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Oxygen saturation and heart rate in children at high altitude. A different response of Aymaras and non-Aymaras with chronic exposure at 3500 m

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ABSTRACT: This work aims to determine if there is a difference between the cardiorespiratory response of children who chronically live at high altitude (Aymaras and non-Aymaras) compared to children that arrive as tourist at a high altitude of 3500 m (Putre, Chile). The subjects were children (Aymaras and non-Aymaras) who were born and live in Putre and children who came to the same location for a tourist visit. We used Oxygen saturation (%) and heart rate (HR, bpm) were evaluated by pulse oxymetry in children from Putre. The results showed similar levels of oxygen saturation were observed among chronic Aymaras and non-Aymara children. A lower oxygen saturation was found in children with acute exposure when compared with chronic children ($p<0.0001$). The HR of Aymaras and non-Aymara chronic children was lower than that observed in the non-native children ($p<0.05$). In contrast acute children had a higher HR than chronic children ($p<0.001$). Negative relationships were observed with correlation values ($p<0.01$) between oxygen saturation and HR in all groups. We concluded that chronic Aymara children exhibited a higher slope and correlation between oxygen saturation vs HR compared to chronic children who are non-Aymaras, suggesting that chronic natives are more sensitive to hypoxia. And, chronic non-Aymara children have an early blunting response to hypoxia. Further studies are needed to understand the physiological mechanisms in this population group.

KEYWORDS: children, heart rate, oxygen saturation, chronic exposure, high altitude, Aymaras, non-Aymaras.

INTRODUCTION

There are several types of human responses to high-altitude exposure. As for the time of exposure, it is possible to classify them as acute (Ward *et al.*, 1995), chronic intermittent (Richalet *et al.*, 2002) or chronic (Beall, 2006). The chronic type of exposure represents groups of people living at high altitudes. The main lines of study have been carried out mainly in adults, with only a few conducted in native populations of children living at high altitudes.

The comparison of oxygen saturation values in children chronically living at high altitude reveal that normal oxygen saturation at 1610 m is 93-94% (Thilo *et al.*, 1991). Oxygen saturation values of 93.3% (93-93.6%) in 1-24 month old children in Bogota at 2600 m (Lozano *et al.*, 1992). A study performed in Andean children (0.5-14 years) at 3200-3400 m reported a range of oxygen saturation values between 82-98% (Pomeroy *et al.*, 2013). Finally, a study published in children aged 5-16 years old at an altitude of 4340 m found oxygen saturation values of 85.7±5% (Schult & Canelo-Aybar, 2011).

A study of Tibetan and Han newborns (people of Han descent who moved to Tibet from the lowlands of China in 1951) compared the time course

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of oxygen saturation during the first four months of life and found a greater oxygen saturation in Tibetan children. This study suggests that hereditary characteristics selected through prolonged residence at high altitude resulted in adequate arterial oxygen saturation in native people during neonatal and early childhood (Niermeyer *et al.*, 1995). Subsequently, in a study of oxygen saturation throughout the life cycle from 1 week to 80 years in a Tibetan population, a constant increase in mean oxygen saturation was observed during the first decade (Beall, 2000). The author proposed a certain progressive influence of the phenomenon of child development on oxygen saturation; however, there are no ventilation studies in this age range.

Currently, no study has been conducted in the population of children (Aymara or non-Aymara) who were born and live chronically at high altitude. The objective of our study was to evaluate oxygen saturation and heart rate in Aymara and non-Aymara children born and chronically living at high altitude and, in addition, compare their values with non-native children who are tourists at high altitude.

MATERIAL AND METHOD

Location. The town of Putre (3500 m) located 145 km northeast of Arica in the province of Putre-Parinacota in the north of Chile.

Study population. A total of 30 chronic Aymara children were included in the study, all of them with a chronological age of less than 5 years. The chronological age was obtained after asking the parents about their birthday. All chronic children were contacted in the kindergarten of the school in the city of Putre, who receive and cater for children from 3 to 5 years old. Of the 30 chronic children living at high altitude, 20 children have an Aymara kinship (12 boys / 8 girls). To identify the heritage of the Aymaras we used the paternal surname of the mother and the father (then it was considered that four surnames define the inheritance of the Aymaras), this approach is not perfect, but it has been used in series of studies of the Andean population (Soria *et al.*, 2013; Pomeroy *et al.*, 2015). 10 non-Aymara children (4 boys / 6 girls) of parents who work in the city of Putre and were born with a permanence of at least 5 years at high altitude. Finally, a group of 20 non-Aymara children (11 boys / 9 girls) who came to Putre (3500 m) as tourists was included in the study, all of them ascended and descended on the same day. This population of acute non-Aymara children was taken when they entered the primary care center in the town of Putre due to symptoms of acute mountain sickness. Previously, to initiate any evaluation procedure, the parents were asked if they were interested in participating in our study, then the parents of the children read and signed the consent forms before authorizing the participation of their children in the study. This study follows the Helsinki protocol and was approved by the Ethics Committee of the Universidad Católica del Norte.

Cardiorespiratory evaluation. Arterial oxygen saturation (SpO2,%) and heart rate (HR, bpm) were assessed by pulse oximetry in chronic children (Aymara and non-Aymara) in healthy high school children located in the city of Putre. The children were considered healthy if they had not had an upper respiratory disease in the last month and showed no signs of heart or lung disease as clinically demonstrated, in addition, the parents indicated no history of prematurity or any complications during pregnancy. The evaluation procedure consisted in the evaluation of oxygen saturation and heart rate after 5-10 minutes at rest to obtain stable measurements. The evaluations performed on children were repeated every day at the same time and by the same evaluator for 5 consecutive days, in order to reduce the variability in heart rate and oxygen saturation. The values reported in this study are the average of the fourth and fifth days. The measurements were made with pulse oximetry (8500M Nonin Medical Inc., Plymouth, MN) using a pediatric finger sensor (model 8000AP Nonin).

Additionally, in acute non-Aymara children (tourists), upon arrival at the primary care centre, the oxygen saturation values and heart rate were evaluated using the same equipment and the Lake Louise survey for children (CLLS) and parents (LLS) were administered (Moraga *et al.*, 2002; Moraga *et al.*, 2008). In the case of a single child who had symptoms of acute mountain sickness (AMS) associated with low oxygen saturation (<80%), it was concluded that they had severe AMS and was treated with oxygen (0.5-1 liter / min for 30 to 60 min) according to the previously described (Moraga *et al.*, 2008).

Statistics analysis. Cardiorespiratory measurements were expressed as mean ± standard deviation (SD), median, 95% IC and range. A tentative threshold point for hypoxemia and tachycardia was considered as the mean oxygen saturation with two standard deviations and heart rate the mean HR with two standard deviations (Schult & Canelo-Aybar, 2011; Subhi *et al.*, 2009). The difference between groups was tested by analysis of variance followed by rank analysis with the Newman-Keuls test. The AMS in acute non-Aymara children and parents was expressed as a percentage. Pearson´s correlation test was used in order to evaluate the correlation for heart rate vs. oxygen saturation. Data was considered significant when $P < 0.05$ (GraphPad, Prism 6.0).

RESULTS

The age of the populations studied is in accordance with the range for kindergarten students in our country and in others (3-5 years). The mean ages were 4.0 ± 0.5 years, 4.1 ± 0.8 years and 4.0 ± 1.0 years for acute non-Aymara children, chronic Aymara children, and chronic non-Aymara children, respectively.

The evaluation of cardiorespiratory variables revealed that chronic Aymaras have a lower HR than non-Aymara chronic children and acute non-Aymara children (Figure 1 and Table I). Additionally, greater oxygen saturation was observed in chronic Aymara and non-Aymara children compared with acute non-Aymara children (Figure 2 and Table I). The data show that the mean values for oxygen saturation and heart rate are inversely related in the study groups. To evaluate this point, we established a correlation between oxygen saturation and heart rate in each group of children. The graph in Figure 3 and the data in Table 2 show that all children had a significantly higher inverse correlation. In addition, chronic Aymaras and acute non-Aymaras presented a higher slope compared to non-Aymara chronic children, suggesting a lower increase in HR with less oxygen saturation in non-Aymara chronic patients.

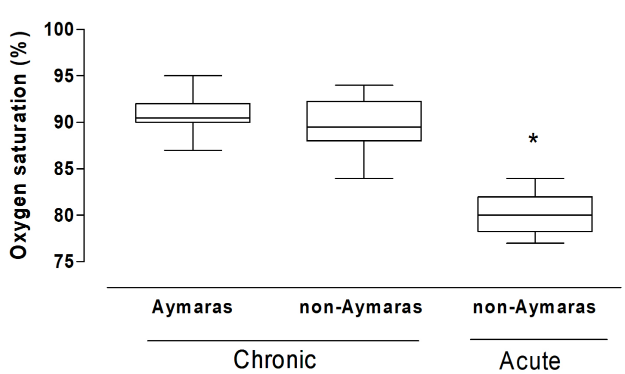

Figure 1. Data shown as box-and-whisker plot. Each box represents the mean for oxygen saturation (SpO2 %) and standard deviation in chronic (Aymaras and non-Aymaras) and acute children at 3500 m. Asterisk (*) represents $p<0.05$ for chronic vs acute conditions.

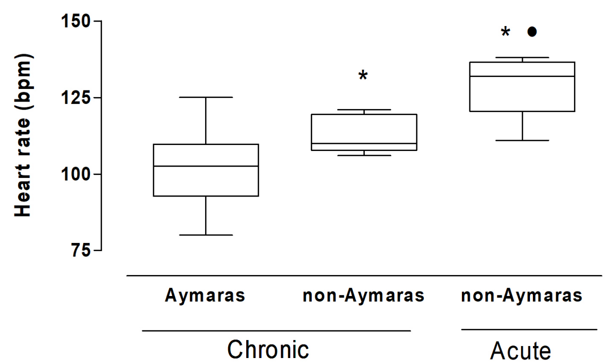

Figure 2. Data shown as box-and-whisker plot. Each box represents the mean for heart rate (bpm) of chronic children (Aymaras and non-Aymaras) and acute children at 3500 m. Asterisks (*) represent significant differences between Aymaras vs non-Aymaras ($p<0.05$); closed circle (●) represents a significant difference between acute and chronic conditions ($p<0.05$).

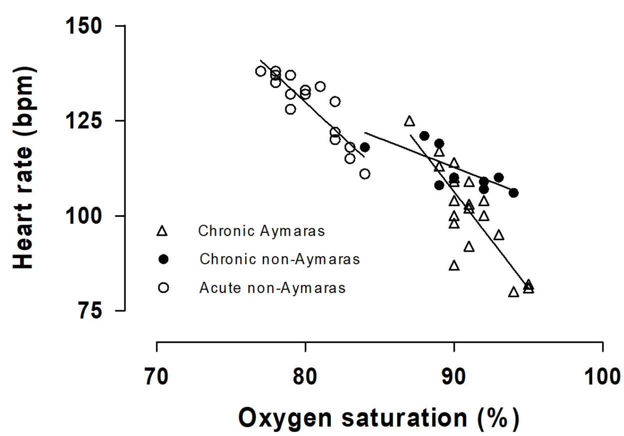

Figure 3. Relationship between heart rate (bpm) vs oxygen saturation (SpO2%). Open triangles represent chronic Aymaras (equation regression $y = -5.077x + 563.3$, $r2 : 0.6928$, $p<0.0001$), closed circles represent chronic non-Aymaras (equation regression $y = -1.522x + 249.7$, $r2 : 0.5492$, $p<0.01$) and open circles represent acute non-Aymaras (equation regression $y = -3.654x + 422.2$, $r2 : 0.8015$, $p<0.0001$) .

Table I.- Cardiorespiratory variables in children with chronic and acute exposure.

	Chronic		Acute
	Aymaras	Non-Aymaras	Non-Aymaras
SpO2 (%)			
Mean±SD	91±2	90±3	80±2●
95% IC	90-92	88-92	79-82
Mean(-2SD)	87	84	-
Median	90	88	78
Range	87-95	84-94	77-84
Heart rate (bpm)			
Mean±SD	101±(3)	112±(2)*	129±(3)*●
95% IC	96-107	109-117	124-133
Mean (+2DS)	107	116	-
Median	102	110	132
Range	80-125	106-121	111-138

Asterisks (*) represent significant differences between chronic Aymaras vs chronic non-Aymaras (p<0.05); closed circles (●) represent significant differences between acute and chronic non-Aymaras conditions (p<0.05).

Table II.- Correlation analysis obtained from heart rate vs oxygen saturation in children at high altitude (Putre).

	Chronic		Acute
	Aymaras	Non-Aymaras	Non-Aymaras
SpO2 (%)			
Mean±SD	91±2	90±3	80±2●
	Aymaras	Non-Aymaras	Non-Aymaras
Slope	-5.077 ±0.797*	-1.522 ±0.488 ●	-3.654 ±0.486
"r" Pearson	-0.832	-0.741	-0.895
P values	P<0.0001	P<0.01	P<0.0001
Heart rate (bpm)			
Mean±SD	101±(3)	112±(2)*	129±(3)*●
95% IC	96-107	109-117	124-133

Values of slopes are expressed as mean± SD. * represents significant differences between slope of chronic Aymaras vs chronic non-Aymaras and acute non-Aymaras (p<0.0001) and closed circles (●) represent significant differences between slope of chronic non-Aymaras vs acute non-Aymaras (p<0.01).

The evaluation of the two standard deviations below the mean oxygen saturation cut in Aymara and non-Aymara children with chronic exposure showed values close to 87 and 85%, respectively (Table I). In addition, we also estimated a limit for two standard deviations above the mean heart rate in Aymara and non-Aymara children with chronic exposure and we obtained values close to 107 bpm and 116 bpm, respectively (Table I).

When evaluating AMS in acute non-Aymara children the higher percentage of AMS (90% 18/20) we observed and higher score of AMS 11.5±2.5 without differences related to gender. Furthermore, 9/20 (45%) children whose oxygen saturation dropped lower than 80% were given oxygen supplementation and after one hour were indicated to return to sea level. Parents had a lower percentage of AMS (27%) in comparison with children.

DISCUSSION

The results obtained in our study show that children with chronic exposure (Aymara and non-Aymara) have higher oxygen saturation than children with acute exposure at high altitude (3500 m). In addition, the heart rate was lower in the chronic Aymaras than in the non-Aymara chronic and non-Aymara acute. These results indicate that chronic (Aymara) children exposed at high altitude have a cardiorespiratory response that is more adapted to life at high altitude.

Children chronically exposed to high altitude.

We recognize three important points in our results: First, we found similar values in Aymara and non-Aymara chronic children living at 3500 m. A similar pattern was reported showing a downward trend in the difference in SpO2 values in Tibetan children versus Han children over 5 years old at an altitude of 3200 and 3800 m (Weitz & Garruto, 2007). In contrast, a wide difference in oxygen saturation was reported in infants from 1 to 4 months against Han (Niermeyer *et al.*, 1995), which was explained by the author because of the effect of pulmonary vasoconstriction expressed in the population of Han. Additionally, studies conducted in Andean children (0.5-14 years old) at 3200-3400 m reported a range of oxygen saturation values between 82-98% (Pomeroy *et al.*, 2013). Subsequently, studies conducted in 4-10 and 7-10-year-old children in La Paz (3650 m) showed oxygen saturation values of 94 ± 1 and 89 ± 3%, respectively (Hill et al 2016a; Hill et al ., 2016b).

Second, our study showed the difference in HR between the populations studied, in which lower HR was observed in chronic Aymara children compared to non-Aymara chronic and non-Aymara acute. There are only a few studies that have examined HR in a similar population and altitude. In the study performed by Huicho *et al.* (2001), they reported an inverse relationship between HR and age in a mestizo population (6 to 18 years) at 4100 m, where 6 year-old children had HR values of 98 ± 11.8 bpm, in addition, the lowest HR was described in ethnic Aymara children at 4340 m with values of 86.5 ± 13.4 bpm for children aged 5 to 6 years (Schult Canelo-Aybar, 2011). A reduction in HR could be explained by a reduction in the metabolic rate associated with growth and maturation and could constitute a better degree of adaptation to high altitude (Huicho *et al.* 2001).

Finally, we found an inverse correlation between heart rate and oxygen saturation in all participants. In addition, a higher slope and similar values were observed between the chronic Aymaras and the acute non-Aymaras living at 3500 m. This evidence was interpreted as a blunting in the HR response to lower values of arterial oxygenation (measured by SpO2 %) in chronic non-Aymara children that live at 3500 m, but additional studies are required to support this conclusion.

It is well established that the loss of sensitivity to hypoxia occurs in adults who have long-standing hypoxemia because they live at high altitude (Chiodi, 1957; Weil *et al.*, 1971; Lahiri *et al.*, 1976), suggesting that this phenomenon is acquired and could produce a partial attenuation after 10 years and practically a complete one after 20 years (Severinghaus, 1966; Byrne-Quinn *et al.*, 1972).

However, very few studies have been performed in children to evaluate this point and some results are controversial. For example, a study comparing the hypoxic ventilatory response (HVR) and the hypercapnic ventilatory response (HCVR) among school-age (sea-level) students and adults concluded that children had a greater cardiac response to hypoxia (as determined by a higher HVR) than adults (Marcus *et al.*, 1994). In addition, another study conducted in chronic Aymara children living at high altitude (Leadville, 3100 m) demonstrated that the loss of HVR in children (9-10 years of age) does not occur in the neonatal period, but could be acquired as adults (Byrne-Quinn *et al.*, 1972). In addition, the study by Cotton & Grunstein (1980) in newborns at high altitude showed two ventilatory patterns, responders and non-responders, to the hypoxic lesion. A prospective study in children aged 3-5 years in Denver-Colorado at 1600 m, showed an increase in the central rate of apnea, apnea and hypopnea, and oxygen desaturation compared to children at sea level (Burg *et al.*, 2013). Finally, a similar study performed with high-altitude children (Tibetans and Aymaras) compared ventilation and HRV in both children and adults, and found that Tibetans aged 9 to > 20 had an increase in HVR, in contrast with the Aymaras from 13 to > 20 years of age who exhibited a maintained HRV (Beall *et al.*, 1997). However, there are no studies of HVR in children of this age range. Taken together, we suggest that the greater slope described in our study with chronic Aymara children is due to a greater sensitivity to hypoxia, while the lower slope described in chronic non-Aymara children is due to a strong sensitivity to hypoxia at 3500 m.

Finally, the SpO2 (%) threshold point described in our results showed average SpO2 2(SD) values for chronic Aymara and non-Aymara children of 87% and 84%, respectively. In this sense, it is known that oxygen saturation decreases with increasing altitude as described previously (Beall, 2006; Lozano *et al.*,1992; Subhi *et al.*, 2009). A systematic review of SpO2 (%) in healthy children from 1 to 5 years of age at a high altitude found a threshold for hypoxemia from 85% to 3200 m (Subhi *et al.*, 2009). No chronic group of children presented hypoxemia values at 3500 m, in contrast to what was observed in acute children. All acute children, who were not Aymaras, required oxygen administration when they arrived at the hospital primary care center. In this sense, this information could be useful in all primary care centers located at high altitude.

Some limitations of the present study have been considered. First, our study included a small number of subjects, but it represents the largest number attending kindergarten at the Putre School. Secondly, lung function and echocardiographic studies were not performed in our study, due to the difficulty of obtaining these types of evaluations in the Aymara communities. Finally, future research should examine a larger number of participants using a prospective, controlled study to evaluate the time course of oxygen saturation, heart rate, electrocardiogram, echocardiography, and polysomnography study in neonates and children up to 5 years of age who live at high altitude.

CONCLUSIONS

Our results show that children between 3 and 5 years of age who were born and live at a great height (3500 m) have a higher oxygen saturation (chronic Aymara and chronic non-Aymara), but two different HR patterns: a lower HR (chronic Aymara) and an increased HR (chronic non-Aymara). In contrast, non-Aymara children with acute exposure showed profound oxygen desaturation associated with tachycardia and a higher incidence of acute mountain sickness, indicating that there is a risk of taking children to a high altitude of more than 3500 m.

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LÓPEZ, V.; MORAGA, D.; CALDERÓN-JOFRE, R. & MORAGA, F. A. Oxygen saturation and heart rate in children at high altitude. Saturación de oxígeno y ritmo cardiaco de niños en zonas de gran altitud. Una respuesta distinta entre Aymaras y no Aymaras con exposición crónica a 3500 m. *J. health med. sci., 6(2)*:123-129, 2020.

RESUMEN: El objetivo de este trabajo es determinar si existe alguna diferencia entre la respuesta cardiorespiratoria de niños que han vivido crónicamente a gran altitud (Aymaras y no Aymaras) comparados con niños llegados como turistas en grandes alturas de 3500 m (Putre, Chile). Los sujetos fueron niños (Aymaras y no Aymaras) que nacieron y vivieron en Putre y niños que llegaron a la zona por una visita turística. Utilizamos saturación de oxígeno (%) y ritmo cardíaco (HR, bpm). Los niños de Putre fueron evaluados utilizando la pulsioximetría. Los resultados mostraron niveles similares de saturación de oxígeno entre los niños crónicos Aymaras y no Ayamaras. En los niños con exposición aguda se encontró una baja saturación de oxígeno al compararse con los niños crónicos ($p<0.0001$). El HR de los niños crónicos Aymaras y no Aymaras fue menor que el observado en niños no nativos ($p<0.05$). En cambio, los niños con síntomas agudos tenían una mayor HR que los niños crónicos ($p<0.001$). Se observaron relaciones negativas con los valores de correlación ($p<0.01$) entre la saturación de oxígeno y HR en todos los grupos. Concluimos que los niños crónicos Aymaras mostraban una gran pendiente y correlacion entre la saturación de oxígeno contra el HR comparado con los niños crónicos no Aymaras, sugiriendo que los nativos crónicos son más susceptibles a la hipoxia, y que los niños crónicos no Aymaras tiene una respuesta temprana a la hipoxia. Se necesitan estudios posteriores para entender los mecanismos fisiológicos en este grupo de población.

PALABRAS CLAVES: niños, ritmo cardiaco, saturación de oxígeno, exposición crónica, gran altitud, Aymaras, no Aymaras.

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