Oxygen saturation, periodic breathing and apnea during sleep in infants 1 to 4 month old living at 2,560 meters above sea level

Santiago Ucrós, MD, Claudia Granados, MD, MS, Karem Parejo, MD, Fernando Guillén, MD, Fausto Ortega, MD, Sonia Restrepo, MD, Fabián Gil, MS and Miriam Guillén

ABSTRACT
There are few data in the literature related to polysomnography in infants in altitudes from 2,200 m to 2,800 m. The main objective of this investigation was to describe oxygen saturation (SpO₂) levels during sleep in infants aged between 1 and 4 months living at an altitude of 2,560 m. The secondary objectives were the description of periodic breathing (PB) and apnea indexes. Polysomnography was performed in 35 healthy infants 1-4 months in Cuenca (Ecuador) at 2,560 m. The median for SpO₂ was 92% and 4.9% for PB. The median for the central apnea index was 23.7/hour and 15.4/hour when related to PB. No correlation was found between PB and SpO₂. Conclusion: SpO₂ was lower than the values at sea level and PB and central apnea index were higher. When apneas associated with PB were not considered, the central apnea index was similar to that found at sea level.

Key words: sleep, infant, altitude, oxygen, polysomnography.

INTRODUCTION
Pulse oximetry has become a routine tool in clinical practice, to the point that it has been proposed as a new vital sign. Oxygen saturation of haemoglobin (SpO₂) values in infants during wakefulness are established at different altitudes. However, data in children at high altitudes during sleeping periods are much scarcer. These kinds of studies have been conducted in Colombia, Bolivia, Peru, China, Bolivia, USA and Argentina.

The research hereby presented was undertaken with the main purpose of describing SpO₂ levels during sleep in infants aged between 1-4 months living at 2,560 m. A description of PB and apnea indexes was included as secondary objectives.

METHODOLOGY
The study was carried out in Cuenca, Ecuador, a city located at 2,560 m above sea level. The protocol was approved by the ethical committees of the institutions which participated in the study.

In this cross-sectional study, the sample calculation was made using the TAMAMU 1.1 program. Estimates were made assuming a type one error of 0.05 with a standard deviation of 3.4 for the SpO₂ mean (based on the results from the study made at the Universidad del Bosque, Bogotá, Colombia) and a two-tailed accuracy level of 2%. A descriptive analysis of the recorded variables, by means of the Kruskal-Wallis test. P <0.05 values were considered to be statistically significant.

In Cuenca, the authors searched for healthy infants at the Growth and Development Outpatient Clinic in the Hospital del Río. Infants included in the study were required to meet the following criteria: a normal full term pregnancy, birth weight of 2,500 g or higher, no previous...
medical history of perinatal pathology and no general or respiratory illness. Babies with current or previous contact with second hand tobacco smoke were also excluded.

Parents accepting the terms of the research signed an informed consent. Polysomnographies were conducted in a hospital room adapted for the study allowing infants to be accompanied by their mothers at all times.

A BWII polysomnography was used for polysomnography measurements, which is Food and Drug Administration (FDA) approved and American Academy of Sleep Medicine (AASM) 100% compliant (Charles, IL, USA). SpO$_2$ was measured with a Nonin oximeter sensor model 8008J. All sleep studies involved at least 180 minutes of total sleep time (TST). The polysomnography interpretation was made according to the AASM recommendations (2012 version). Respiratory breathing was defined according to the definition of the AASM as “an event with ≥3 episodes of central apnea lasting >3 seconds separated by ≤20 seconds of normal breathing. Central apneas that occur within a run of periodic breathing should be scored as individual apneas as well.” Central apneas were differentiated between those associated with respiratory breathing and those arising as isolated events, via manual analysis of each of the polysomnographies.

To determine whether there was any correlation between SpO$_2$ and the PB, the ratio of the length time during which the infant had a SpO$_2$≥91% and the time when the SpO$_2$ was <91% was used. We called this ratio the Sleep Saturation Ratio (SSR). This correlation was assessed with the Spearman correlation coefficient.

**RESULTS**

A total of 35 infants complied with the inclusion criteria. The polysomnographies were performed between October 19, 2012 and May 5, 2013. The group comprised 18 boys and 17 girls, nine were between 30 and 59 days old, thirteen were 60 to 89 days old and thirteen were 90 to 120 days old. The age groups for SpO$_2$, PB and CAI showed no statistical differences. These parameters showed a non-normal distribution, with a bias towards the right (see main results in Table 1).

The median for SpO$_2$ was 92% (Figure 1). The SpO$_2$ difference between the 5$^{th}$ and 25$^{th}$ percentile values was 4%, and the same value was found between the 25$^{th}$ and 95$^{th}$ percentiles (Figure 2). The SpO$_2$ values for the infants in this study frequently fell below 80%, with dips characteristically short and followed by swift recovery.

The proportion of PB had a median of 4.9%. The PB median for rapid eye movement (REM) sleep was 9% and 2.3% for non rapid eye movement (NREM) sleep, yielding a statistically significant difference (p= 0.0001). The CAI had a median of 23.7/hour. The median of CAI in relation to PB was 15.4/hour, while the median for isolated CAI was 4.5/hour. The mean time for

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<tr>
<th>Table 1. Polysomnography respiratory parameters in 35 infants 1-4 months of age living at 2,560 m above sea level</th>
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<tbody>
<tr>
<td><strong>Age (weeks)</strong></td>
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<tr>
<td><strong>TST (minutes)</strong></td>
</tr>
<tr>
<td><strong>Active/REM sleep time (minutes/%)</strong></td>
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<tr>
<td><strong>Quiet/NREM sleep time (minutes/%)</strong></td>
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<tr>
<td><strong>SpO$_2$ in TST % PB</strong></td>
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<tr>
<td><strong>TCAI/hour</strong></td>
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<td><strong>ICAI/hour</strong></td>
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<td><strong>PBRAI/hour</strong></td>
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<td><strong>SpO$_2$ lowest value in TST</strong></td>
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<td><strong>SSR</strong></td>
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TST: Total Sleep Time; p: percentile; PB: Periodic Breathing; TCAI: Total Central Apnea Index; ICAI Isolated Central Apnea Index; PBRAI: Periodic Breathing Related Apnea Index; SSR: Sleep Saturation Ratio.
central apneas was 5.15 s. The median for central hypopnea was 0. Obstructive and mixed apnea indexes were 0/hour. The median for the SSR was 3.9. No correlation was found between SSR and PB (Figure 3).

DISCUSSION
In this study we present the description of the SpO2 and other respiratory polysomnography parameters in infants 1-4 months of age, at 2,560 m above sea level. The SpO2 we found was clearly lower than values described at sea level by Schlüter et al, who for children aged 1-4 months reported a median of 98.1% (p5, 95% – p95, 99.5%).10 PB, on the other hand, was significantly higher than data recorded at sea level by Kelly et al, which was lower than 1% in infants 2-4 months11 and by Schlüter et al, who found PB below 0.5% in children aged 1-4 months.10 The fact that PB increases with altitude has physiological bases12 and has been previously reported in infants.13 In our study, PB was significantly higher during REM sleep compared with NREM sleep; this finding is recognized since 1977.14

The data on CAI that we have found is higher than that reported by Schlüter et al, at sea level, who recorded a median of 5-10/hour for infants aged 1-4 months.10 However, in our data, when central apneas associated with PB were discounted, the CAI median was close to the value reported by these authors. These results indicate that the discrimination between isolated apneas and PB associated apneas becomes important in high altitude conditions, in this age group. If ignored, the CAI values will be largely a reflection of the PB percentage. An increase in central apneas associated with PB was reported by Parkins et al with findings similar to ours. These authors analyzed the breathing pattern in 34 children with a mean age of 3.1 months exposed to oxygen at 15% (equivalent to a barometric pressure of 582 mm Hg), and found that apneas associated with PB increased 3.5 times with the simulated altitude, whereas the increment of isolated apneas was only of 0.15.13

Recently a study similar to ours at 2,640 m of altitude was published.2 The results agree in relation to SpO2, but CAI and PB were higher in our results. The authors report an important

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**Figure 1. Oxygen saturation during sleep in infants aged 1-4 months living at 2,560 m above sea level and comparison with values at sea level**

<table>
<thead>
<tr>
<th>Percentile</th>
<th>SpO2 (%)</th>
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<tbody>
<tr>
<td>P5</td>
<td>86</td>
</tr>
<tr>
<td>P25</td>
<td>90</td>
</tr>
<tr>
<td>P50</td>
<td>92</td>
</tr>
<tr>
<td>P75</td>
<td>93</td>
</tr>
<tr>
<td>P95</td>
<td>94</td>
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</table>

a, b, c: Oxygen saturation percentiles 5, 25 and 75 during sleep at sea level in infants aged 1-4 months.14

SpO2: oxygen saturation.

**Figure 2. Oxygen saturation percentiles during sleep in infants 1 to 4 months of age at 2,560 m above sea level**

**Figure 3. No correlation between sleep saturation ratio and % of periodic breathing in infants aged 1-4 months living at 2,560 m above sea level (r = 0.057, p = 0.278)**

SpO2: oxygen saturation.

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The absence of correlation between PB and SpO$_2$ represented by the SSR suggests that low SpO$_2$ is attributable to the decreased inspiratory PO$_2$ characteristic of high altitudes and not to the increase in PB. In consequence, the clinical decision to provide supplementary oxygen should be based on the SpO$_2$ data and not with the intention of changing the PB or CAI parameters.

The obstructive sleep apnea index and the mixed apnea index were 0 in all the infants taking part in this study. Values approaching 0 for these parameters have been previously reported at sea level, by Schlüter in Germany$^{10}$ and by Kato$^{15}$ in Belgium.

The fact that the difference between the SpO$_2$ in the 5th to 25th percentiles was the same that the one observed between the 25th and 95th percentiles shows a relevant difference in the physiological behavior of this parameter during sleep in about 25% of the babies. The reason why this happens and whether there are any consequences should be evaluated in further investigations. It could be hypothesized that some babies have a higher level of pulmonary vascular reactivity in response to the hypobaric hypoxia.

Considering the haemoglobin dissociation curve, the data obtained for SpO$_2$ in this study can be useful as an approximation to what happens in a range of ± 300m around 2,500 m of altitude, where large populations live, including cities like México DF with 21 million inhabitants, Bogotá (Colombia) with 8 million, Addis Ababa (Ethiopia) with 2.7 million, Sana’a (Yemen) with 2.5 million, Quito (Ecuador) with 2.3 million, Arequipa (Peru) and Toluca (México) with 0.8 million and Cochabamba (Bolivia), Quetzaltenango (Guatemala) and Asmara (Eritrea) with 0.6 million.

Acknowledgements

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REFERENCES