Oxygen saturation, periodic breathing, and sleep apnea in infants aged 1-4 months old living at 3200 meters above sea level

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ABSTRACT

Objectives: To describe, in infants aged 1-4 months old living at 3200 meters above sea level (MASL), oxygen saturation (SpO_2), sleep apnea indices, and periodic breathing (PB) during sleep. Polysomnographies were done in 18 healthy infants.

Results: The median SpO_2 was 87%, and the median PB was 7.2% for the total sleep time. The median central sleep apnea index was 30.5/hour, which decreased to 5.4/hour once sleep apneas associated with PB were excluded. The 5th percentile for SpO_2 was 76% among awake infants, and 66% among asleep infants.

Conclusions: The SpO_2 was lower than that observed at sea level, whereas PB and the central sleep apnea index were higher, once sleep apneas associated with PB were excluded. The latter was similar to that observed at sea level. At 3200 MASL, different cut-off points are required for a normal SpO_2, one for infants during the waking state and one for infants during sleep.

Key words: *sleep, infant, altitude, oximetry, polysomnography.*

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INTRODUCTION

Hemoglobin oxygen saturation (SpO_2) in infants has been established in the waking state at different altitudes.[1-4] However, there are limited data on infants' SpO_2 during sleep. Studies have been conducted in this regard in Colombia,[5-7] Bolivia,[1] China,[3] the United States,[4] and Argentina.[8] There are no publications available regarding normal SpO_2 in infants aged 1-4 months old during sleep at 3000-3500 meters above sea level (MASL) or in relation to periodic breathing (PB) or sleep apnea indices. The only study published on polysomnographies done in infants living above 3500 MASL was conducted in Argentina at 3775 MASL.[8]

In clinical practice, SpO_2 during sleep in infants living in high altitudes is commonly misinterpreted because it is based on values obtained from infants during the waking state. This leads to unnecessary hospitalizations, oxygen overuse, and the need to do paraclinical tests to look for an explanation for an alleged hypoxemia. Major consequences result from this situation, both at a financial and an emotional level, and it becomes especially relevant when considering the significance of bronchiolitis in the first months of life.

The main purpose of this study was to describe SpO_2 during sleep in infants aged 1-4 months old living at 3200 MASL. The secondary objectives included to describe sleep apnea indices, and PB and its association with SpO_2.

METHODOLOGY

This was a prospective, cross-sectional study conducted in Cañar, Ecuador, at 3200 MASL. The protocol was approved by the Ethics Committees of Fundación Santa Fe de Bogotá, Universidad del Azuay in Ecuador, and Universidad Javeriana in Bogotá. In addition to these institutions, the study also involved investigators from Hospital Luis Fernando Martínez in Cañar (Ecuador), and Clínica Shaio and Hospital de la Misericordia in Bogotá (Colombia). Polysomnographies were performed between December 2012 and December 2013. A descriptive analysis was done using median values and percentiles, considering the asymmetrical distribution of data for SpO_2, PB, and central sleep apnea index (CSAI). *P* values lower than 0.05 were considered statistically significant.

Infants included in the study were born at term, had a birth weight of at least 2500 g, and had no perinatal or current disease. All study participants were locals and had always lived in Cañar, like their parents. Families who agreed to participate signed an informed consent form. Polysomnographies were performed in a hospital room, where infants were accompanied by their mothers. The BWII system (Neurovirtual, Doral FL, USA) was used to do the polysomnographies, which is approved by the Food and Drug Administration (FDA) and meets the requirements of the American Academy of Sleep Medicine (AASM). SpO_2 was measured using a Nonin 8008J oximeter (Nonin Medical Inc, Minneapolis, MN). Polysomnographies were required to comprise at least 180 minutes of total sleep time (TST) to be included in the study. Polysomnographies were interpreted as per the AASM's recommendations. The definition of PB used in this study was that established by the AASM: "PB is classified as an event characterized by 3 or more central apneas of more than 3 seconds in duration, separated by no more than 20 seconds of normal breathing. Central sleep apneas occurred within a periodic breathing episode should also be recorded as a separate apnea event" (i.e., sleep apneas associated with desaturation and/or microarousals). Isolated central sleep apneas were differentiated from those associated with PB by means of an individual analysis for each test.

The sample size was calculated based on estimations made assuming a type I error of 0.05, a standard deviation of 3.4 for the average SpO_2 (based on a study by Universidad del Bosque in Bogotá),[5] with a 95% confidence interval and a 2% absolute accuracy.

To establish if there was a correlation between SpO_2 and PB, the relationship between time (minutes) elapsed with a SpO_2 ≥88% and time (minutes) elapsed with a SpO_2 <88% was determined. This cut-off point was selected based on the median SpO_2. This coefficient was referred to as sleep saturation coefficient (SSC) and it was used to establish a correlation between SpO_2 and PB, which was assessed using the Spearman's test.

RESULTS

Out of 35 infants who had a polysomnography done, 18 met the minimum time requirement. SpO_2, PB, and CSAI had an abnormal distribution, with a clear deviation towards the right. The main results are summarized in *Table 1*.

The median SpO_2 was 87%; the difference in SpO_2 between the P5 and the P25 was 20%, whereas it was 5% between the P25 and the P95 (*Figure 1*). The lowest recorded SpO_2 was 33%. The median SpO_2 among awake infants was 89% (P5 76%-P95 91%).

The median PB was 7.2%. The median CSAI was 30.5/hour and the median isolated central sleep apnea index (ICSAI) was 5.4/hour, whereas the median CSAI associated with PB was 19.9/hour. The average duration of central sleep

Table 1. *Respiratory parameters of polysomnographies done in 18 infants aged 1-4 months old at 3200 MASL*

Age (weeks)	Average 8.1	SD 3.3	
TST (minutes)	Average 229.4	SD 35.9	
REM sleep time (minutos/%)	Average 99.4 (43.2%)	SD 27.3	
Non-REM sleep time (minutos/%)	Average 129.7 (56.7%)	SD 27.1	
SpO_2 in the waking state	Median 89%	p5 76%	p95 91%
SpO_2 during TST	Median 87%	p5 66%	p95 91%
PB during TST	Median 7.2%	p5 1.2%	p95 78.7%
TCSAI/hour	Median 30.5	p5 8.8	p95 217.5
ICSAI/hour	Median 5.4	p5 2.0	p95 85.8
CSAIAPB/hour	Median 19.9	p5 2.2	p95 204.4
Lowest SpO_2 recorded in each test	Median 71%	p5 31%	p95 81%

REM: rapid eye movement; SD: standard deviation; SpO2: oxygen saturation; TST: total sleep time; P: percentile; PB: periodic breathing; TCSAI: total central sleep apnea index; ICSAI: isolated central sleep apnea index; CSAIAPB: central sleep apnea index associated with periodic breathing.

apneas was 5.7 seconds (SD 1.0). The median central hypopnea value was 0; the same value was obtained for obstructive and mixed sleep apneas. The median SSC was 1.15. No correlation was observed between PB and SSC (r= -0.36, *p*= 0.14).

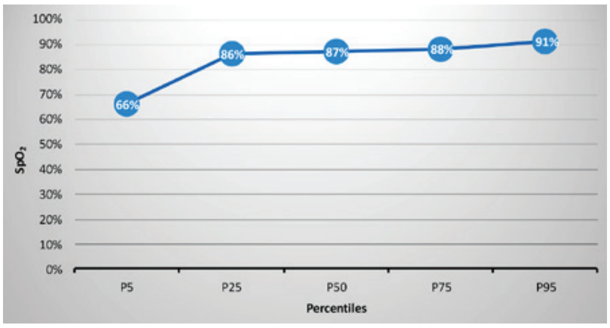
DISCUSSION

In this study, we describe SpO_2 and other polysomnography respiratory parameters in infants aged 1-4 months old at 3200 MASL. The median SpO_2 was 88%, which was lower than that reported at sea level, where infants aged 1-4 months old had a SpO_2 of 98.1%,[9] and was also lower than that reported by us at 2560 MASL, which was 92%.[6] The P5 of SpO_2 was 76% among awake infants and 66% among asleep infants; this means that, at this altitude, it is necessary to have two different cut-off points for a normal SpO_2 of younger infants, depending on whether it is measured during the waking state or during sleep. This does not occur at sea level, where the 90% value is useful for both awake and asleep infants (*Figures 2 and 3*). This is a highly relevant issue for acute respiratory tract infection programs where pulse oximetry has become an essential tool for making clinical decisions.[10,11]

The median PB was 7.2% and was significantly higher than that published at sea level, which was reported to be 1.1% among young infants,[12] and was also higher than that reported at 2560 MASL, which was 4.9%.[6] The CSAI was higher than that observed at 2560 MASL[6] and much higher than that published at sea level. Once central sleep apneas associated with PB are excluded, the CSAI was similar to that observed at sea level; this confirms that the difference between isolated central sleep apneas and those associated with PB was critical in this age group living in high altitudes.

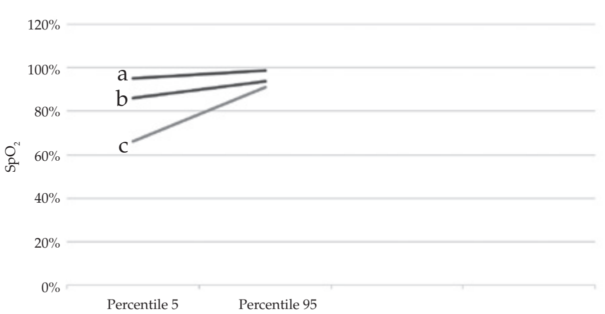
The lack of a correlation between SpO_2 (assessed as per the SSC) and PB suggests that the lower SpO_2 compared to that observed at sea level may be explained by the reduced oxygen pressure typical of high altitudes, not by the increase in PB. In this study, no obstructive or mixed sleep apneas were observed, neither were they found previously in this age group at both sea level[9] and in high altitudes.[6]

Figure 1. *Oxygen saturation percentiles during sleep in 18 infants aged 1-4 months old at 3200 MASL*



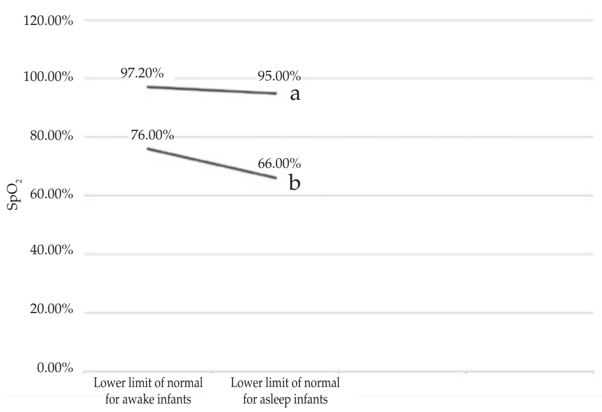
SpO_2: oxygen saturation.

Figure 2. *Oxygen saturation. Percentiles 5 and 95 for sea level, 2560 MASL, and 3200 MASL in infants aged 1-4 months old during sleep*



SpO_2: oxygen saturation.
a. Sea level: ref. 11.
b. 2560 MASL: ref. 6.
c. 3200 MASL: this study.

Figure 3. *Lower limit of normal of oxygen saturation in infants aged 1-4 months old during the waking state versus during sleep at sea level and at 3200 MASL*



a. Sea level: ref. 11.
b. This study.
SpO_2: oxygen saturation

The fact that 25% of infants have a SpO_2 that is significantly different from the remaining 75% may be explained by a higher pulmonary vascular reactivity (PVR). Studies conducted in Kyrgyzstan[13] have demonstrated that pulmonary pressure at high altitudes is genetically determined by mediators that regulate PVR. We believe that PVR may be a determining factor for the fact that some individuals have a significantly lower SpO_2 during sleep. An early detection of these individuals may be useful to establish their risk for pulmonary hypertension.

A limitation of this study is that out of the 35 infants who had a polysomnography done, only 18 were included because the rest did not reach a TST of at least 180 minutes.

CONCLUSIONS

At 3200 MASL, SpO_2 among healthy infants aged 1-4 months old was lower than that observed at sea level, whereas PB and CSAI were higher. However, once central sleep apneas associated with PB are excluded, the CSAI was similar to that observed at sea level. At 3200 MASL, different cut-off points are required for a normal SpO_2, one for infants during the waking state and one for infants during sleep. ■

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