Hemoglobin changes (Hb) in miners exposed to high altitude and associated factors

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Abstract

Aim: *To determine the variation of hemoglobin (Hb) in two groups of miners working at different altitudes.* **Methodology:** *A longitudinal study conducted in a private company. Hb was obtained from entrance exams and annual checks of workers at two locations: at sea level and at Peruvian highlands (4,100 m), taken by trained staff and equipment calibrated to environmental conditions. We analyzed variations in the course of the years with the PA-GEE statistical test; p values were obtained.* **Results:** *Of the 376 workers, 89% (322) were men, the median age was 32 years (range 20-57) and 84% (304) were at high altitude. In multivariate analysis, male sex ($p < 0.001$), body mass index (BMI; $p = 0.021$) and working at high altitude ($p < 0.001$) were associated with the greatest variation of Hb in time, adjusted for age, length, and type of work.* **Discussion:** *These findings should be considered for health surveillance of workers exposed to similar conditions to prevent chronic mountain sickness.* **Conclusion:** *The change in Hb of miners was associated with male sex, BMI, and work at high altitude.*

KEY WORDS: *Occupational medicine. Altitude. Hemoglobin. Longitudinal study.*

Introduction

The physiology of human adaptation to high altitudes is one of basic science and high-altitude medicine main lines of research[1], especially owing to the increasing numbers of people originating from seal level that work an reside at high altitudes[2]. This generates, among other things, exposure to zones with lower atmospheric pressure and less amounts of available oxygen[3,4], and if the migrant does not undergo an adequate adaptation process this can bring about several natural changes and even health problems (on the long-term)[1], with susceptibility to physiological changes that must be studied in order to be able to adequately implement altitude-related sicknesses relevant prevention[5].

Hemoglobin (Hb) increase in high altitude conditions is mainly stimulated by hypoxia[6], although there are other factors that might influence on the magnitude of this response[7,8], but assessments of changes in populations exposed for work-related migration are insufficient. Numerous studies have been carried out on erythropoiesis improvement during training at high and moderate altitude[8,9], with any of these suggesting better habituation is obtained when longer time is spent under such conditions[9,10]. Although studies in populations native to zones of high altitude generally show higher Hb levels[11,12], there are few studies published on populations native to low altitude spending long periods at high altitude, with most studies being carried out descriptively[13-15]. In view of this, the purpose of this study was to determine if there is Hb variation over time during exposure to height in workers of a mining company.

Methodology

Type of study and sample

A secondary data analysis, cross-sectional analytical study was carried out using data reported on

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occupational files of workers of a single company that has two sites at different altitudes. Data of workers who underwent medical occupational examination between the years 2007 and 2010, and who had measurements of the variables used in the study were included. Workers with incomplete or missing data were excluded (0.1% exclusion).

A census-type convenience sampling was used. The assessed workers belonged to the economically active population of each of the cities where the company sites were located (these workers came from the cities of Lima and Trujillo), both at sea level, and their site was not changed during the data collection period. According to Peruvian regulations, at admission to their working center, they were assessed with a pre-occupational examination, where their health status was verified and any preexisting pathology was ruled out, and studied workers were therefore healthy and had Hb levels within normal ranges. Annually, they underwent a similar examination to that at admission, out of which follow-up data were obtained for this work. Of note, the company has a smoking restriction policy, which reduces the effects of tobacco on study subjects' Hb variations.

Procedures and variables

There was access available to the database of the high-altitude site and of the site located at sea-level. A double capture process was carried out, after which one of the authors performed the crossing of bases and quality control. The bases were created in the Microsoft Excel program for Windows 2007; the workers were codified for this process in order for them to remain unidentified, and the matrix base was handled only by the main authors.

The dependent variable was the Hb value found at each measurement of the company's workers. This variable was obtained by hematocrit manual determination and subsequent calculation for real values in patient serum, where the results were obtained by spectrophotometry. This was carried out by health professionals with years of experience in the field of occupational medicine. Equipment and teams were regularly monitored by the company –periodic equipment calibration– and other state and external audit companies. At both sites, calibrated equipment and sterile materials were used for blood extraction.

The independent variables that were considered for the analysis were gender (category of interest: male gender), age (measured as a quantitative variable), job position (category of interest: operator position), year of the take (measured as a quantitative variable) and site of work (category of interest: site located at high altitude, 4100 masl at the La Libertad mountain range).

Statistical analysis

The Stata statistical program, version 11.1 for Windows 2007 (Stata Corp LP, College Station, TX, USA), was used for statistical analysis. For categorical variables descriptive statistics, frequencies and percentages were used, and for quantitative variables, median and ranges (simple or interquartile) were used, and for post-analysis, the Shapiro Wilk test. For bivariate analytic statistics, Mann-Whitney U-test (for quantitative independent variables) and the chi-square test (categorical independent variables) were used, and for multivariate models, population-averaged generalized estimating equations (PA-GEE) were used, which allow for results to be adjusted for time, considering the time variable as the year of Hb take. This was carried out using the binomial family and the log link function, in order to find the association coefficients. In addition, the robust models were taken into account for large sample adjustment. A p-value < 0.05 was considered to be statistically significant.

Ethical aspects

Ethical regulations on works with human beings of the Declaration of Helsinki of 1975 were complied with.

Results

One thousand four-hundred and seventy-eight measurements made to 376 workers were obtained. Of these, 88.9% were males (322), median age was 32 years (range: 20-57 years of age) at baseline measurements, 84% of workers (304) were at the high altitude site, and median years working for the company was 2 (interquartile range: 1.3-2.4 years). The other descriptive variables are shown in table 1. Baseline Hb according to workplace height had a median of 14.9 mg/dL (13.6-15.8 mg/dL) at sea level and 16.7 mg/dL (15.7-17.2 mg/dL) at high altitude (Fig. 1).

The bivariate analysis showed that there were differences in Hb values with other variables, except for age and years of seniority; variables that were different were gender, operator type of work, weight and BMI ($p < 0.001$), with the latter two showing positive correlation. The site altitude showed direct correlation with Hb as well ($p < 0.01$), all this without adjustments for time (Table 2).

Table 1. Socio-occupational characteristics of assessed workers according to working site

Variable	Working site		Total	p*
	Sea level	High altitude		
	58 (16%)	304 (84%)	362	
Gender				
Female	20 (34.5%)	20 (6.6%)	40	< 0.01
Male	38 (65.5%)	284 (93.4%)	322	
Age† (years)	33 (29-43)	32 (27-37)	32 (28-38)	0.06
Type of work				
Administrative	51 (87.9%)	41 (14.6%)	92	< 0.01
Operator	7 (12.1%)	240 (85.4%)	247	
Years of seniority†	1 (0-6)	2 (1.5-2.2)	2 (1.3-2.4)	< 0.05
Weight† (kg)	72 (64-82)	71 (64.5-79.6)	71.3 (64.5-80)	0.65
Height† (m)	1.7 (1.63-1.75)	1.7 (1.6-1.7)	1.67 (1.63-1.72)	0.20
BMI† (kg/m^2)	25.5 (23.3-27.1)	25.4 (23.7-27.5)	25.5 (23.7-27.5)	0.78
Obesity				
Yes	6 (10.3%)	27 (8.9%)	33	0.72
No	52 (89.7%)	277 (91.1%)	329	
Hemoglobin	14.9 (13.6-15.8)	16.7 (15.7-17.2)	16.4 (15.5-17.2)	< 0.01

*Mann-Whitney U-test (quantitative independent variables) and chi-square test (categorical independent variables).
†Median and interquartile range.

In the multivariate analysis, age (p = 0.100), type of work (p = 0.823) and seniority in the job (p = 0.992) were found not to be associated with Hb variation, but gender (p < 0.001), BMI (p = 0.021) and site altitude (p < 0.001) were, with time being used as an adjustment for each worker. The results are shown in table 3.

Discussion

There was a progressive Hb increase, according to time variation, in the workers exposed to high altitude in comparison with those who worked at sea level. The results are similar to those assessed in a study that

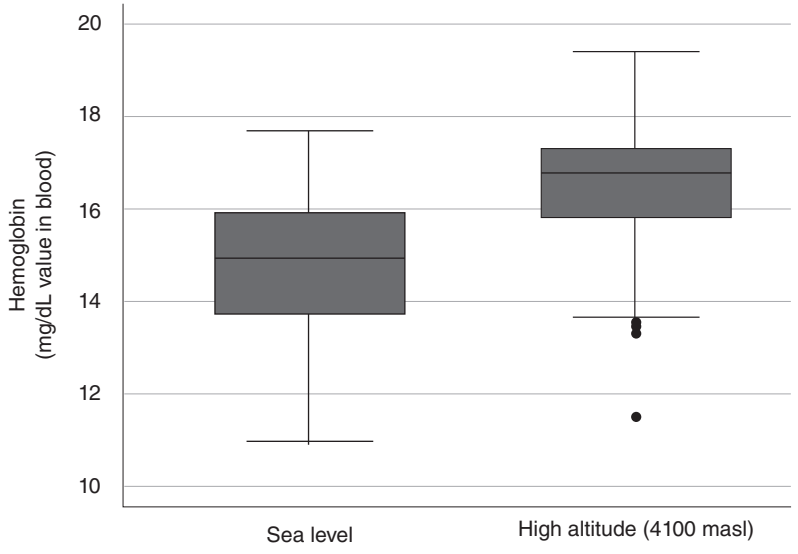

Figure 1. *Hemoglobin box and whisker plot according to working site in Peruvian miners.*

Table 2. Hb values analysis according to the characteristics of workers of two sites of a mining company

Variable	Mg/dL	
	Median (IQR) or correlation coefficient	p
Gender		
Female	14.3 (13.2-14.7)	
Male	16.7 (15.8-17.3)	< 0.001*
Age† (years)	0.05	0.393‡
Type of work		
Administrative	15.7 (14.4-16.7)	< 0.001*
Operator	16.7 (15.7-17.2)	
Years of seniority in the job†	0.02	0.654‡
Weight† (kg)	0.23	< 0.001‡
Height† (m)	0.17	< 0.01‡
BMI† (kg/m^2)	0.20	< 0.001‡
Working site		
Sea level	14.9 (13.6-15.8)	< 0.001*
High altitude (4100 masl)	16.7 (15.7-17.2)	

*Mann-Whitney U-test.
†Median (IQR) for categorical variables values. Correlation coefficient for quantitative variables values.
‡Spearman correlation test.
IQR: interquartile range.

enrolled male students of a military academy located at 2210 masl, where it increased by a mean of 5.5% over 1 year[10], and to those in another where it increased more than 10% in a college student population after 2.5 years[16]. One study carried out in a group of soldiers reported they had their Hb increased by 11% after chronic and intermittent exposure to altitude for 22 years[17]. The same relationship occurred in a group of swimmers who, at a simulated altitude of 2320 masl had their Hb levels increased by 7.2 ± 3.3% more than they would do at sea level, and this increase lasted up to 3 weeks after the altitude simulated increase[18]. Although exposure times were different, similar change results were obtained with 14 runners who were exposed to a simulated altitude of 3000 masl (10 daily hours for 21 days), which was sufficient hypoxic stimulus to increase their Hb level[7]. A similar situation occurred in 26 swimmers who had their Hb increased with exposure to high altitude, regardless of the type of training regimen[19]. This was also substantiated with 12 mountain climbers who in 4 weeks climbed to 4850 and 7600 masl and displayed large Hb increases[20]. Hb increase is probably due to a decrease of total plasma volume and increased erythropoiesis as a response to hypoxia by renal regulation[1,11,15,17,20].

Hb increase occurred to a greater extent in males, which may be comparable to a study conducted in a population living at high altitude, where there was higher increase in Hb in men than in women[21]. A similar relationship was observed in a study carried out in China, where an increase of Hb with the level of altitude is described to be higher in men than in women; this relationship occurs more often in certain population groups[22]. However, some studies failed to find between-gender differences, such as one carried out in a group of swimmers where the ascent to altitude showed a gender-independent Hb increase[18]. This findings' difference is probably due to the fact that the adaptation groups are different – these were athletes and with shorter time of exposure than we have assessed. The decreased capability to increase Hb in childbearing age women in comparison with men is mainly due to the reduced iron stores caused by a constant loss of blood resulting from menstruation[23], as described in a group of women living at more than 3000 masl in Bolivia[24]. Iron stores are very important, which should prevent us about a possible risk factor in women working at high altitude, in whom Hb level should be continued to be controlled according to the adaptation they might exhibit.

Table 3. Multivariate analysis of Hb values according to the characteristics of workers of two sites of a mining company

Variable	Coefficient	95% CI	p
Male gender	6.14	4.52-8.34	< 0.001
Age (years)	1.01	0.99.1.01	0.100
Type of work operator	1.02	0.84-1.23	0.823
Seniority (years)	1.00	0.98-1.01	0.992
BMI (kg/m^2)	1.02	1.01-1.05	0.021
High geographic altitude site	3.93	2.93-5.29	< 0.001

Coefficients, 95% confidence intervals (95% CI) and p-values obtained with time-adjusted population-averaged generalized estimating equations (PA-GEE) using the binominal family, the log link function and robust models.

A positive relationship was also observed with Hb increase as BMI increased. These data suggest that people with more elevated BMI might experience higher Hb increase in altitude. Obese people have been reported to show poorer acute acclimation to high altitude, which triggers a decrease in saturation and higher incidence of acute mountain sickness[25]. A study conducted in healthy adults of the Peruvian Andes mentions that, for each increased BMI unit, saturation decreases by 0.21%[26]. It is also possible for this saturation decrease to occur by night[27], owing to the exacerbation altitude causes to sleep disorders and apnea[28]. This adaptation mechanism might trigger the exacerbation if others in order to balance the adaptive response, with this being a hypothesis that would explain our finding. An exaggerated increase in red blood cells might have not so beneficial consequences, since it slows down blood hemodynamics and decreases arterial O_2 transport capacity, thus producing headaches and neurological alterations, among other symptoms grouped in the chronic mountain sickness syndrome, also known as Monge's disease[29,30]. This is why this population group should be monitored according to their physiological changes, in addition to generating plans for weight improvement, in order for the produced change not to cause major alterations.

One of the limitations of this study was the lack of other hematologic markers for adaptation assessment; however, Hb is one of the important factors that change with ascent to altitude and, given the sample size, the results could be thought of as being close to reality. In addition, although iron and ferritin levels were not measured, all workers had a good health status and Hb values were within normal range, according to regulations of the company the surveyed subjects worked in, which wouldn't allow this type of alterations in its personnel. Another limitation was given by the fact that this was a secondary data analysis (where the primary investigation searched for an association of age with metabolic syndrome[31]) and the high altitude site had therefore four times more data than the one located at sea level, with this being originated by the fact that this was a study carried out in a company dedicated to this activity and, like others in the field, has much more personnel that works at the high altitude operation; this is why these data are important: to enable the comparison with those of other similar companies.

We conclude that, according to the studied data, Hb in workers of the assessed mining company increases with the passage of years, with this increase being larger in males, in workers operating at the high geographic altitude site and who have higher BMI. Continuing with the performance of occupational medical surveillance programs is recommended in this type of workers, since monitoring all workers exposed to high altitude is necessary, given that they undergo an adaptation process that will generate changes on their physiology.

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Conflict of interests

RGC and LPP were occupational physicians of the company where the research was carried out during the study period.

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