

Sleep-related hypoxaemia and excessive erythrocytosis in Andean high-altitude natives

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ABSTRACT: To determine whether nocturnal hypoxaemia contributes to the excessive erythrocytosis (EE) in Andean natives, standard polysomnographies were performed in 10 patients with EE and in 10 controls (mean haematocrit $76.6 \pm 1.3\%$ and $54.4 \pm 0.8\%$, respectively) living at an altitude of 4,380 m. In addition, the effect of O₂ administration for 1 h prior to sleep, and the relationship between the hypoxic/hypercapnic ventilatory response and the apnoea/hypopnoea index (AHI) during sleep were studied.

Awake arterial oxygen saturation (Sa_aO₂) was significantly lower in patients with EE than in controls ($83.7 \pm 0.3\%$ versus $85.6 \pm 0.4\%$). In both groups, the mean Sa_aO₂ significantly decreased during sleep (to $80.0 \pm 0.8\%$ in EE and to $82.8 \pm 0.5\%$ in controls). The mean Sa_aO₂ values remained significantly lower in patients with EE than in controls at all times of the night, and patients with EE spent significantly more time than the controls with an Sa_aO₂ of <80%. There were no differences between the two groups in the number and duration of the apnoeas/hypopnoeas. None of these variables were affected by O₂ administration. In both groups the AHI positively correlated with the hypercapnic ventilatory response.

Andean natives undergo minor respiratory disorders during sleep. The reduction in oxygen saturation found in subjects with excessive erythrocytosis was small, yet consistent and potentially important, as it remained below the threshold known for the increase in erythropoietin stimulation. This may be an important factor promoting erythropoiesis, but its relevance needs to be further explored.

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Excessive erythrocytosis (EE) and hypoxaemia are the major features of a syndrome known as "chronic mountain sickness" (CMS) [1, 2] affecting millions of highlanders around the world and particularly common among Andean natives. The pathogenesis of EE is still unclear. In fact, while the increased erythropoiesis in highlanders is considered a mechanism of adaptation to the hypoxic environment, it is not clear why some of these subjects develop EE. One possible explanation is that a blunted hypoxic ventilatory response observed in highlanders with EE may induce a chronic hypoventilation that worsens the hypoxaemia [3]. Other authors have suggested that sleep-related hypoxaemia may be the cause of EE [2, 4]. This suggestion is based on the observation that hypoventilation is a physiological feature of the sleep state at sea-level as well [5]. In addition, substantial nocturnal hypoxaemia has been reported in highlanders at 3,100 m and 3,658 m [6, 7] and sleep-disordered breathing (SDB) is a common finding in lowlanders ascending to high altitude [8–10]. COOTE and co-workers [11, 12] were the first to perform sleep studies in healthy Andean natives above 4,000 m and to determine the presence of nocturnal periodic breathing associated with a moderate fall in arterial oxygen saturation (Sa_aO₂). This finding led these authors to emphasise the importance of studying the nocturnal respiratory pattern in detail in these subjects. This should allow definitive conclusions to be drawn about the importance of nocturnal

hypoventilation and/or SDB in the development of polycythaemia. However, to date, a comparison of the nocturnal respiratory profile between Andean highlanders with and without EE has never been performed.

Therefore, the frequency and duration of nocturnal apnoea/hypopnoea episodes, oxygen saturation, and sleep parameters in a group of patients with EE were compared with a group of controls that were permanent residents in the Andean town of Cerro de Pasco (Peru) at an altitude of 4,380 m.

The occurrence of SDB at altitude could be related to an altered hypoxic and/or hypercapnic ventilatory response [10, 13, 14]. However, the ventilatory control of lowlanders during acute exposure to altitude is markedly different from that found in altitude natives [3, 15]. Therefore, in order to investigate a possible correlation between the hypoxic/hypercapnic ventilatory response and the presence of SDB in the subjects, the ventilatory response to isocapnic hypoxia and to normoxic hypercapnia was assessed by classic rebreathing manoeuvres.

Finally, in a preliminary report, it was suggested, at least during wakefulness, that the depressed ventilation described in patients with EE may be reversed by the acute (1 h) administration of O₂ [15]; similarly, a recent study showed an increase in ventilation during O₂ administration in similar patients [16]. These previous references thus provided a rationale for testing whether the 1-h administration of O₂

prior to sleep could improve oxygen saturation (and consequently sleep parameters) during the night.

Methods

Subjects

The experiments were conducted in the Andean town of Cerro de Pasco, Peru, at an altitude of 4,380 m, during September 1–28, 2001. Two groups (EE and controls) of 10 subjects were selected for this study, on the basis of their haematocrit (Ht) and haemoglobin (Hb). The values for establishing the presence of EE were chosen according to studies from LEON-VELARDE and co-workers [17, 18] who measured Hb in the population of Cerro de Pasco and found a 95 percentile of 21.3 g·dL⁻¹, which corresponds to a Ht of ~64%. The SD of Ht and Hb in the healthy middle-aged male population in Cerro de Pasco is 3.13% and 1.21 g·dL⁻¹, respectively [19]. Therefore, the EE group was comprised of those subjects with an Ht of ≥70% and Hb of ≥22.5 mg·dL⁻¹, and the control group of subjects with an Ht ≤60% and Hb ≤19.5 mg·dL⁻¹. Two groups of 10 subjects were established with these characteristics and provided a chance of ≥99% for detecting significant differences in these variables. All the subjects were selected from the male population of Cerro de Pasco among those who fulfilled these criteria. All subjects were Mestizos who were born and had lived their life at that altitude (no visit to a lower altitude in the last 12 months) and none of them was employed as a miner. The characteristics of the subjects are shown in table 1. Lung function was assessed by performing a standard flow/volume spirometric curve with a Microlab 3500 (Sensormedics, Milan, Italy). The calibration of the pneumotachygraph was checked by a known air volume by a calibrated syringe. The CMS score was assessed by a previously described [17] questionnaire on clinical symptoms and signs (table 1).

Study protocol and polysomnography

All subjects underwent two consecutive nights of standard polysomnography in Cerro de Pasco, in the "Laboratorio del Instituto de Investigaciones de la Altura" of the Universidad Peruana Cayetano Heredia of Lima, Peru. In the first night of the study, the polysomnography was performed under basal conditions while in the second night O₂ was administered by a facial mask for 1 h prior to sleep. For each patient the O₂ flow was regulated in order to maintain Sa_{o2} above sea-level values (>96%). Polysomnographic recordings were performed

Table 1.—Demographic, clinical and haematological data of the subjects

	EE	Controls	p-value
Age yrs	38.9±2.5	38.5±1.4	NS
BMI kg·m ⁻²	23.3±0.2	23.4±0.8	NS
Haematocrit %	76.6±1.3	54.4±0.8	<0.0001
Haemoglobin g·dL ⁻¹	23.5±0.3	16.9±1.0	<0.0001
Red blood cells ×10 ⁹ ·L ⁻¹	7.4±0.1	5.5±0.1	<0.0001
CMS score	23.8±3.3	10.3±3.2	<0.0001
FVC L	4.43±0.80	4.55±0.54	NS
FEV ₁ L	3.52±0.65	3.80±0.44	NS

Data are presented as mean±SEM unless otherwise stated; BMI: body mass index; CMS: chronic mountain sickness; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; NS: nonsignificant.

using a Compumedics P-Series, 18-channel sleep recorder (Abbotsford, Victoria, Australia) with a standard set-up according to the American Sleep Disorders Association [20]. Sleep stages were identified by electroencephalogram (EEG; C3/A2 and C4/A1), electro-oculogram and by a bipolar submental electromyogram (EMG); all recordings were obtained from surface electrodes. Thoracic and abdominal excursions were detected by inductance plethysmographic bands. Airflow was detected by a nasal-oral thermocouple and Sa_{o2} by a finger pulse oximeter. The electrocardiogram was monitored from precordial leads. Sleep stages were scored according to RECHTSCHAFFEN and KALES [21]. Sleep efficiency was defined as the total sleep time (TST) divided by total registration time. Arousals were defined as an EEG shift in the α or θ frequency having a duration of >3 s associated with an increase in chin EMG [22]. Arousal index was defined as the number of arousals·h sleep⁻¹. Apnoeas and hypopnoeas were defined as a complete cessation or a >50% decrease in airflow, respectively, for ≥10 s, associated with a decrease in Sa_{o2} of ≥3%. Obstructive apnoeas were distinguished from central apnoeas by the presence of respiratory effort (thoracic/abdominal excursions). The apnoea/hypopnoea index (AHI) was defined as the number of apnoeas or hypopnoeas per hour of sleep according to standard definitions [20]. The drop in Sa_{o2} (ΔSa_{o2}) during each apnoea/hyperpnoea episode was measured and averaged for the whole study period and is labelled mΔSa_{o2}. The mean Sa_{o2} during 10 min of recording before sleep was defined as "awake Sa_{o2}". The average of the Sa_{o2} during the whole sleep time is defined as "mean sleep Sa_{o2}".

Hypoxic and hypercapnic ventilatory response

On the first and second study day, in order to determine the hypoxic (HVR) and the hypercapnic ventilatory response (HCVR), the subjects were studied in the seated position (in the morning at rest for ≥2 h, and ≥2 h after a light breakfast with no tea or coffee), and connected to a rebreathing circuit through a mouthpiece, as previously described [23–25]. To assess the response to progressive hypoxia, end-tidal carbon dioxide (ETCO₂) was kept constant by passing a portion of the expired air into a scrubbing circuit before returning it to the rebreathing bag. Conversely, when the response to progressive hypercapnia was tested, O₂ was continuously supplied to the rebreathing circuit in order to maintain Sa_{o2} at sea-level normoxic levels (>95%). The rebreathing tests terminated when Sa_{o2} reached 70% (hypoxic response) or when ETCO₂ reached 7.3 kPa (55 mmHg; hypercapnic response). ETCO₂ was continuously monitored by COSMOplus (Novamatrix, Wallingford, CT, USA) connected to a mouthpiece, and Sa_{o2} by a 3740 Ohmeda Pulse Oximeter (Ohmeda, Englewood, CO, USA). The COSMOplus was precalibrated against known gas mixtures. The airway flow was continuously measured by a Fleish pneumotachygraph (Metabo Epalinges, Lausanne, Switzerland), connected to a differential pressure transducer (RS part N395-257; RS Components Ltd, Corby, UK) connected in series in the expiratory part of the rebreathing circuit. The calibration of the pneumotachygraph was checked before and after each rebreathing manoeuvre. All signals were acquired on a Macintosh personal computer (G3 model; Apple, Cupertino, CA, USA) at the frequency of 300 per sample channel. The respiratory flow signal was integrated by software, and each breath was identified by an automatic and interactive program. Breathing rate, tidal volume, and minute ventilation (*V*'E) relative to each breath were recognised with their corresponding values of Sa_{o2} and ETCO₂. The chemoreflex

sensitivity to hypoxia or hypercapnia was obtained from the slope of the linear regression of $\dot{V}E$ versus Sa,O_2 or $ETCO_2$, respectively [23–25].

Statistical analysis

Differences between groups were analysed using the unpaired t-test or the Mann-Whitney U-test. Differences between groups and sleep and respiratory variables in the two groups and by effects of O_2 administration were also tested by mixed-design analysis of variance. Data are presented as mean \pm SD. Linear regression was used to assess correlations between parameters.

Results

Demographic characteristics of the subjects with haematological and clinical data are shown in table 1. No significant difference was observed in the lung function of the two groups (table 1). The mean slopes of the HCVR were similar in EE and controls, whereas the HVR slopes were slightly lower in EE than in controls, but the difference was not significant (HVR -0.43 ± 0.07 L \cdot min $^{-1}\cdot\%$ Sa $_2$ O $_2^{-1}$ and -0.67 ± 0.1 L \cdot min $^{-1}\cdot\%$ Sa $_2$ O $_2^{-1}$ for EE and controls, respectively; HCVR 1.31 ± 0.16 L \cdot min $^{-1}\cdot$ mmHg CO $_2^{-1}$ and 0.97 ± 0.1 L \cdot min $^{-1}\cdot$ mmHg CO $_2^{-1}$ for EE and control, respectively).

Sleep variables

During the first study night no significant differences were observed in the TST, sleep efficiency, stages II, III, IV and rapid eye movement (REM) sleep, and the arousal index between the EE and the controls (table 2). Only stage I of sleep was slightly longer in the controls. The arousal index did not correlate with any of the haematological, clinical, demographic or polysomnographic variables of the subjects. For both groups all sleep variables remained unchanged during the second night of the study, in which O_2 was administered for 1 h before sleep (table 2).

Respiratory variables during wakefulness and sleep

During wakefulness, patients with EE had a significantly lower Sa,O_2 compared with controls ($83.7\pm 0.3\%$ versus $85.6\pm 0.4\%$, $p<0.01$). In both groups, the mean values of Sa,O_2 significantly decreased, by a similar small extent during sleep (to $80\pm 0.8\%$ in EE and to $82.8\pm 0.5\%$ in controls,

$p<0.05$; fig. 1). At all times of the night, the mean Sa,O_2 values remained significantly lower in EE than in controls (fig. 1). The percentage of time that the two groups spent at various Sa,O_2 per cent ranges is shown in figure 2. Although both groups spent $>50\%$ of the time in the Sa,O_2 range 81–85%, the controls spent more time than EE subjects with an Sa,O_2 of $>80\%$, whereas EE subjects spent more time than the controls with an Sa,O_2 of $<80\%$ ($\sim 38\%$ of the night in the range 76–80%). Since the TST was the same for both groups, the same findings would be observed if the data were evaluated in terms of actual time spent at each level of Sa,O_2 , rather than in terms of percentage. Overall, the subjects with EE spent $10,343\pm 1,856$ s (*i.e.* nearly 3 h) between 76–80% Sa,O_2 , whereas the controls spent $3,039\pm 1,543$ s (only ~ 50 min) in the same Sa,O_2 range ($p<0.01$).

In both EE and controls, REM sleep was not associated with episodes of marked hypoventilation and the lowest Sa,O_2 levels reached were similar during non-REM and REM sleep (table 3).

Both groups exhibited recurrent episodes of periodic breathing characterised mainly by hypopnoeas alternated with hyperpnoeas (fig. 3), while frank central apnoeas were more rare. In only one patient with EE obstructive apnoeas were present. The values of AHI, duration of hypopnoeas and $m\Delta Sa,O_2$ were similar in the two groups (table 3). With an AHI of ~ 10 , the severity of the sleep disorder could be defined as "mild", according to the standard criteria for sea level [26]. The AHI showed a fair correlation with subjects' age ($r^2=0.22$, $p<0.05$) and, more consistently, with the slope of HCVR ($r^2=0.59$, $p<0.05$) but not with the slope of HVR. Administration of O_2 prior to sleep in the second night of the study did not alter any of these respiratory parameters (table 3).

Discussion

The new findings of this study are that Andean high-altitude natives, with or without EE, undergo mild respiratory disorders during sleep, and that subjects with EE have a slightly, but highly consistent, lower nocturnal Sa,O_2 and spend significantly more time than controls with an Sa,O_2 of $<80\%$ during the night. These mild respiratory abnormalities were not affected by 1-h administration of O_2 prior to sleep.

In contrast to the many studies on SDB in lowlander visitors to altitude, very few studies have addressed the question of breathing during sleep in high-altitude natives, particularly in those with EE. This study clearly indicates that in Andean natives the occurrence of SDB among patients with EE is similar to high-altitude natives with relatively normal haematocrit in terms of frequency and duration of the periodic breathing. However, although the absolute extent

Table 2.—Sleep variables recorded during the first night (basal) and second night (after oxygen administration) night in excessive erythrocytosis (EE) and in controls

	Basal EE	After oxygen EE	Basal controls	After oxygen controls
TST min	333 \pm 15	348 \pm 14.5	312 \pm 20.7	335 \pm 13
Sleep efficiency %	79.4 \pm 3.5	83.8 \pm 3.1	74.4 \pm 4.9	81.3 \pm 3.2
Stage 1 (% of TST)	5.2 \pm 0.7	4.2 \pm 1.3	9.3 \pm 1.4	7.2 \pm 1.6
Stage 2 (% of TST)	55.6 \pm 4.2	49.6 \pm 5.2	50.9 \pm 3.7	55.4 \pm 3.9
Stage 3 (% of TST)	25.5 \pm 3.1	26.0 \pm 4.4	17.5 \pm 2.1	18.7 \pm 1.9
Stage 4 (% of TST)	8.8 \pm 2.1	8.4 \pm 2.0	8.7 \pm 2.4	8.9 \pm 1.7
REM (% of TST)	9.8 \pm 1.9	11.0 \pm 2.9	11.5 \pm 3.6	9.5 \pm 2.6
REM latency min	108 \pm 30	102 \pm 43	126 \pm 22	104 \pm 28
Arousals index	12.0 \pm 1.8	11.2 \pm 0.8	12.7 \pm 1.3	10.7 \pm 2.1

Data are presented as mean \pm SEM unless otherwise stated; TST: total sleep time; REM: rapid eye movement; All p-values of EE versus controls, and basal versus after oxygen are nonsignificant.

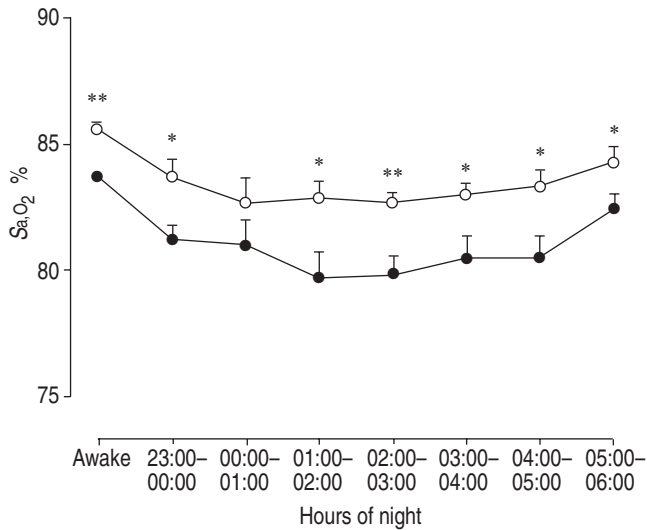


Fig. 1.—Time course of the nocturnal arterial oxygen saturation (S_{a,O_2}) in 10 subjects with excessive erythrocytosis (EE; ●) and in 10 controls (○). Values are expressed as mean \pm SEM. The S_{a,O_2} decreased significantly ($p<0.01$) from the awake state throughout the sleep period in both EE and control groups. *: $p<0.05$ EE versus control; **: $p<0.01$ EE versus control.

of nocturnal desaturation was the same for EE and controls, EE subjects, who had lower S_{a,O_2} during the day, maintained a lower S_{a,O_2} during the night. This difference was small in absolute terms, but very consistent and prolonged during the entire period of the night, and, in addition, it allowed the EE group to spend a substantial period of the night with an S_{a,O_2} of $<80\%$. Transient oxygen desaturations, even reaching very low values in S_{a,O_2} , are not considered an important stimulus for the production of erythropoietin, whereas clinical conditions such as chronic obstructive pulmonary diseases and chronic respiratory failure, characterised by stable and prolonged hypoxaemia may be associated with polycythaemia [27]. Therefore, it is likely that the percentage of sleep time spent below a specific given level of S_{a,O_2} may be a determinant of the haematopoietic response to hypoxia, even in the absence of transient dramatic desaturations.

The authors found that EE patients spent one-half of the night with an S_{a,O_2} in the range of 81–85%, and 38% of the night in the range of 76–80%, whereas the healthy controls spent most of the time with an S_{a,O_2} of $>81\%$. This points to a possible S_{a,O_2} cut-off value of $\sim 80\%$, below which the haematopoiesis may be stimulated. The presence of a threshold of 80% S_{a,O_2} for the stimulation of erythropoietin

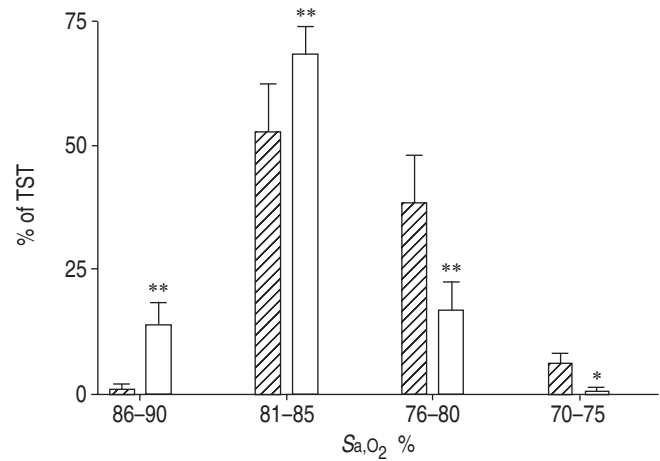


Fig. 2.—Histogram showing the percentage of time spent in different arterial oxygen saturation (S_{a,O_2}) ranges for excessive erythrocytosis patients (▨) and controls (□). Groups were compared using a Mann-Whitney U-test *: $p<0.05$ versus control; **: $p<0.01$ versus control.

has been clearly documented previously [28]. Therefore, it is possible that a mean reduction of 3–4% in nocturnal S_{a,O_2} , which has no effect in normal subjects, may drag patients with EE that have lower diurnal S_{a,O_2} below a value that is critical for erythropoiesis. This exactly crosses the difference between the controls and EE subjects (fig. 1), and may thus explain at least in part why, even in the absence of major respiratory disorders some subjects develop polycythaemia, while others do not, despite intergroup small differences in S_{a,O_2} . At an altitude of 3,100 m (Leadville, Colorado) and at 3,658 m (Lhasa), it has been found that nocturnal hypoxaemia in polycythaemic subjects is more marked compared with the EE group (although polycythaemia is less severe at lower altitude) [6, 7]. One possible explanation is that there may be differences between ethnic groups. It is also possible that the different altitude at which these studies were performed may have determined these different results. While at lower altitude a more severe SDB is necessary in order to induce excessive polycythaemia, at higher altitude even a mild SDB could induce moderate/severe polycythaemia, whereas a more severe SDB could be incompatible with life.

The finding that SDB, though not severe, occurs in the Andean population at 4,380 m is *per se* of interest. In fact periodic breathing was not reported in a small group of Himalayan Sherpas at an altitude of $>5,000$ m [13]. If these differences were confirmed by larger studies on both populations, then nocturnal respiratory instability in the

Table 3.—Respiratory variables recorded during the first night (basal) and second night (after oxygen administration) in excessive erythrocytosis EE and controls

	Basal EE	After oxygen EE	Basal controls	After oxygen controls	p-value [#]	p-value [†]
Awake VE L·min ⁻¹	12.9 \pm 0.5		12.0 \pm 0.5		NS	
Awake ET CO_2 mmHg	39.9 \pm 1.0		38.3 \pm 0.9		NS	
Awake S_{a,O_2} %	83.7 \pm 0.3	96.6 \pm 0.4 ⁺	85.6 \pm 0.4	97.1 \pm 0.5 ⁺	<0.01	<0.01
Mean sleep S_{a,O_2} %	80.0 \pm 0.8***	80.3 \pm 0.6	82.8 \pm 0.5***	83.6 \pm 0.6	<0.05	NS
Lowest NREM S_{a,O_2} %	69.3 \pm 2.7	68.3 \pm 4.1	74.8 \pm 1.0	74.7 \pm 2.1	NS	NS
Lowest REM S_{a,O_2} %	71 \pm 2.9	71.8 \pm 1.3	78.5 \pm 1.2	78.8 \pm 1.3	NS	NS
AHI	10.0 \pm 4.5	13.2 \pm 7.0	8.7 \pm 2.7	7.0 \pm 2.0	NS	NS
Mean duration of the apnoea/hypopnea s	24.2 \pm 1.5	19.5 \pm 1.7	20.3 \pm 1.4	20.8 \pm 0.9	NS	NS
$\Delta S_{a,O_2}$ %	5.4 \pm 0.6	4.5 \pm 0.6	4.6 \pm 0.2	5.0 \pm 0.2	NS	NS

Data are presented as mean \pm SEM unless otherwise stated; V'E: minute ventilation; ET CO_2 : end-tidal carbon dioxide; S_{a,O_2} : arterial oxygen saturation; REM: rapid eye movement; NREM: non-REM; AHI: apnoea/hypopnoea index; [#]: EE versus controls; [†]: basal control versus after oxygen control; ⁺: S_{a,O_2} during oxygen administration; NS: nonsignificant; ***: $p<0.001$ versus awake S_{a,O_2} .

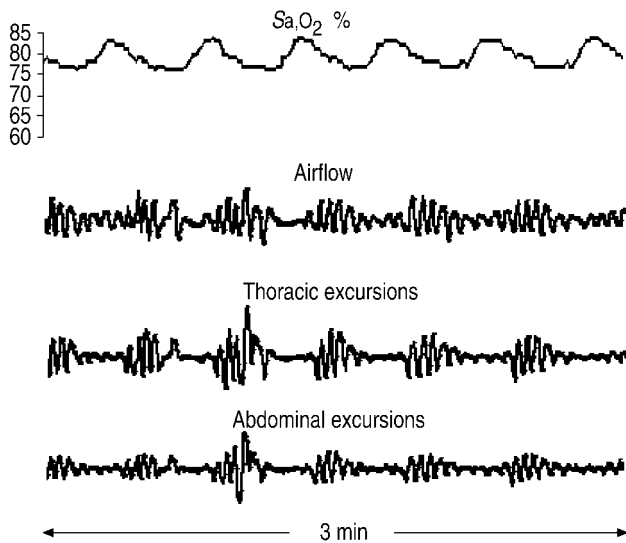


Fig. 3.—Example of periodic breathing from the polysomnographic record of a single patient. S_{a,O_2} : arterial oxygen saturation.

Andeans may be considered a sign of poor adaptation to altitude.

Both hypoxia and hypocapnia have been suggested as the stimuli that trigger and sustain periodic breathing at altitude [29, 30]. In sea-level natives ascending to altitude, SDB is related to an increased HVR [13, 14] but in long-term residents at altitude the HVR is blunted [3, 31], therefore it is likely that other mechanisms may determine the nocturnal respiratory instability in these subjects. These findings support the hypothesis that the fall in arterial carbon dioxide tension (P_{a,CO_2}) may be a determinant factor. The AHI did not correlate with basal $ETCO_2$, in agreement with a previous report [32] but correlated significantly with the HCVR. Since a fall in P_{a,CO_2} below the apnoeic threshold depends on the individual chemoreflex sensitivity, it is not surprising that the AHI correlated with HCVR rather than with the $ETCO_2$ level itself. The concept that a high gain of central chemoreflex response may lead to nocturnal periodic breathing has been evidenced from many studies in animal and humans [29]. Briefly a low $ETCO_2$ at basal condition may induce hyperventilation with further decrease in CO_2 below the apnoeic threshold. The hyperventilation that occurs after each apnoea further decreases the CO_2 level triggering the next apnoea and finally leading to a vicious circle. In patients with high hypercapnic chemoreflex sensitivity these responses are enhanced and apnoeas more likely to occur. This mechanism is similar to what is shown at sea level in patients with chronic heart failure experiencing nocturnal (and also diurnal) periodic breathing; in addition, for these patients a clear correlation has been shown between HCVR and SDB [33].

Despite this, a significant difference in HCVR was not found in the two groups, in agreement with a recent study [34], and with the rest of the literature. This suggests that this factor may be able to explain the occurrence of sleep abnormalities (which in fact were present in both EE and controls to a similar extent), as it does in some patients at sea level, but it does not necessarily play a partial role in the origin of EE, whose cause is probably more related to the lower S_{a,O_2} . The lack of difference in HVR in the two groups could be due to the relatively small number of subjects studied, but again a normal or slightly reduced HVR may not be necessarily the cause of the reduced S_{a,O_2} . A depressed HVR is a common finding in Andean natives living at high altitude, regardless of the presence of EE [4, 16, 31], and even recent studies confirmed the presence of very small differences

between these two groups of subjects [16]. The age of the subjects also has some influence in the occurrence of nocturnal respiratory instability as a slight but significant positive correlation with the AHI was found. There is some evidence that age can be a risk factor for nocturnal periodic breathing also in lowlanders at sea level in the presence of some pathological conditions [35].

All sleep variables were similar in the two groups and this is in agreement with data reported at the same [11, 12] or at a lower altitude [6]. In contrast, lowlanders undergo profound changes in sleep pattern during the first days after ascending to altitude, then improve with acclimatisation [8, 36]. Taken together these observations suggest that sleep is a physiological variable characterised by a fairly rapid adaptation to the environmental conditions and is not negatively influenced by chronic exposure to altitude.

This study indicates that Andean natives, with or without excessive erythrocytosis, undergo mild respiratory disorders during sleep, and that subjects with excessive erythrocytosis have a slightly (but highly significant) lower nocturnal arterial oxygen saturation and spend more time than controls with an arterial oxygen saturation below 80% during the night. Since an arterial oxygen saturation of 80% has been previously identified as a threshold for erythropoiesis, further studies are needed to establish whether or not a link exists between these changes in nocturnal arterial oxygen saturation and excessive erythrocytosis.

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