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Original Scientific Paper

Disappearance of isocapnic buffering period during increasing work rate exercise at high altitude

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Background **At sea level, ventilation kinetics are characterized during a ramp exercise by three progressively steeper slopes, the first from the beginning of exercise to anaerobic threshold, the second from anaerobic threshold to respiratory compensation point, and the third from respiratory compensation point to peak exercise. In the second ventilation phase, body CO_2 stores are used to buffer acidosis owing to lactate production; it has been suggested that this extra CO_2 production drives the ventilation increase. At high altitude, ventilation increases owing to hypoxia. We hypothesize that ventilation increase reduces body CO_2 stores affecting ventilation kinetics during exercise.**

Design **In eight healthy participants, we studied the ventilation kinetics during an exercise performed at sea level and at high altitude (4559 m).**

Methods **We used 30 W/2 min step incremental protocol both at sea level and high altitude. Tests were done on a cycloergometer with breath-by-breath ventilation and inspiratory and expiratory gas measurements. We evaluated cardiopulmonary data at anaerobic threshold, respiratory compensation point, peak exercise and the VE/VCO_2 slope.**

Results **At high altitude: (a) peak V_{O_2} decreased from 2595 ± 705 to 1745 ± 545 ml/min ($P < 0.001$); (b) efficiency of ventilation decreased (VE/VCO_2 slope from 25 ± 2 to 38 ± 4, $P < 0.0001$); (c) at each exercise step end-tidal pressure change for CO_2 was lower; and (d) the isocapnic buffering period disappeared in seven over eight participants and was significantly shortened in the remaining participant.**

Conclusion **Exercise performed at high altitude is characterized by two, instead of three, ventilation slopes.** ***Eur J Cardiovasc Prev Rehabil*** **15:354–358 © 2008 The European Society of Cardiology**

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Introduction

At sea level, during exercise, ventilation increases [1]. Unfortunately, at the present time, we do not have a clear understanding of the control of ventilation during exercise [2]. Several mechanisms are reported to play a role including the amount of carbon dioxide production (VCO_2), acidosis, efficiency of ventilation, gas exchange capacity at alveolar and muscular level, and reflexes arising from lungs, chemoreceptor, muscles, brain and so on [3,4]. In an exercise performed with a progressive increase in workload, ventilation increase has a kinetic characterized by three slopes, whereas VCO_2 increase is characterized by two slopes and the oxygen uptake (V_{O_2}) increase by only one [5]. It has been proposed that each ventilation increase slope is owing to the effect on ventilation of a metabolic/acid state balance specific for the exercise phase examined [6]; however, the reverse

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has also been suggested, that is, that ventilation affects the metabolic/acid state balance [7]. Regardless of the mechanism involved, the first ventilation slope is between the beginning of exercise and the anaerobic threshold. In this exercise phase, ventilation increase is associated to $\dot{V}O_2$ increase. The second ventilation slope is observed between the anaerobic threshold and the end of the isocapnic buffering period, which identifies the 'so called' respiratory compensation point. Wasserman *et al.* [5,6,8] hypothesized that this second ventilation slope is related to VCO_2 production arising from carbonate buffering of lactate (anaerobic energy production) on top of aerobic energy production; the former implies the progressive consumption of a portion of body CO_2 stores. Above the respiratory compensation point, the buffering of lactate by the bicarbonate system is incomplete and exercise-induced acidosis becomes uncompensated and arterial pH starts to decrease. It is still to be discussed if, and to what extent acidosis is an additional driving force for ventilation at this exercise step [5,6,8,9].

At altitude, ventilation at rest and during exercise is higher compared with sea level, with hypoxia being the driving force for such an increase [10]. We hypothesized that hypoxia-induced hyperventilation should influence the ventilation slopes observed at sea level so that an exercise performed at high altitude might be characterized by different kinetics of ventilation. Indeed, at high altitude the increase in ventilation needed to keep up with the low inspired pO_2, is associated to a reduction of arterial pCO_2, which implies a reduction of CO_2 body stores [11]. Accordingly, the second ventilation slope observed at sea level, which is linked to the utilization of body CO_2 stores, at high altitude should disappear or, at least, be greatly reduced.

To evaluate if ascent to high altitude influences ventilation kinetics, we performed a progressively increasing workload cardiopulmonary exercise test at sea level, and on the second/third day at high altitude (Capanna Regina Margherita, Monte Rosa, Italian Alps, 4559 m) in eight normal volunteers. Starting from the pioneering experience of Angelo Mosso more than 100 years ago, several high altitude studies have been performed at the Capanna Regina Margherita. This shelter is the highest in Europe and hosts a library devoted to high altitude research and expeditions [12].

Methods

Study participants and protocol

Eight normal nonathlete individuals without relevant alpine experience (six male and two female; mean age 44 ± 16 years) participated in the study. All participants live in the Milan area (90–200 m); each participant performed two maximal cardiopulmonary exercise tests at sea level and one at Capanna Regina Margherita. We used the same cyclo-ergometer (Microlife Corporation, Dunedin, Florida, USA) and metabolic cart (Oxycon Mobile software v. 4.6, VIASYS Healthcare GmbH, Wuerzburg, Germany) in all tests. The first sea level test, always preceding the high altitude test, was used for familiarization purposes and its results were discarded. The second test at sea level was done before ($n = 3$), or at least 2 weeks after descent from high altitude ($n = 5$). Ascent to Capanna Regina Margherita from Milan was performed in 2 days, by car (up to Alagna 1191 m), cable car (up to punta Gnifetti 3200 m) and then by foot. All participants spent a night in an intermediate shelter (Capanna Gnifetti 3647 m) and ascended to Capanna Regina Margherita the day after, under the supervision of alpine guides. The exercise was performed on the second or third day after arriving at Capanna Regina Margherita. During the first 2 days of their stay at Capanna Regina Margherita, participants did not perform any additional relevant physical activity. Participants remained at Capanna Regina Margherita for 7–10 days.

The exercise protocol was characterized by at least 10 min of rest, 3 min of unloaded pedalling and subsequent 30 W load increases every 2 min up to exhaustion. We measured, breath-by-breath, ventilation, inspired and expired gases. One lead ECG, blood pressure, pulse oxymetry data and heart rate were also obtained.

Tests were evaluated by two expert readers. The anaerobic threshold was identified by V-slope analysis of $\dot{V}O_2$ and VCO_2 increase and confirmed by specific behaviour of O_2 ($VE/\dot{V}O_2$), ventilatory equivalent and O_2 end-tidal pressure change ($PetO_2$) [13]. The respiratory compensation point was identified when VE over VCO_2 increased and end-tidal pressure changes for CO_2 ($PetCO_2$) decreased [5]. VE/VCO_2 slope was measured from the beginning of loaded exercise to the respiratory compensation point.

The study was approved by the Istituto Auxologico Italiano Ethics Committee as a substudy of a larger research project investigating the effects on human subjects of hypoxia induced by high altitude. All participants signed a written informed consent before participating in the study.

Statistical analysis

Data are reported as means ± SD. Mean values of the cardiopulmonary exercise tests (except time) are 20 s averages. All data were evaluated with the database SPSS-PC + 13.0 (SPSS-PC + Inc., Chicago, Illinois, USA). Data were analyzed by paired Student's *t*-test. A *P* value of < 0.05 was considered to indicate statistical significance.

Table 1 Cardiopulmonary exercise test variables

	Baseline		Anaerobic threshold		Respiratory compensation		Peak exercise	
	Sea level	High altitude	Sea level	High altitude	Sea level	High altitude	Sea level	High altitude
HR (beat/min)	80 ± 21	81 ± 15	109 ± 21	116 ± 15	147 ± 20$^{\#}$	117 ± 15	165 ± 12§	145 ± 22
VCO_2 (ml/min)	292 ± 49	296 ± 75	1374 ± 407§	969 ± 245	2400 ± 722*	1009 ± 300	3120 ± 888$^{\#}$	2023 ± 594
$V\mathrm{O}_2$ (ml/min)	313 ± 33	327 ± 74	1416 ± 363§	1002 ± 240	2131 ± 609*	1029 ± 268	2595 ± 705$^{\#}$	1745 ± 545
RR (breath/min)	14 ± 4	19 ± 6	20 ± 7	21 ± 6	28 ± 7$^{\#}$	21 ± 6	38 ± 8$^{\#}$	44 ± 11
VT (l)	0.9 ± 0.3	0.8 ± 0.3	2.1 ± 0.5	2.0 ± 0.7	2.5 ± 0.5	2.1 ± 0.7	2.7 ± 0.4§	2.3 ± 0.4
VE (l/min)	11 ± 2	15 ± 5	40 ± 12	42 ± 11	72 ± 24$^{\#}$	43 ± 14	104 ± 32	99 ± 30
$PetCO_2$ (mmHg)	37 ± 4*	24 ± 3	39 ± 4*	26 ± 2	37 ± 4*	26 ± 2	33 ± 3*	21 ± 3
$PetO_2$ (mmHg)	106 ± 7*	57 ± 4	106 ± 5*	56 ± 3	112 ± 6*	56 ± 3	118 ± 5*	65 ± 3

Data were recorded as means over 20 s and reported as mean ± SD. HR, heart rate; $PetCO_2$, end tidal CO_2 pressure; $PetO_2$, end tidal O_2 pressure; RR, respiratory rate; VCO_2, carbon dioxide production; VE, ventilation; $V\mathrm{O}_2$, oxygen consumption; VT, tidal volume. $^{*}P<0.0001$; $^{\#}P<0.001$; $^{\S}P<0.05$ sea level versus high altitude.

Table 2 Exercise tolerance and time to anaerobic threshold and respiratory compensation point

	Sea level	High altitude
Exercise tolerance (s)	851 ± 240*	586 ± 181
Time to AT (s)	337 ± 118§	256 ± 85
Time to RC (s)	654 ± 185*	261 ± 96
Time difference between AT and RC (s)	317 ± 87*	5 ± 15
Time difference between AT and peak exercise (s)	514 ± 145$^{\#}$	330 ± 151
Time difference between RC and peak exercise (s)	197 ± 111§	324 ± 153

Data are expressed as mean ± SD. AT, anaerobic threshold; RC, respiratory compensation point. $^{*}P<0.0001$; $^{\#}P<0.001$; $^{\S}P<0.05$ sea level versus high altitude.

Results

All participants were able to perform a maximal test or what they claimed was a maximal test. Indeed, peak exercise respiratory exchange ratio was 1.19 ± 0.06 and 1.17 ± 0.09 at sea level and high altitude test, respectively. Data reported in Table 1 refer, for both sea level and high altitude tests, to rest, anaerobic threshold, respiratory compensation point and peak exercise. $PetCO_2$ was always lower at high altitude. The ventilatory efficiency, measured by means of VE/VCO_2 slope, was 25 ± 2 at sea level and 38 ± 4 at Capanna Regina Margherita ($P < 0.0001$). Exercise capacity was lower at high altitude in terms of $V\mathrm{O}_2$ reached (Table 1), Watts reached and exercise tolerance (Table 2). Indeed, exercise tolerance was 851 ± 240 s at sea level and 586 ± 180 s at high altitude ($P < 0.0001$), and Watts reached were 217 ± 64 W at sea level and 150 ± 39 W at high altitude ($P < 0.01$). In addition, the anaerobic threshold occurred earlier at high altitude (Table 2). The respiratory compensation point was superimposed to the anaerobic threshold (i.e. simultaneous increase in VE/VCO_2, $VE/V\mathrm{O}_2$ and $PetO_2$ and reduction in $PetCO_2$) in seven out of eight participants (Fig. 1). In one participant, the time difference between the anaerobic threshold and the respiratory compensation point was not abolished but only reduced, being 301 s at sea level and 43 s at high altitude. Percent changes in time between the various exercise parts are reported in Table 2.

Discussion

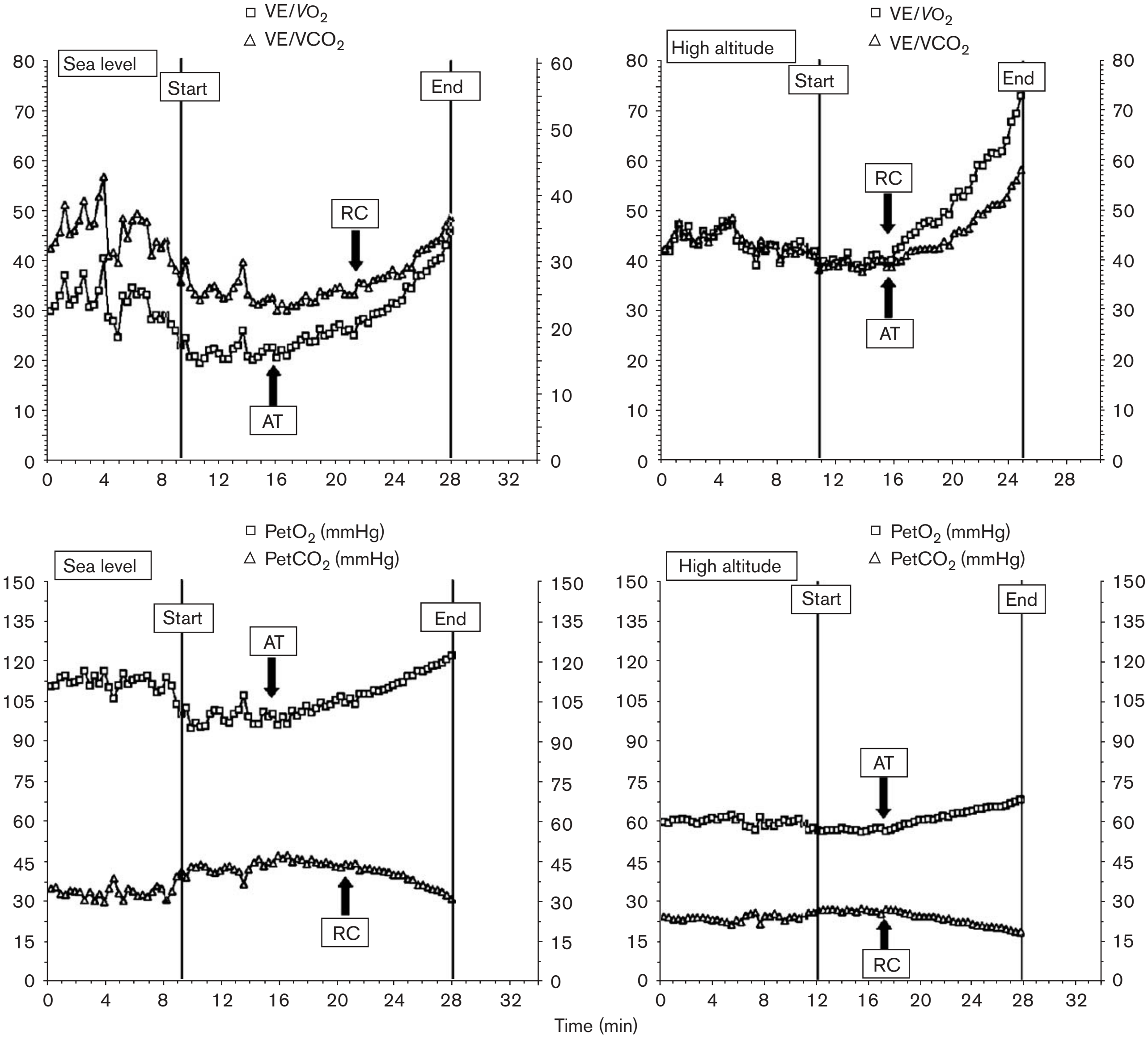
This study shows that in seven out of eight participants, at high altitude, ventilation in a progressive exercise test has a kinetic characterized by two slopes instead of the three observed at sea level, and that the isocapnic buffering period disappears in these seven participants, and it is significantly shortened in the remaining one. In other words, the second ventilation phase observed at sea level, known to be associated with the utilization of body CO_2 stores, disappeared or was greatly shortened at altitude.

Owing to the need of collecting blood pressure, pulse oxymetry data and heart rate, at definite workload (which are not included in the present report), we performed a step incremental exercise protocol characterized by 30 W load increment every 2 min. This implies a not linear increment of ventilation during exercise, which makes the calculation of ventilatory kinetics difficult and possibly criticizable. Accordingly, we avoided reporting slopes ventilation/time relationship [13,14].

It is a common notion that at high altitude ventilation increases. The cause of high altitude increase in ventilation is hypoxia [11,15]. When considering the mechanisms responsible for the two slopes observed at high altitude, as at sea level, the first slope is related to the effects of $V\mathrm{O}_2$ increase on ventilation [6]. Above the respiratory compensation point, which in seven out of eight participants is superimposed to the anaerobic threshold, and in the eighth participant is immediately after the anaerobic threshold, ventilation increase is likely driven by acidosis. That hypoxia or $V\mathrm{O}_2$ are not the main driving force for ventilation in the second part of exercise at altitude is suggested by the fact that $PetO_2$ is higher, as at sea level, at peak exercise compared with anaerobic threshold. This indicates that ventilation is exceeding the $V\mathrm{O}_2$ metabolic demand.

The disappearance at high altitude of the isocapnic buffering period is likely owing to the preexercise high ventilation which has reduced the CO_2 body stores

Fig. 1



Different behaviour of O_2 and CO_2 ventilatory equivalents (VE/$\dot{V}O_2$ and VE/VCO_2) and end-tidal pressure changes for O_2 ($PetO_2$) and CO_2 ($PetCO_2$) in the same participant at sea level (panels on the left) and at high altitude (panels on the right). The anaerobic threshold was identified by V-slope analysis of $\dot{V}O_2$ and VCO_2 increase. The respiratory compensation point was identified when VE over VCO_2 increased and end-tidal pressure changes for CO_2 ($PetCO_2$) decreased. Note that the respiratory compensation point (RC) was superimposed to the anaerobic threshold (AT) when the exercise is performed at high altitude. Data are reported as mean of 20 s.

available for exercise-induced acidosis buffering [11]. Indeed, $PetCO_2$ at high altitude is much lower than at sea level (Table 1). Consequently, our observation fits with the Wasserman's hypothesis of an effect on ventilation kinetics during exercise of the metabolic/acid state balance [5,6,8].

It should be emphasized that we have described the changes in ventilation kinetics during exercise at altitude, and that we have not evaluated the role of CO_2 and acidosis on the ventilatory control during exercise. Indeed, besides CO_2 and acidosis other regulatory mechanisms such as metabo and ergoreflexes [3,4], temperature changes and so on might be of primary importance on regulation of ventilation during exercise at altitude, and none were evaluated in this study. Furthermore, because CO_2 balance is reset after a prolonged permanence at high altitude [16], our results should be interpreted only within the frame of the time course of the present experiment, and data cannot be extrapolated to a population living at high altitude or to participants remaining at altitude for longer times.

Similarly, exercise performed immediately after a quick ascent to altitude might show different results.

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Conflict of interest: none.

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