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Chilean Miners Commuting from Sea Level to 4500 m: A Prospective Study

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ABSTRACT

Richalet, Jean-Paul, Manuel Vargas Donoso, Daniel Jiménez, Ana-María Antezana, Cristián Hudson, Guillermo Cortès, Jorge Osorio, and Angélica Leòn. Chilean miners commuting from sea level to 4500 m: a prospective study. *High Alt Med Biol* 3:159–166, 2002.—The development of mining activities in North Chile involves a great number of workers intermittently exposed to high altitude for a long period of time (chronic intermittent hypoxia, CIH). A $2^1/_2$-year prospective study aimed to characterize this model of exposure to CIH and to know whether this condition may progressively lead to a chronic pattern. Twenty-nine miners, aged 25 ± 5 yr, working 7 days at HA (3800 to 4600 m) and resting 7 days at sea level (SL) were studied. Subjects underwent a physical examination, EKG, hematological status, maximal exercise test, ventilatory and cardiac response to hypoxia (F_{iO_2} = 0.114) at rest and exercise, pulmonary vascular response to hypoxia by echocardiography, and 24-h monitoring of EKG and arterial pressure. Basal evaluations were performed at SL before the first exposure to hypoxia. HA measurements were daily AMS score, sleep status, and 24-h monitoring of EKG and arterial pressure. All these measurements were repeated after a mean period of 12, 19, and 31 months. Hematocrit increased but reached values lower than those observed in chronic permanent exposure. Systemic and pulmonary arterial pressures measured at SL did not change, but were higher in hypoxia. Right ventricle showed a slight dilatation. Exercise performance at SL declined with exposure to CIH to reach a 12.3% decrease after 31 months of CIH, associated with a 6.8% decrease in maximal heart rate. Signs of ventilatory acclimatization were observed after 12 months. Symptoms of AMS and sleep disturbances were still seen on the first 2 days at HA, whatever the time of exposure to CIH. In conclusion, CIH induced a clear acclimatization process. Subjects did not reach a health status comparable to that seen in permanent residents at HA and remained at risk of acute altitude-induced illnesses.

Key Words: chronic intermittent hypoxia; altitude; acclimatization; pulmonary artery pressure; hematocrit; sleep disturbances

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INTRODUCTION

THE DEVELOPMENT OF MINING ACTIVITIES in North Chile involves a great number of workers intermittently exposed to high altitude for a long period of time. This is a new model of hypoxic exposure, distinct from acute (alpinism) or chronic (permanent residence) exposure to altitude hypoxia (Fig. 1). It will be called here *chronic intermittent hypoxia* (CIH). Industrial mining activities in South America started in the 16th century with conquest by the Spaniards. These activities always involved populations living and working permanently at high altitude (4000 to 4500 m), as in Potosi (Bolivia) or Cerro de Pasco (Peru) (León-Velarde et al., 2000; Vasquez and Villena, 2001). The geographical situation is different in North Chile, where the band of high altitude land is narrow (a few hundred kilometers), allowing rapid transportation from high altitude to sea level (a few hours). The discovery of mining resources at high altitude and the availability of easy transportation allowed the development of mining facilities at high altitude with workers not living permanently on the mining site. Thus, commuting from sea level (resting periods) to mining sites at high altitude (working periods) became a new and rapidly developing work pattern specific to North Chile. This model is very different from other models of intermittent hypoxia, which mainly deal with daily short exposures (minutes or hours) for studying the effect of training in intermittent hypoxia (Katayama et al., 1999; Garcia et al., 2000) or sleep apnea syndrome (Somers et al., 1995).

A PROSPECTIVE STUDY

A $2^1/_2$-year prospective study was started in February 1998 to characterize this model of exposure to CIH and to know whether this condition may progressively lead to a chronic pattern or to an intermediate status between acute and chronic exposure. Some physiological or pathophysiological features specific to CIH may also appear. This study was sponsored by the Chilean government and private organizations through a FONDEF project (n°D-9711068). For the first time, an ambitious research program was launched to explore the physiological changes and/or pathological events associated with CIH during mining activities.

POPULATION STUDIED

Twenty-nine miners, aged 25 ± 5 yr (18 to 41), working 7 days at HA (3800 to 4600 m) and resting 7 days at sea level (SL) were studied. None of them had any experience of high alti-

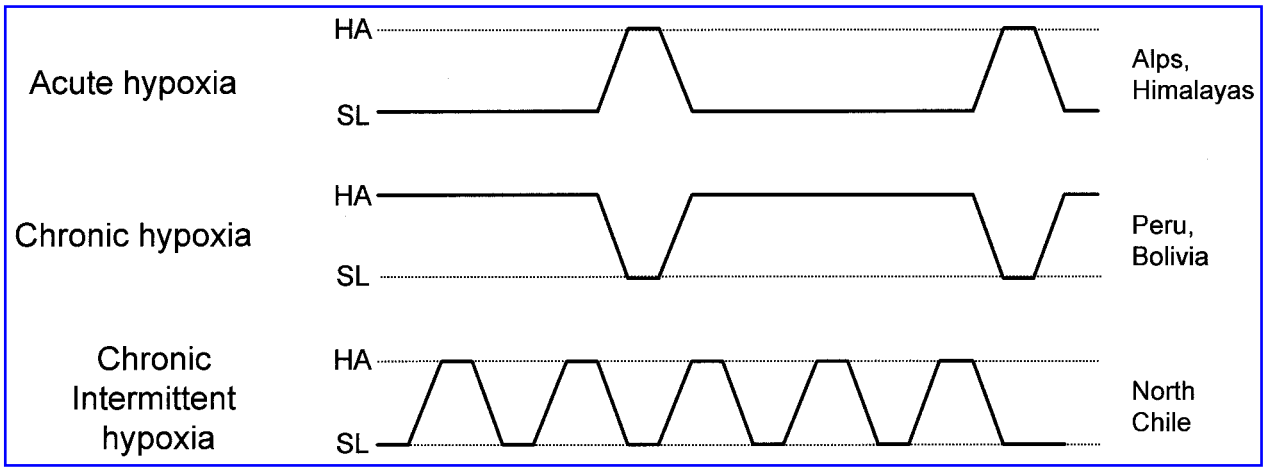

FIG. 1. Three models of exposure to hypoxia. Acute hypoxia corresponds to subjects living at sea level and exposed for a few minutes, hours, or days at high altitude. Chronic hypoxia concerns people living permanently at high altitude and eventually exposed for short periods of time (days) to normoxia. Chronic intermittent hypoxia is defined as long-term (several months or years) intermittent exposure to hypoxia.

tude for the two preceding years or any particular medical history. The mine was a copper mine run by the Doña Inés de Collahuasi Mining Company. During their stay at the mining facilities, working activities were held between 4300 and 4600 m, but restaurants for evening meals and dormitories were located at 3800 m (Fig. 2). Subjects were technicians, engineers, and truck drivers.

PROTOCOL

A complete clinical and physiological evaluation was performed, including physical examination, EKG, thorax X ray, spirometry, hematological status, maximal exercise test, body composition, ventilatory and cardiac response to hypoxia ($F_{i_{O_2}} = 0.114$) at rest and exercise (Richalet et al., 1988; Gamboa et al., 2001), pulmonary vascular response to hypoxia at rest by Doppler echocardiography in normoxia and after a 20-min inhalation of a hypoxic gas mixture ($F_{i_{O_2}} = 0.114$), and 24-h monitoring of EKG and arterial pressure. The maximal exercise test was performed on a cycloergometer, using a 3-min step by step increase of 50 W until exhaustion.

These evaluations were performed at SL before the first exposure to hypoxia and between days 3 and 6 at sea level during the period of exposure to CIH.

The following measurements were done at HA: daily Lake Louise AMS score (the first measurement was done after the first night, 24 h after arrival at HA), sleep status (modified Spiegel questionnaire) during each night spent at HA, 24-h monitoring of EKG and arterial pressure on day 2 at HA, and hematological status on day 6. All these measurements were repeated after a mean period of 12, 19, and 31 months to evaluate the impact of an intermit-

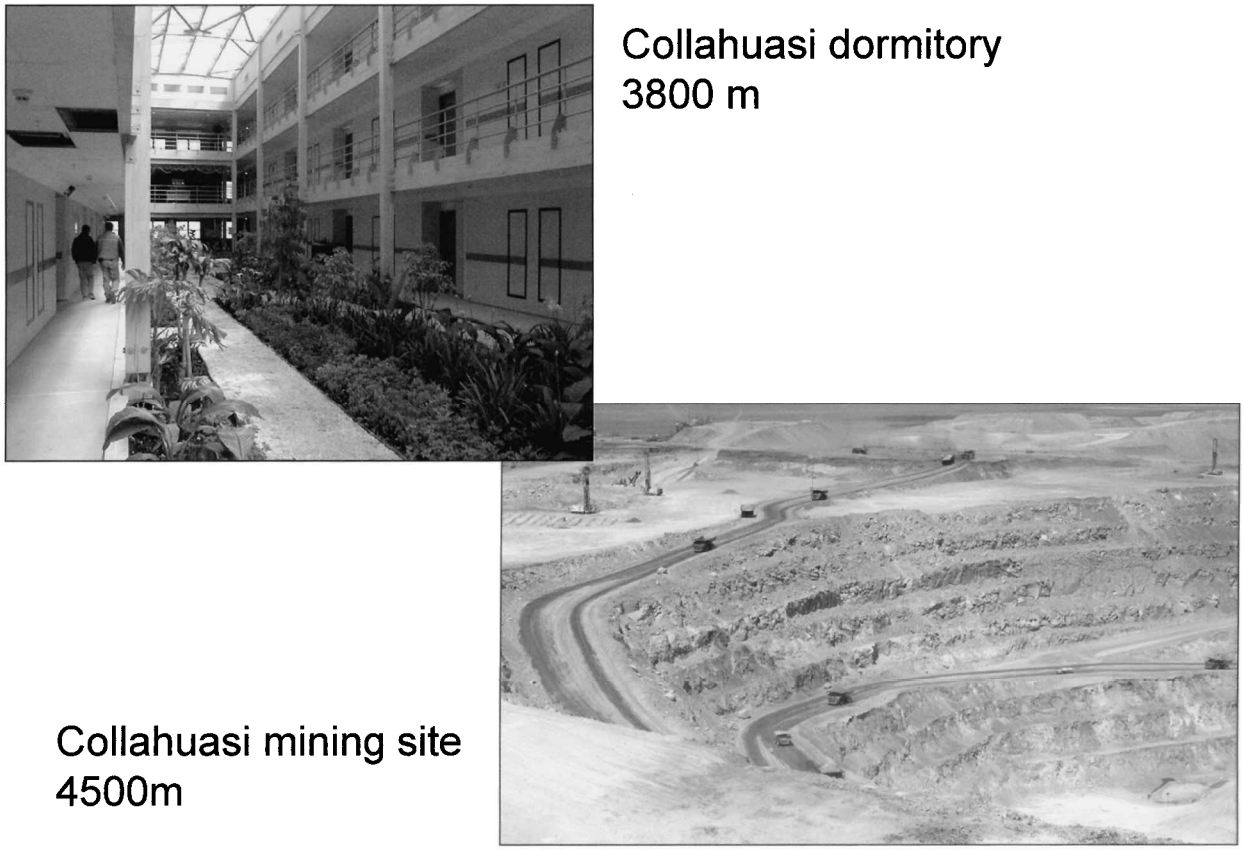

FIG. 2. Views of the Collahuasi mine: upper left, dormitories at 3800 m; lower right, one of the open-air mining sites, located at 4500 m.

tent hypoxic challenge on the health status of miners.

This prospective study was only a part of an overall study on CIH in miners in the frame of the FONDEF project. Other studies were performed concerning the following:

- Effect of various shift patterns (7 d/7 d vs. 20 d/3 d vs. 4 d/3 d) on physical performance, acclimatization process, and clinical status
- Ergonomy of mining activities and the cost (evaluated by heart rate) of some specific work posts
- Effects of oxygen enrichment on altitude-induced sleep disturbances
- Characteristics of subjects intolerant to high altitude (recurrent history of HAPE or HACE), using echocardiography in hypoxia and perfusion of L-arginine

In the same program, an animal model of intermittent exposure to hypoxia was also developed at the Universidad Arturo Prat in Iquique (Chile).

RESULTS

The results of each protocol will be presented in detail elsewhere. The main results of the prospective study are summarized here.

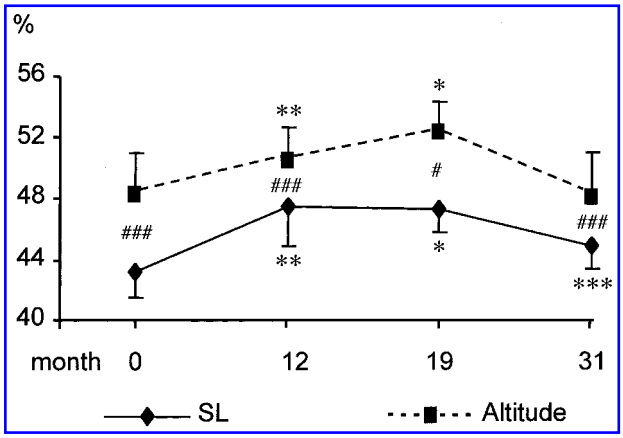

FIG. 3. Hematocrit before (0) and after 12, 19, and 31 months of exposure to CIH. Mean ± SD. Time versus 0: *, **, ***: $p < 0.05$, 0.01, 0.001, respectively. Altitude versus sea level (SL): #, ##, ###: $p < 0.05$, 0.01, 0.001, respectively. Student's paired t test was used for all parameters to evaluate the differences between conditions of exposure to CIH.

- Hematocrit increased, measured at both sea level and high altitude, at 12 and 19 months and returned to values similar to initial preexposure values after 31 months of CIH. Increase of hematocrit due to acute exposure to high altitude was similar at all times (Fig. 3).
- Body weight and body composition did not change significantly (results not shown).
- Mean systemic arterial pressure, both during daytime and nighttime, showed a tendency to decrease with time. Values at high altitude were higher than at sea level (Fig. 4A and B).
- Systolic pulmonary artery pressure, both in normoxia and after an acute hypoxic challenge, did not change significantly with time of exposure, except after 31 months, when lower values were found in hypoxia (Fig. 5). Right ventricular end-diastolic diameter, evaluated by echocardiography, increased from 18.6 ± 3.3 mm to 22.4 ± 2.4 mm at 19 months of exposure to CIH ($p < 0.001$).
- Exercise performance evaluated by the maximal load sustainable at exercise at sea level decreased by 12.3% after 31 months of CIH, while maximal heart rate decreased by 6.8% at the same time (Fig. 6).
- Hypoxia-induced decrease in arterial O_2 saturation at exercise (30% of normoxic maxV_{O_2}) was smaller after 12 months of exposure and remained stable afterward. Ventilatory response to hypoxia evaluated at the same level of submaximal exercise increased after 12 months of exposure and remained elevated (Fig. 7).
- Symptoms of AMS were similar whatever the time of exposure to CIH. AMS score was, each time, maximal on days 1 and 2 at high altitude (Fig. 8). Quality of sleep was altered during the first two nights at high altitude (worse on the second night) and did not ameliorate with time of exposure (Fig. 9).

DISCUSSION

This is the first study ever performed on a population of subjects intermittently exposed to high altitude for a period of $2^1/_2$ years. Although there were some problems in obtaining the participation of all the subjects throughout

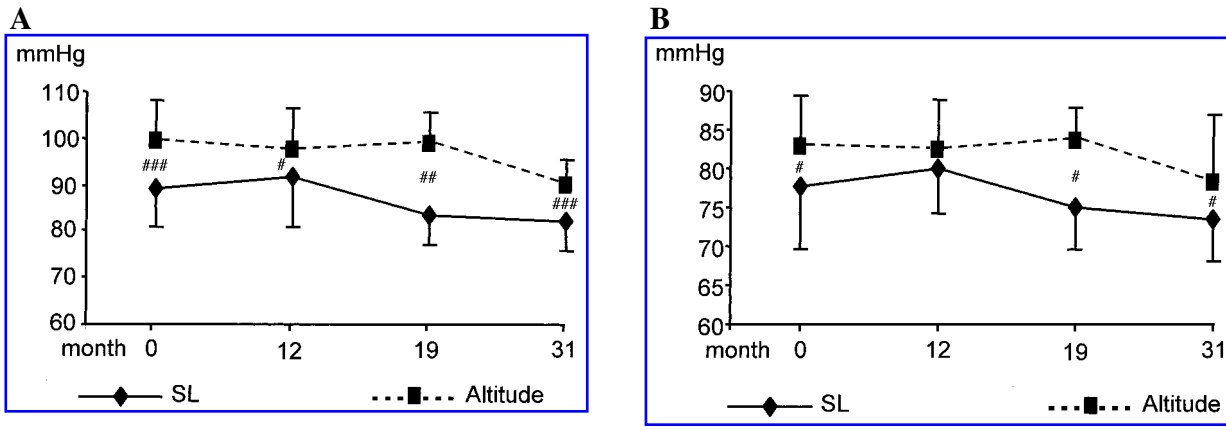

FIG. 4. Mean systemic arterial pressure (A: daytime, B: nighttime) measured from 24-h Holter recording of blood pressure, before (0) and after 12, 19, and 31 months of exposure to CIH. Mean ± SD. Altitude versus sea level (SL): #, ##, ###: $p < 0.05$, 0.01, 0.001, respectively.

the study, the results are very promising and allow new insights into the effect of high altitude in humans. It also allows us to give some recommendations about the future, especially in the prevention of altitude-induced diseases and the maintenance of a good health status.

As an overall result, a period of $2^1/_2$-year exposure to intermittent hypoxia did not induce any significant alteration in the health status of the subjects studied. No subject suffered from severe forms of mountain sickness (HAPE, HACE), but all suffered from benign AMS in the first 2 to 3 days of exposure. Persistent exposure did not decrease significantly the intensity of AMS at each turn. Alteration of sleep is the main disturbance during each period spent at high altitude and may induce fatigue or lack of vigilance during the following day. Thus, monitoring of the health status of workers must not decrease with years of exposure, an acute accident being still possible at any time, even in acclimatized subjects.

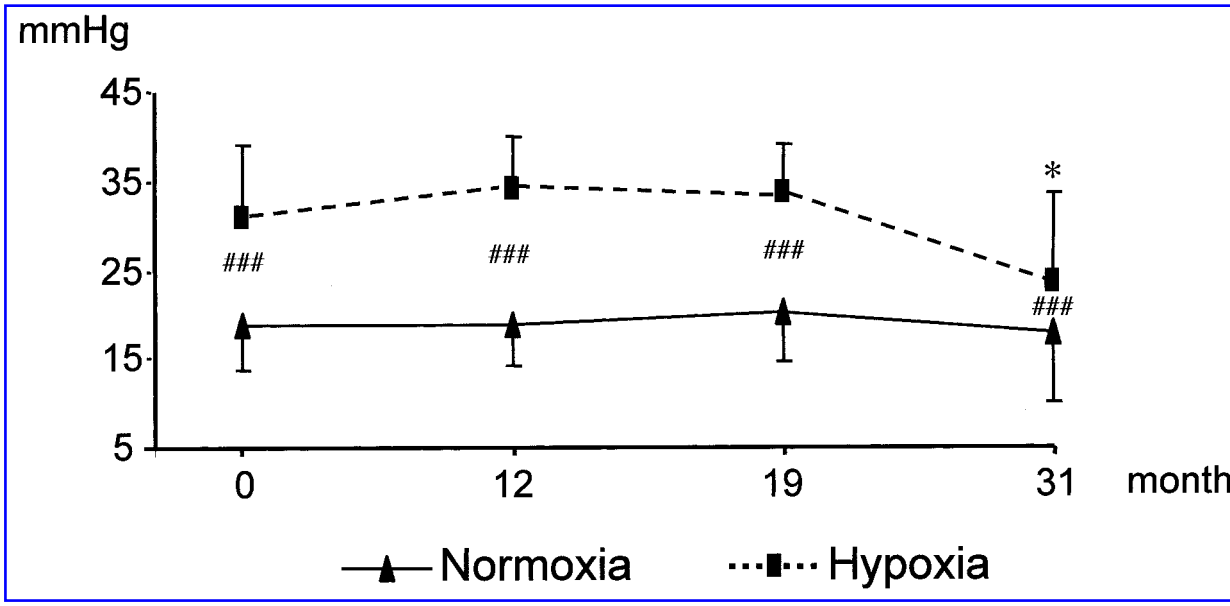

FIG. 5. Systolic pulmonary arterial pressure, evaluated by Doppler echocardiography, before (0) and after 12, 19, and 31 months of exposure to CIH. Mean ± SD. Time versus 0: *: $p < 0.05$. Hypoxia versus normoxia: ###: $p < 0.05$, 0.01, 0.001, respectively.

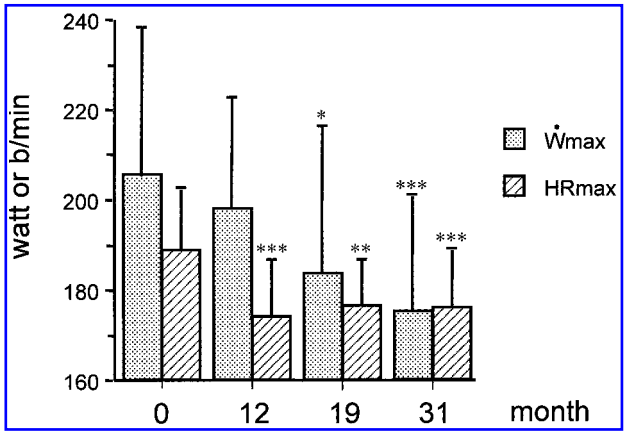

FIG. 6. Work load (Wmax) and heart rate (HRmax) at maximal exercise reached on a bicycle ergometer, before (0) and after 12, 19, and 31 months of exposure to CIH. Mean ± SD. Time versus 0: *, **, ***: $p < 0.05, 0.01, 0.001$, respectively.

Physical performance of the subjects decreased significantly with time. Only part of this decrease can be attributed to the decrease in maximal heart rate induced by the down-regulation of β-adrenergic and upregulation of muscarinic receptors (Richalet et al., 1992). A detraining effect of exposure to hypoxia or excessive sedentarity during the resting periods at sea level is probably also responsible for this effect. Thus, information should be given to the subjects to maintain or to increase their physical activity, especially during the recovery period at sea level. Regular follow-up of physical condition would be of special interest.

Signs of acclimatization to hypoxia are clear, as evidenced by a better O_2 saturation during exercise in hypoxia and an increased ventilatory response to hypoxia. Gas exchange at exercise improves with time. Such an increase in ventilatory response to hypoxia had already been observed, but in much shorter exposures to intermittent hypoxia (Katayama et al., 1999; Garcia et al., 2000). Desaturation at exercise during a hypoxic test remains the best criterion to evaluate the quality of acclimatization at high altitude in active subjects.

The polycythemia induced by altitude exposure is significant, but lower than what is observed in permanent highlanders for which values over 50% have been observed in male subjects living above 4000 m (León-Velarde et al., 2000; Vasquez and Villena, 2001). A level of 50% of hematocrit can be suggested as a criterion for adequate hematological response to CIH.

Cardiovascular changes are limited to a slight adaptation of the right ventricle to increased pulmonary pressure, as witnessed by a small increase in its end-diastolic diameter. Systemic blood pressure and pulmonary blood pressure measured at sea level during the recovery period remained normal. Pulmonary pressure was lower than in subjects living permanently at high altitude (Hultgren, 1997). However, exposure to altitude is always accompanied by high systemic blood pressures. Subjects with preexisting high values of systemic blood pressure should be carefully followed by regular Holter and echocardiography. Subjects with preexisting pulmonary hypertension should be excluded from work at high altitude.

In conclusion, this study provided evidence that a continuous process of acclimatization is going on, even after 31 months of exposure to intermittent hypoxia. Some parameters are stabilized while others are still changing and deserve further evaluation, such as cardiovascular variables or sleep pattern. The follow-up of this prospective group will be essential to determine if this unique condition found in North Chile tends, with time, to mimic the condition of permanent exposure to chronic hypoxia.

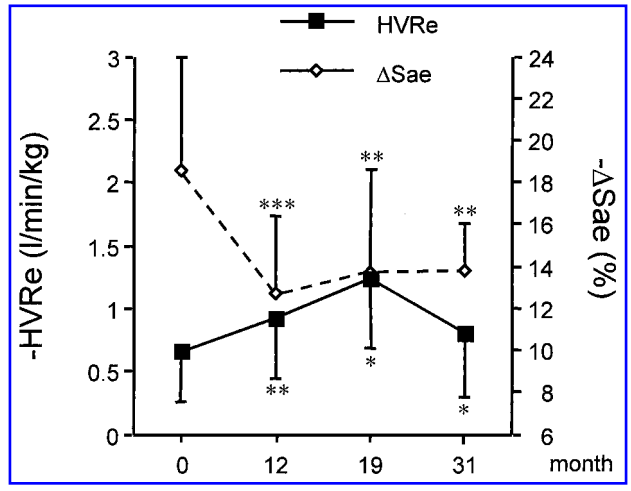

FIG. 7. Hypoxic ventilatory response at submaximal exercise (30% of normoxic maxV_{O_2}) (HVRe) and decrease in arterial O_2 saturation from normoxia to hypoxia (ΔSae) at the same level of exercise, before (0) and after 12, 19, and 31 months of exposure to CIH. Mean ± SD. Time versus 0: *, **, ***: $p < 0.05, 0.01, 0.001$, respectively.

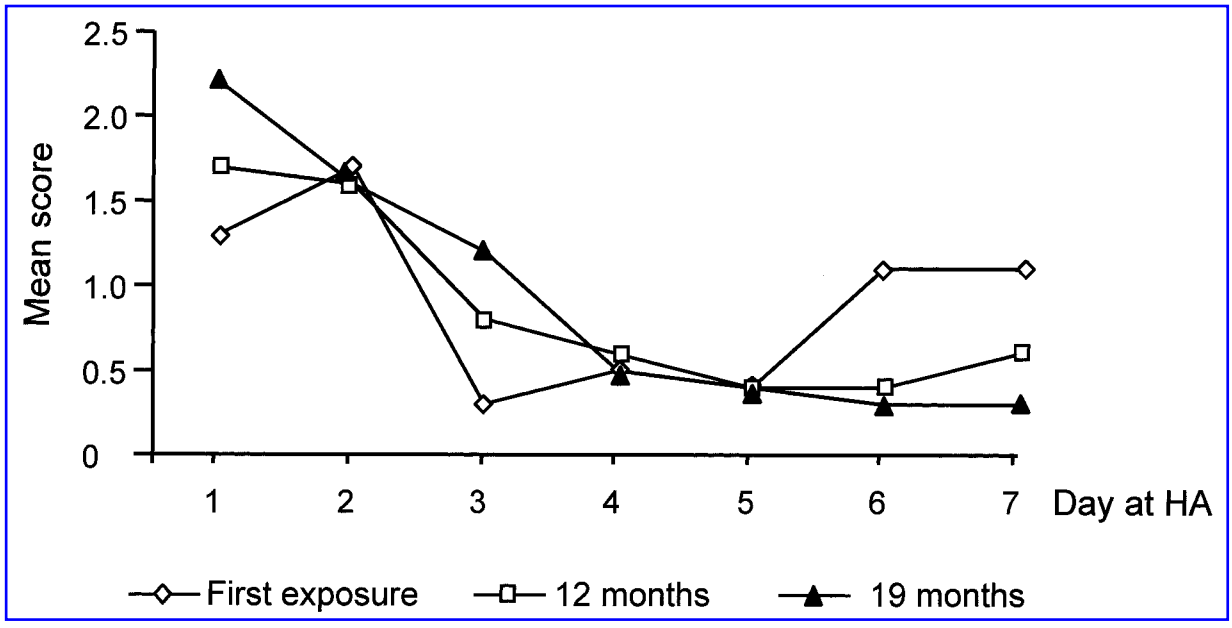

FIG. 8. Score of AMS (Lake Louise) among the subjects exposed for 7 d at high altitude (3800 to 4600 m), during their first exposure and after 12 and 19 months of CIH. Mean values are represented without SD for better clarity. Values are different on days 1 and 2 when compared to the last day ($p < 0.05$). There is no significant difference between 0, 12, and 19 months of CIH.

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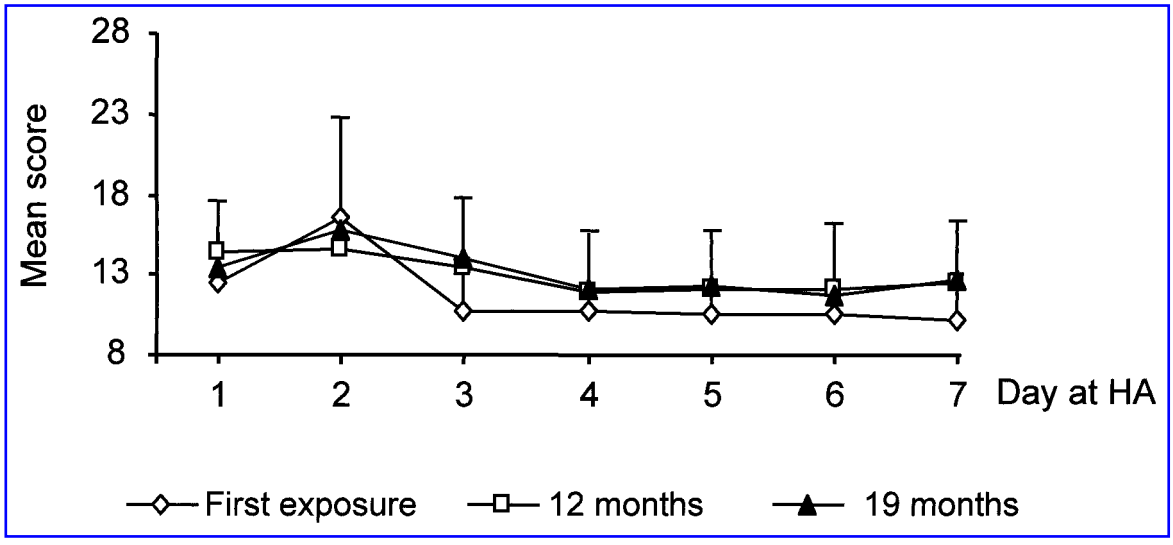

FIG. 9. Quality of sleep (modified Spiegel questionnaire) among the subjects exposed to 7 d at high altitude (3800 to 4600 m), during their first exposure and after 12 and 19 months of CIH. Mean values are represented without SD for better clarity. Values are different on day 2 when compared to the last day ($p < 0.05$). There is no significant difference between 0, 12, and 19 months of CIH.

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