. However, the rapid improvement in cerebral oxygenation that was observed at 4680 m and 3475 m was reaffirmed, as was the effect of the soda lime CO_2 scavenger in decreasing both SpO_2 and cerebral rSO_2 (Table 3).

The higher baseline cerebral rSO_2 seen at 5005 m than at 4680 m initially appears anomalous. The NIRS technique is particularly suitable for multiple measurements of trends rather than single absolute measurements of cerebral oxygenation. The higher baseline rSO_2 seen at 5005 m is probably partly a reflection of the much lower rate of ascent on this particular expedition. Subjects were much better acclimatized, having taken 13 days to ascend to 5005 m, whereas ascent to 4680 m was over 3 days and that to 3475 m was in a single day. Baseline SpO_2 at 4680 m following a rapid ascent (3 days) was 75.1% (10.3%), whereas at 5005 m, following a much slower ascent (13 days), it was 79.5% (4.5%). The subjects would probably have had a higher haematocrit at 5005 m. The observed rise in total cerebral haemoglobin from 107.5 (26.3) μmol/l of tissue at sea level to 132.1 (37.4) μmol/l ($P < 0.04$) supports this hypothesis.

The concept that carbon dioxide might be beneficial at altitude is not a new one [19]. More recently, supplemental carbon dioxide has been suggested in the treatment of acute mountain sickness [20], but this has not been confirmed by others [21]. Carbon dioxide has two powerful effects at all altitudes. First, by stimulating the respiratory centre, the rate and depth of respiration are increased. This can profoundly affect SpO_2 [12] and can also increase the arterial partial pressure of O_2 [22]. Secondly, carbon dioxide is a powerful cerebral vasodilator, causing a rapid increase in cerebral blood flow and increasing trans-cranial Doppler middle cerebral artery velocities at altitude [23]. The combination of increases in PiO_2 and $PiCO_2$ appears to have a synergistic effect. For these reasons, it seems likely that the accumulation of carbon dioxide in a portable hyperbaric chamber is beneficial, and that carbon dioxide extraction may be counter-productive. The use of supplemental 3% carbon dioxide at ambient pressures at altitude has been studied [22]. However, the optimum concentrations of carbon dioxide at differing altitudes need to be determined, and we suggest that measurement of cerebral regional oxygenation is a useful end-point to monitor, as it is likely to predict response to treatment.

In conclusion, these studies have demonstrated for the first time that compression in a portable hyperbaric chamber at altitude improves cerebral oxygenation, and that the improvement is due in part to the increase in PiO_2; in addition, the increase in $PiCO_2$ has a measurable physiological effect.

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