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Continuous positive airway pressure increases haemoglobin O_2 saturation after acute but not prolonged altitude exposure

Piergiuseppe Agostoni[1,2]*, Gianluca Caldara[3], Maurizio Bussotti[1], Miriam Revera[3,4], Mariaconsuelo Valentini[3,4], Francesca Gregorini[3], Andrea Faini[3], Carolina Lombardi[3,4], Gregorz Bilo[3], Andrea Giuliano[3], Fabrizio Veglia[1], Giulio Savia[3], Pietro A. Modesti[5], Giuseppe Mancia[3,4], and Gianfranco Parati[3,4] on behalf of the HIGHCARE Investigators

[1]Centro Cardiologico Monzino, IRCCS, Istituto di Cardiologia, Università di Milano, Via Parea 4, 20138 Milan, Italy; [2]Division of Critical Care and Respiratory Medicine, Department of Medicine, University of Washington, Seattle, WA, USA; [3]Department of Cardiology, S.Luca Hospital, Istituto Auxologico Italiano, Milan, Italy; [4]Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, Italy; and [5]Department of Internal Medicine, University of Florence, Florence, Italy

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Aims It is unknown whether subclinical high-altitude pulmonary oedema reduces spontaneously after prolonged altitude exposure. Continuous positive airway pressure (CPAP) removes extravascular lung fluids and improves haemoglobin oxygen saturation in acute cardiogenic oedema. We evaluated the presence of pulmonary extravascular fluid increase by assessing CPAP effects on haemoglobin oxygen saturation under acute and prolonged altitude exposure.

Methods and results We applied 7 cm H_2O CPAP for 30 min to healthy individuals after acute (Capanna Margherita, CM, 4559 m, 2 days permanence, and <36 h hike) and prolonged altitude exposure (Mount Everest South Base Camp, MEBC, 5350 m, 10 days permanence, and 9 days hike). At CM, CPAP reduced heart rate and systolic pulmonary artery pressure while haemoglobin oxygen saturation increased from 80% (median), 78–81 (first to third quartiles), to 91%, 84–97 ($P < 0.001$). After 10 days at MEBC, haemoglobin oxygen saturation spontaneously increased from 77% (74–82) to 86% (82–89) ($P < 0.001$) while heart rate (from 79, 64–92, to 70, 54–81; $P < 0.001$) and respiratory rate (from 15, 13–17, to 13, 13–15; $P < 0.001$) decreased. Under such conditions, these parameters were not influenced by CPAP.

Conclusion After ascent excessive lung fluids accumulate affecting haemoglobin oxygen saturation and, in these circumstances, CPAP is effective. Acclimatization implies spontaneous haemoglobin oxygen saturation increase and, after prolonged altitude exposure, CPAP is not associated with HbO_2-sat increase suggesting a reduction in alveolar fluids.

Keywords Arterial blood oxygen saturation • High altitude pulmonary oedema • Hypobaric hypoxia at altitude • Positive pressure ventilation

Introduction

High-altitude pulmonary oedema (HAPE) is observed in 2–5% of low landers when climbing[1,2] and, most frequently, within 1–3 days after arrival at altitude.[3] HAPE is more frequent if ascent is rapid,[1,4] associated with heavy exercise[5,6] and in the so-called susceptible subjects usually defined as subjects with a previous history of HAPE.[7–9] At altitude, HAPE-susceptible subjects have some pulmonary haemodynamic derangement even in the absence of any clinical manifestation of HAPE.[8] A higher risk of HAPE is also reported in subjects with smaller lungs and higher pulmonary vascular pressure,[10–12] probably due to the relationship between pulmonary artery pressure changes and vascular cross-sectional area.[10] So, albeit clinically overt HAPE is relatively rare, it has

* Corresponding author. Tel: +39 2 58002270, Fax: +39 2 58002283, Email: piergiuseppe.agostoni@ccfm.it

been suggested that subclinical interstitial oedema is present in most recreational and professional climbers.[10,13] Indeed, Cremona et al.[10] observed that three out of every four subjects, after rapid ascent to a high altitude, have an increase in closing volume which they related to increased pulmonary extravascular fluids, whereas Grocott et al.[13] reported an increased alveolar–arterial oxygen pressure gradient at least at an extreme altitude. At present, no definite information is available about the effects of a prolonged permanence at a high altitude on acute extravascular pulmonary fluid increase.

High-altitude pulmonary oedema is, at least at its onset, a haemodynamic hydrostatic oedema characterized by high pulmonary artery pressure.[7,8,14,15] So, in this regard, it is similar to cardiogenic oedema observed in patients at sea level. Cardiogenic pulmonary oedema is frequently treated using positive pressure ventilation [continuous positive airway pressure (CPAP)],[16–18] and also HAPE could benefit from this intervention, starting from the pioneering personal experience of Oelz.[19] Indeed, CPAP in the presence of increased extra vascular lung fluid, allows improvement of oxygen transport across the alveolar capillary membrane by mechanical removal of accumulated alveolar fluid.[19–21]

The present research project was undertaken to assess the effects of CPAP on arterial haemoglobin oxygen saturation in subjects after either a rapid ascent to high altitudes and after a more gradual ascent followed by prolonged sojourn at high altitudes. The former experiments were performed at Capanna Regina Margherita (CM, 4559 m) which was reached from sea level in less than 2-day hike with CPAP effects being assessed on the second day of altitude exposure. The latter experiments were performed at Mount Everest South Base Camp (MEBC, 5400 m) reached with a 9-day hike, with CPAP effects being assessed 10 days after arrival at MEBC. The final aim of our study was to indirectly evaluate the degree of pulmonary extravascular fluid increase under acute or prolonged exposure to high-altitude hypoxia by assessing the effects of CPAP on HbO_2-sat in these conditions.

Methods

In all conditions of our study, we included subjects who, at the time of CPAP application, showed no evidence of HAPE. Continuous positive airway pressure effects at CM were assessed within the frame of the 2005 Monte Rosa Research Expedition which included a group of 39 subjects. During this expedition, subjects did not receive any research drug. Twenty-three out of 39 subjects were randomly assigned to CPAP application. Continuous positive airway pressure effects at MEBC were assessed within the frame of the HIGHCARE (HIGH altitude CArdiovascular REsearch) project, which included a total of 47 subjects. In this project, subjects were randomized to receive an angiotensin II receptor blocker (Telmisartan 80 mg, $n = 24$) or placebo ($n = 23$). Sixteen out of these 47 subjects were randomly assigned to CPAP application (eight under telmisartan; eight under placebo) (*Table 1*). Subjects not involved in the CPAP studies, both at CM and MEBC, had the same characteristics of the subjects involved in the CPAP studies (*Table 1*). High-altitude sickness prevention by any drug was not allowed in both CM and MEBC expeditions.[22,23] At sea level, before ascent to a high altitude, a general safety medical check-up was performed on all subjects at S. Luca Hospital in Milan (Italy).

Table 1 Anthropometric data of subjects

	Capanna Regina Margherita	Mount Everest South Base Camp	*P*-value
Subjects involved in the CPAP studies			
Sex (M/F)	17/6	15/1	0.21
Age (years)	42 (32–53)	47 (42–53)	0.20
BMI	23 (22–25)	24 (21–25)	0.70
Subjects not involved in the CPAP studies.			
Sex (M/F)	13/3	16/13	0.06
Age (years)	34 (30–60)	36 (32–41)	0.27
BMI	23 (21–24)	24 (21–24)	0.49

Age and BMI data are reported as median and inter-quartile range (first and third quartiles). M, male; F, female; BMI, body mass index. Sex differences were analysed by Fisher's test; age and BMI differences by Wilcoxon rank-sum test.

High-altitude ascent technique and laboratory setting

Capanna Margherita is located on the top of one of the Monte Rosa peaks in the Swiss-Italian Alps at an altitude of 4559 m. Capanna Margherita was reached from Alagna Valsesia (altitude 1130 m) with subjects ascending first by cable-car up to Punta Indren (3200 m) and then on foot to the Gnifetti hut (altitude 3647 m). After an overnight stay, the hike was continued up to CM. All subjects arrived at CM in less than 36 h from initial departure.[24] CPAP experiments were done the day after arrival at CM. Mount Everest South Base Camp is located at 5400 m on the south wing of Mt Everest (Nepal), on the 'Ice Fall Glacier'. Mount Everest South Base Camp was reached during a 9-day hike. We moved from Kathmandu (1200 m) to Lukla (2800 m) by plane and reached Namche Bazar (3500 m) the same day by helicopter. We stopped 3 days in Namche Bazar for initial research/safety measurements and acclimatization. Following a 2 days hike, we then reached Periche (4200 m) where we stopped 1 day for further acclimatization. Thereafter, with a further 2 days hike, we reached MEBC. Experiments at Monte Rosa were performed in CM, a comfortable heated hut, at 4559 m.[7,8,24] Experiments at MEBC were performed at 5400 m in a heated tent, fortunately on 2 sunny days with a warm temperature. In both conditions, subjects were made as comfortable as possible and in no case did they complain of any sort of discomfort due to cold temperatures during the research measurements. In both CM and MEBC, laboratory temperature and barometric pressure were recorded.

During the HIGHCARE Expedition, a safety check was performed in the morning between the first and the second day after arrival at Namche Bazar and at MEBC, as well as between Days 10 and 11 of permanence at MEBC. During these checks, we measured several parameters including heart rate, systemic blood pressure, respiratory rate, and pulmonary artery blood pressure by echocardiography. Mountain sickness severity was assessed by means of the Lake Louise Score (LLS).[25]

Continuous positive airways pressure ventilation

Continuous positive airways pressure was applied using a nasal mask (HC405 Fisher & Pikel, Aukland, New Zealand) in a sitting position using a standard commercial instrument (S8 ResMed, Bella Vista, Australia) regulated to administer a pressure of 7 cm H_2O.

Transcutaneous haemoglobin oxygen saturation was measured constantly before, during, and after CPAP application (pulse oxymeter, Life Scope I, Nihon Kohden, Tokyo, Japan). Pulmonary pressure was measured before and immediately after CPAP application by means of Doppler Ultrasound (Vivid I; General Electric, Tirat Carmel, Israel). Systemic blood pressure (by an oscillometric validated device, OMRON M5-I, Omron, Tokyo, Japan), heart rate, and respiratory frequency were also recorded at the same times.

At MEBC, on the day following the 7 cm H_2O CPAP (Day 22 of ascension), four subjects also underwent 15 cm H_2O CPAP application for 30 min, to explore the possibility of a greater effect with a higher positive airway pressure.

Statistical analysis

Subjects were selected for the CPAP experiments, both at CM and MEBC, by means of a computer-generated randomization list. Assuming a standard deviation of 6 (%) for the main outcome (SpO_2), the sample size of 23 subjects in the study at CM allowed a statistical power of approximately 80% to assess as significant, with a two-tailed $\alpha = 0.05$, a within-subject difference of about 4 (%) (allowing a 20% excess number of subjects, due to the use of a non-parametric test). For the study at MEBC, the sample size of 16 subjects allowed the same statistical power to assess as significant a within subject difference of about 5 (%). Owing to the relatively limited sample size allowed by the difficult experimental conditions, and to the skewed distribution of most of the examined variables, data are summarized as median and inter-quartile range. Data were analysed using non-parametric tests. Within the group, variations were assessed using the Wilcoxon signed-rank test; between-group comparisons were made using the Wilcoxon rank-sum test. Gender distribution between the two groups was evaluated using the Fisher test. Changes during high-altitude exposure in the Mt Everest expedition were assessed by repeated measurements, non-parametric Friedman test followed by *post hoc* analysis corrected by the Bonferroni method. $P < 0.05$ were considered as significant. All tests were two-sided and were performed using SAS statistical package V9.13 (SAS Institute Inc., Cary, NC, USA).

Results

Anthropometric data for subjects at CM and MEBC were not different (*Table 1*). Sex distribution difference did not reach statistical significance and did not influence the CPAP response. Mean atmospheric pressure and oxygen air pressure were 440 and 92 mmHg at CM and 400 and 84 mmHg at MEBC during CPAP experiments. All subjects who underwent 7 cm H_2O CPAP tolerated the manoeuvre well, both at CM and MEBC. Before CPAP at MEBC, telmisartan and placebo-treated subjects did not differ in terms of haemoglobin oxygen saturation, heart rate, respiratory rate, and systemic and pulmonary blood pressure, respectively (*Table 2*). The response to CPAP was similar, so that data are reported regardless of treatment. Subjects who did not participate in the CPAP research protocol, both at CM and MEBC, had cardiorespiratory parameters similar to those of subjects who participated in the CPAP protocol.

After short-term high-altitude exposure at CM, application of 7 cm H_2O CPAP for 30 min reduced heart rate and systolic pulmonary artery pressure but did not influence systemic blood pressure (*Table 3*), whereas haemoglobin oxygen saturation was significantly increased by CPAP from 80 to 91% ($P < 0.001$). Haemoglobin oxygen saturation increase became evident 5 min after starting CPAP application and remained so throughout (*Figure 1*). On the contrary, after long-term high-altitude exposure at MEBC none of the above-reported parameters was influenced by CPAP (*Table 3*, *Figure 1*). Specifically, haemoglobin oxygen saturation was 81 and 80% before CPAP and after 30 min of 7 cm H_2O CPAP, respectively. As an average, comparing pre-CPAP conditions under short-term high-altitude exposure with those at prolonged high-altitude exposure, heart rate was the only parameter evaluated that was different (*Table 3*). Interestingly, average haemoglobin oxygen saturation was the same in the two pre-CPAP conditions. At CM, neither LLS, haemoglobin oxygen saturation nor pulmonary vascular pressure correlated to the haemoglobin oxygen saturation changes during CPAP.

Lake Louise Score was 3.5 (2.0–4.8) at CM and 0.0 (0.0–0.2) after 10 days stay at MEBC ($P < 0.001$).[25]

Haemoglobin oxygen saturation, heart rate, and respiratory rate varied during chronic adaptation to high altitudes in the HIGHCARE expedition. In *Figure 2*, data collected at Milan (95 m), Namche Bazar (3500 m, i.e. on Days 2 and 3 of ascent towards MEBC), on Days 1

Table 2 Cardiorespiratory parameters after 10 days at Mount Everest South Base Camp

	Telmisartan subjects ($n = 8$)			Placebo subjects ($n = 8$)			Δ Pre-CPAP and 30′ CPAP telmisartan vs. placebo (*P*-value)
	Pre-CPAP	30′ CPAP	30′ Post-CPAP	Pre-CPAP	CPAP	30′ Post-CPAP	
HbO_2-sat (%)	84 (78–85)	81 (78–87)	83 (78–88)	81 (77–83)	80 (76–83)	81 (78–84)	0.94
HR (b.p.m.)	74 (70–92)	70 (65–81)	75 (66–85)	78 (67–85)	75 (63–85)	72 (66–80)	0.24
RR (b.p.m.)	11 (9–13)	13 (11–16)	15 (13–16)	16 (13–20)	14 (10–18)	13 (18–17)	0.14
SBP (mmHg)	126 (113–147)	125 (101–145)	127 (119–137)	136 (123–142)	132 (123–139)	140 (124–152)	0.29
DBP (mmHg)	80 (70–86)	76 (71–91)	80 (78–81)	79 (71–90)	86 (84–92)	88 (84–93)	0.29
PAPs (mmHg)	31 (26–36)	31 (24–36)	31 (22–35)	35 (29–41)	37 (36–38)	34 (33–38)	0.94

Data are reported as median and inter-quartile range (first and third quartiles). CPAP, continuous positive pressure ventilation. Continuous positive airway pressure data were collected on continuous positive airway pressure at the end of 30 min continuous positive airway pressure application. HbO_2-sat, arterial haemoglobin saturation for oxygen; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PAPs, pulmonary artery systolic pressure. In the last right column, *P*-values for differences between pre-continuous positive airway pressure and 30′ continuous positive airway pressure in subjects assuming telmisartan vs. subjects assuming placebo are reported.

Table 3 Cardiorespiratory parameters pre-continuous positive airway pressure and during continuous positive airway pressure (30 min) at Capanna Regina Margherita and Mount Everest South Base Camp

	Capanna Regina Margherita			Mount Everest South Base Camp			Δ Pre-CPAP at CM vs. Δ pre-CPAP at MEBC (*P*-value)
	Pre-CPAP	30′ CPAP	*P*-value	Pre-CPAP	30′ CPAP	*P*-value	
HbO_2-sat (%)	80 (78–81)	91 (84–97)	<0.001	81 (78–85)	80 (78–85)	0.80	<0.001
HR (b.p.m.)	88 (77–101)	84 (77–86)	<0.001	76 (68–91)*	73 (63–85)	0.01	0.24
RR (b.p.m.)	17 (14–21)	16 (14–18)	0.79	13 (11–17)	13 (10–17)	0.52	0.62
SBP (mmHg)	126 (122–134)	130 (122–136)	0.89	131 (119–144)	132 (111–140)	0.23	0.61
DBP (mmHg)	87 (81–90)	90 (83–96)	0.57	80 (71–88)	84 (74–92)	0.26	0.51
PAPs (mmHg)	35 (31–40)	33 (24–35)	0.005	32 (27–40)	37 (33–38)	0.60	0.03

Data are reported as median and inter-quartile range (first and third quartiles). CPAP, continuous positive airway pressure; HbO_2-sat, arterial haemoglobin saturation for oxygen; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PAPs, pulmonary artery systolic pressure. *P*-values represent significance vs. the same parameter pre-continuous positive airway pressure in the same conditions.
*$P < 0.05$ vs. HR pre-continuous positive airway pressure at Capanna Regina Margherita.

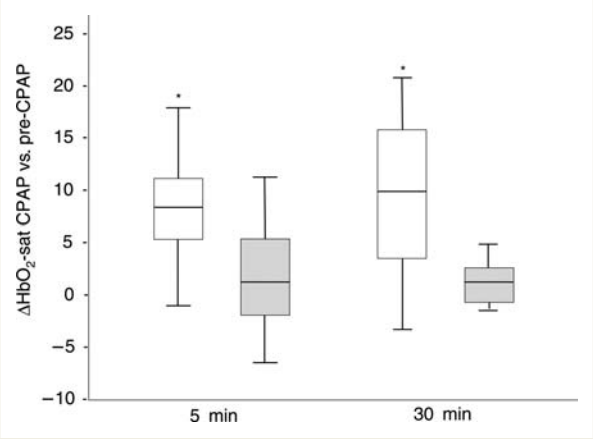

Figure 1 Difference in arterial haemoglobin oxygen saturation between pre-continuous positive airway pressure and during continuous positive airway pressure, after 5 and 30 min, respectively. White columns are data collected at Capanna Regina Margherita, grey columns are data collected at Mount Everest Base Camp. *$P < 0.000$ vs. pre-continuous positive airway pressure condition. Data are shown as median, first and third inter-quartiles and 95% confidence interval values.

and 2 at MEBC (5350 m, Days 10 and 11 of ascent) and on Days 11 and 12 at MEBC (Days 21 and 22 of ascent) are reported. At MEBC after 10 days, haemoglobin oxygen saturation increased (from 77 to 86%; $P < 0.001$) whereas heart rate (from 79 to 70 b.p.m.; $P < 0.001$) and respiratory rate (from 15 to 13 breaths/min; $P < 0.001$) decreased. Lake Louise Score during ascent and MEBC stay is also reported in *Figure 2*.

Four subjects underwent 15 cm CPAP application at MEBC. One subject did not tolerate 15 cm H_2O CPAP. In the remaining three, haemoglobin oxygen saturation was 78% before CPAP and 74% during CPAP (30 min). Heart rate, respiratory rate, and systemic and pulmonary pressures did not show any significant change.

Discussion

These data show that CPAP application after short-term high-altitude exposure improves arterial haemoglobin oxygen saturation, whereas this is not the case in subjects after prolonged high-altitude exposure, even when pre-CPAP haemoglobin oxygen saturation is similar to the acute condition.

These findings suggest that acutely, in line with our hypothesis, some lung fluid accumulation is, at least in part, responsible for low arterial haemoglobin oxygen saturation at high altitudes, but that after prolonged high-altitude exposure no more extravascular fluid is present on the alveolar-capillary membrane which could be shifted away by CPAP.

CPAP is recommended and frequently used for pulmonary oedema treatment at sea level.[16–18] In acute pulmonary oedema, CPAP usually leads to a rapid increase in haemoglobin oxygen saturation. It has been proposed that CPAP acts by shifting excessive lung fluid from the flat part of the alveolar-capillary membrane, where the majority of gas exchange takes place, to the alveolar corner and from there to the extra-alveolar interstitial space.[20,21] This suggested lung fluid shift, although the total amount of lung fluid does not change, may be the factor responsible for the observed improvement in haemoglobin oxygen saturation in patients with acute pulmonary oedema treated with CPAP.[20,21,26–28]

High-altitude pulmonary oedema occurs in a percentage of subjects who reach high altitude, usually 24–72 h after arrival and particularly if the ascent is associated with heavy physical exercise, as it was the case in our study at CM.[1–5] High-altitude pulmonary oedema has a pulmonary haemodynamic involvement that resembles that observed during acute pulmonary oedema at sea level.[7–9,15] Furthermore, Cremona *et al.*[10] produced indirect evidence suggesting that many, if not all, subjects who ascend to high altitudes show evidence of lung fluid increase and, very recently, Grocott *et al.*[13] showed, albeit at extreme altitude, an increase in alveolar–arterial oxygen pressure gradient. Accordingly, studies of both Cremona *et al.*[10] and Grocott *et al.*[13] are suggestive of subclinical pulmonary oedema even in the absence of signs and symptoms of overt pulmonary oedema. Acute hypoxia

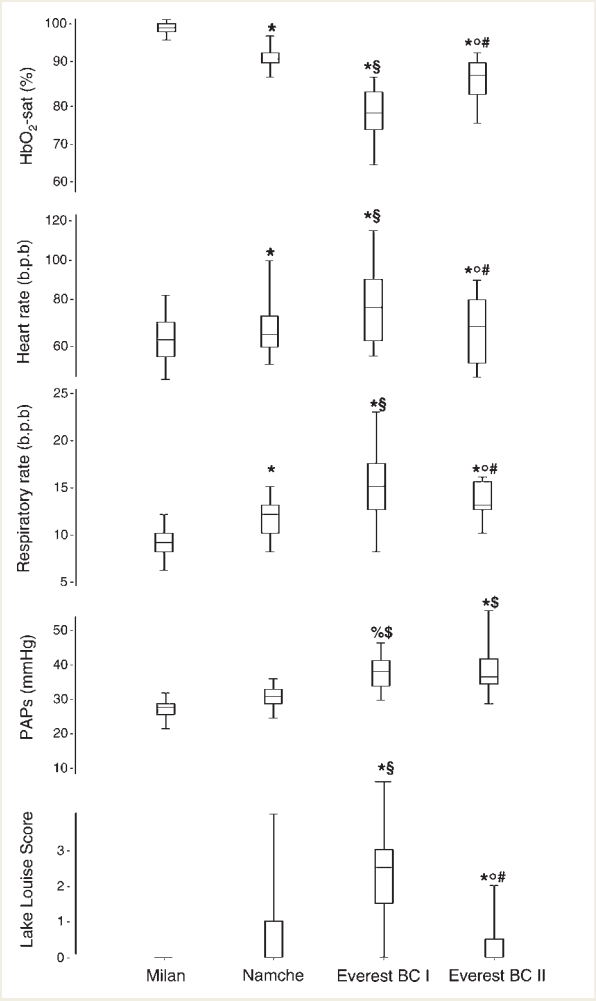

Figure 2 Arterial haemoglobin oxygen saturation (HbO_2-sat), heart rate, respiratory rate, pulmonary artery systolic pressure and Lake Louise Score at Milan, Namche Bazar, and Mount Everest South Base Camp at Days 1–2 and 10–11. Data are shown as median, first and third inter-quartiles and 95% confidence interval values. $^{*}P < 0.001$ vs. Milan; $^{\%}P < 0.01$ vs. Milan; $^{\S}P < 0.001$ vs. Namche Bazar; $^{\$}P < 0.05$ vs. Namche Bazar; $^{\circ}P < 0.005$ vs. Namche Bazar; $^{\#}P < 0.001$ vs. Mount Everest South Base Camp Days 1–2.

may lead to transitory dysregulation of ventilation perfusion matching which CPAP may counterbalance. Interestingly, Loeppky *et al.*[29] showed that even in the first hours of hypobaric hypoxia there is, at rest, a greater desaturation in the subjects developing acute mountain sickness. It should be emphasized, however, that, both at CM and MEBC, none of the subjects showed clinical evidence of overt pulmonary oedema at the time of CPAP application. Regardless of this, we observed that CPAP is effective in increasing low arterial haemoglobin oxygen saturation, similar to when it is applied during acute pulmonary oedema treatment at sea level,[16–18] but this occurs only after short-term exposure to high-altitude hypobaric hypoxia. Furthermore, when CPAP was applied in these acute hypoxic conditions, we observed not only a relevant improvement in arterial haemoglobin oxygen saturation, but also a reduction in heart rate and pulmonary artery pressure. All together, these data are in line with the observations by Cremona *et al.*[10] and Grocott *et al.* suggesting that some subclinical pulmonary oedema is present in many, if not all, subjects who ascend rapidly to high altitudes and that CPAP can counterbalance this lung fluid derangement.

A significant reduction in haemoglobin oxygen saturation was also observed after short-term high-altitude exposure in the HIGHCARE Mt Everest expedition, too. Furthermore, in the acute phase of HIGHCARE expedition, during high-altitude acclimatization, 5 out of the 47 European low-lander subjects (none of whom, as required by the experimental protocol, received any drugs to prevent HAPE, including acetazolamide) experienced severe dyspnoea and other major clinical signs of mountain sickness, which were treated using intravenous steroids, inhalation of oxygen, acetazolamide and a temporary transfer to lower altitude. During the 10-day permanence at MEBC, arterial haemoglobin oxygen saturation improved in all subjects, suggesting that adaptation to high altitudes was associated with a reduction in alveolar extravascular fluid content. Indeed, when CPAP was applied after 10 days of permanence at MEBC, no further haemoglobin oxygen saturation changes were observed. The lack of increase in haemoglobin oxygen saturation with CPAP after prolonged exposure at MEBC was not due to differences in barometric pressure compared with CM, because, even if there is a 650 m altitude difference between CM and MEBC, the difference in barometric pressure and therefore atmospheric partial PO_2 was small, 40 and 8.4 mmHg, respectively, due to differences in latitude.[30,31] Furthermore, subjects treated at MEBC with higher levels of CPAP did not show any increase in arterial haemoglobin oxygen saturation. We interpret these findings as being due, with permanence at high altitude, to an adaptation-induced reduction in the amount of extravascular fluids acutely appearing on the alveolar-capillary membrane, as suggested by the spontaneous haemoglobin oxygen saturation increase concomitantly occurring during the stay at high altitudes (*Figure 2*). Finally, we can reasonably exclude the possibility that, under prolonged exposure to high altitude, CPAP effects on blood oxygen saturation were prevented by the chronic effects of pulmonary hypoxic vasoconstriction, because after 7–10 days of permanence at high altitudes pulmonary pressure was no longer elevated.

This study has several possible limitations that should be acknowledged. First, differences in the laboratory settings should be considered. Indeed, CM is a comfortably heated hut, whereas experiments at MEBC were carried out, although on 2 sunny days, in a heated tent. Second, we limited our observation to transcutaneous haemoglobin oxygen saturation and did not perform direct arterial gas analysis. Indeed, repeated arterial punctures were found somehow unethical by researchers and difficult to accept by volunteers. Third, we did not perform any direct measurement of lung fluids or analysis of lung congestion as previously done by chest X-ray or spirometric techniques; so our suggestions on lung fluid behaviour at altitude are indirectly derived from arterial haemoglobin oxygen saturation changes. Fourth, we did not measure ventilation at CM and at MEBC. It is known that at high altitudes ventilation continues to increase over 2 weeks due to the increased sensitivity of peripheral

chemoreceptors to hypoxia.[32] Because CPAP may act by increasing ventilation, it is possible that at MEBC, after high-altitude adaptation, the supposed CPAP increase in ventilation is blunted, reducing some of the CPAP effects seen at CM. Finally, we do not know whether standard prophylactic treatment with acetazolamide[22] could influence the haemoglobin oxygen saturation before and after CPAP application, an issue that would deserve to be addressed in future studies at high altitudes.

In conclusion, this study suggests that after rapid high-altitude ascent excessive fluids accumulate along the alveolar capillary membrane affecting arterial haemoglobin oxygen saturation and that, in these circumstances, CPAP is effective in increasing haemoglobin oxygen saturation. This study also shows that acclimatization implies an increase in haemoglobin oxygen saturation and a reduction in heart rate, in parallel with a reduction in mountain sickness symptoms. As a result, application of CPAP after long-term high-altitude exposure is no longer associated with an increase in arterial haemoglobin oxygen saturation. A practical implication of our findings is that CPAP application could represent a useful manoeuvre for the treatment of some mountain sickness symptoms related to low blood oxygen saturation under acute exposure to high-altitude hypobaric hypoxia. Even if our data suggest that CPAP was no longer useful after prolonged high-altitude exposure, in subjects without clinical signs or symptoms of pulmonary oedema, we cannot exclude that CPAP very likely remains a useful therapeutic tool in all cases of HAPE,[33,34] regardless of the length of time subjects remain at high altitudes.

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Conflict of interest: none declared.

Appendix

HIGHCARE Investigators

Gianfranco Parati, Piergiuseppe Agostoni, Manuela Bartesaghi, Barbara Bilo, Grzegorz Bilo, Giovanna Branzi, Maurizio Bussotti, Gianluca Caldara, Andrea Cappugi, Kaschina Elena, Andrea Faini, Alessia Giglio, Andrea Giuliano, Francesca Gregorini, Carolina Lombardi, Veronica Mainini, Giuseppe Mancia, Paolo Mazzoleni, Paolo Meriggi, Pietro Amedeo Modesti, Marco Morabito, Alberto Piperno, Barbara Poletti, Stefano Rapi, Miriam Revera, Mauro Romerio, Katarzyna Styczkiewicz, Margherita Tamplenizza, Maria-consuelo Valentini.

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CARDIOVASCULAR FLASHLIGHT

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A multi-modal assessment of a multi-visceral affect of a Wegener granulomatosis

Guillaume Leurent[1,2,3,4]*, Pierre Axel Lentz[5], and Sébastien Henno[6]

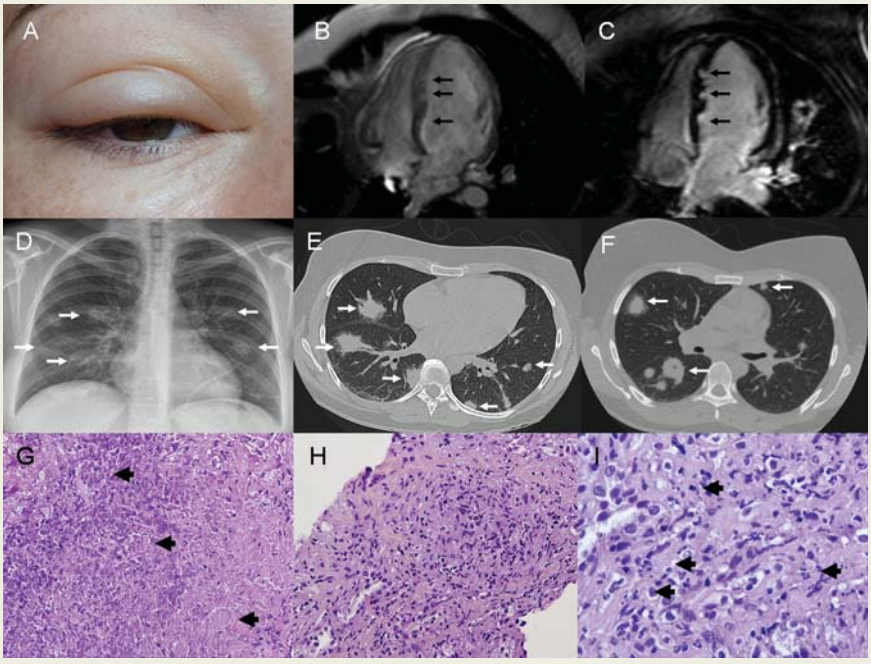
[1]CHU Rennes, Service de cardiologie et maladies vasculaires, Rennes F-35000, France; [2]Université de Rennes 1, LTSI, Rennes F-35000, France; [3]INSERM, U642, Rennes F-35000, France; [4]INSERM, CIC-IT 804, Rennes F-35000, France; [5]CHU Rennes, Département de radiologie et d'imagerie médicale, Rennes, F-35000, France; and [6]CHU Rennes, Service d'anatomie et cytologie pathologiques, Rennes, F-35000, France

* Corresponding author. Tel: +33 299 289 221, Fax: +33 299 282 503, Email: guillaume.leurent@chu-rennes.fr

A 34-year-old woman was hospitalized for acute chest pain. Her personal history was made of an acute inflammation of the right lacrimal gland (*Panel A*), biopsied 2 days before, showing a non-specific inflammation.

EKG was normal, but troponin rose up to 10 ng/mL, and C-reactive protein to 200 mg/L. Renal function was normal, without any proteinuria. Transthoracic echo showed a septal hypokinesia: left ventricular ejection fraction (LVEF) 45%. A catheterization was performed, showing normal coronary arteries.

A cardiac 3 T MR examination was achieved:



- Cine MR realized after the injection of gadolinium confirmed the septal hypokinesia (LVEF 38%), with a contrast enhancement in the same territory (*Panel B*).
- T1-weighted inversion recovery sequences, 10 min later, confirmed the septal inflammation: a delayed contrast enhanced is found in the septal area, with a 'patchy' pattern (*Panel C*). Myocarditis was then diagnosed.

Since the thoracic radiography revealed several bilateral opacities (*Panel* D), a thoracic CT scan was achieved (*Panels E* and *F*): bilateral rounded opacities were found, some of them excavated, without any other anomalies. Transthoracic biopsies were performed, and histological analysis showed 'geographic' necrosis with isolated multinucleated giant cells (*Panel G*), and leucocytoclastic vasculitis (*Panels H* and *I*).

The research for cANCA was strongly positive (337 U/mL), and a Wegener granulomatosis was diagnosed, with myocardial, ophthalmological, and pneumological involvement. Corticosteroid therapy was introduced, allowing a quick improvement of the patient.

Cardiac involvement is a rare manifestation of Wegener granulomatosis. This case illustrates the need to use multi-modal imaging to assess its extension.