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[a], Claudia Granados, MD, MSc[b], Karem Parejo, MD[c], Fernando Guillén, MD[d], Fausto Ortega, MD[e], Sonia Restrepo, MD[f], Fabián Gil, MSc[g] and Miriam Guillén[h]

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 (SpO_2) 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 SpO_2 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 SpO_2. Conclusion: SpO_2 was lower than the values at sea level and PB and central apnea indexwere higher. When apneas associated with PB were not considered, the central apnea indexwas similar to that found at sea level.
Key words: *sleep, infant, altitude, oxygen, polysomnography.*

http://dx.doi.org/10.5546/aap.2015.eng.341

a. Department of Pediatrics. Fundación Santa Fe de Bogotá.
b. Departments of Pediatrics and Clinical Epidemiology and Biostatistics.Pontificia Universidad Javeriana.
c. Department of Neurology and Sleep Lab. Fundación Clínica Shaio.
Bogotá, Colombia.
d. Department of Pediatrics. Hospital del Río. Universidad del Azuay. Cuenca, Ecuador.
e. Department of Pediatrics. Hospital Luis Fernando Martínez. Cañar, Ecuador.
f. Departments of Pediatrics. Hospital de La Misericordia, Fundación Santa Fe de Bogotá, Universidad de los Andes.
g. Biostatistician. Department of ClinicalEpidemiology and Biostatistics. Pontificia Universidad Javeriana.
Bogotá, Colombia.
h. Medical Student. Universidad del Azuay. Cuenca, Ecuador.

E-mail Address:
Santiago Ucrós MD: santiago_ucros@yahoo.com

Funding: This research was supported in part by grants from FundaciónConocimiento, Bogotá, Colombia (Grant PI-FC/001-2012); the education fund from the Pediatrics Department, Fundación Santa Fe de Bogotá; and the research fund from the Azuay University, Cuenca, Ecuador.

Conflict of interest: None.

Received: 2-14-2015
Accepted: 4-23-2015

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 (SpO_2) 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,[1,2] Bolivia,[3] Peru,[4] China,[5] Bolivia,[6] USA[6] and Argentina.[7]

The research hereby presented was undertaken with the main purpose of describing SpO_2 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.[8] Estimates were made assuming a type one error of 0.05 with a standard deviation of 3.4 for the SpO_2 mean (based on the results from the study made at theUniversidad del Bosque, Bogotá, Colombia)[1] and a two-tailed accuracy level of 2%. A descriptive analysis of the recorded was undertaken, using medians and percentiles measurements in view of their asymmetrical distribution. Medians were compared by age group (<30 days, 30 to 60 days, >60 days), for SpO_2, PB, and Central Apnea Index (CAI) 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).[13] 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 $SpO_2 \geq 91\%$ 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 forrapid 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

Table 1. *Polysomnography respiratory parameters in 35 infants 1-4 months of age living at 2,560 m above sea level*

Age (weeks)	Mean 11.1	SD 3.8	
TST (minutes)	Mean 250	SD 32	
Active/REM sleep time (minutes/%)	Mean 112 (45%)	SD 28	
Quiet/NREM sleep time (minutes/%)	Mean 142 (55%)	SD 28	
SpO_2 in TST	Median 92%	p5 86%	p95 94.0%
% PB	Median 4.9%	p5 0.2%	p95 46.8%
TCAI/hour	Median 23.7	p5 0.9	p95 130.2
ICAI/hour	Median 4.5	p5 0.0	p95 47.0
PBRAI/hour	Median 15.4	p5 0.9	p95 105.0
SpO_2 lowest value in TST	Median 77%	p5 61%	p95 85%
SSR	Median 3.9	p5 0.4	p95 26.2

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.

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 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*).

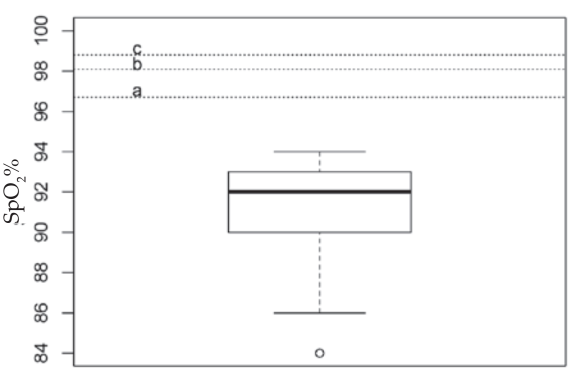
DISCUSSION

In this study we present the description of the SpO_2 and other respiratory polysomnography parameters in infants 1-4 months of age, at 2,560 m above sea level. The SpO_2 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 months[11] 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 bases[12] 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]

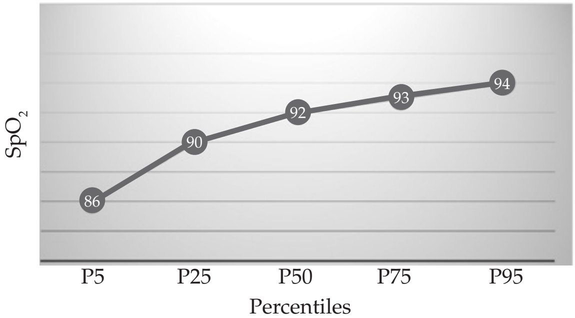
Recently a study similar to ours at 2,640 m

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*



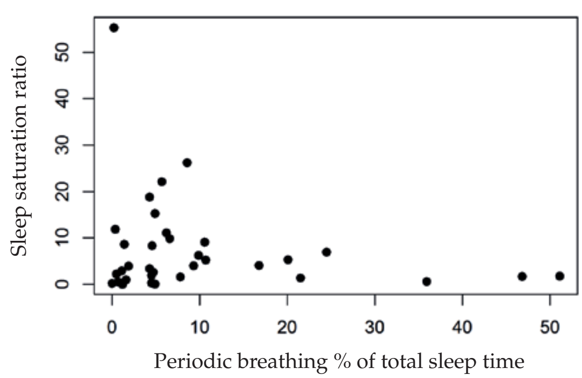
a, b, c: Oxygen saturation percentiles 5, 25 and 75 during sleep at sea level in infants aged 1-4 months.[14]
SpO_2: oxygen saturation.

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



SpO_2: oxygen saturation.

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)*



of altitude was published.[2] The results agree in relation to SpO_2, but CAI and PB were higher in our results. The authors report an important number of obstructive apneas that was not found by us.

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 5^{th} to 25^{th}percentileswas the same that the one observed between the 25^{th} and 95^{th} 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

This research could not have been done without the collaboration of the infant's parents.

We thank Ms. Sandra Rocío Morales for her hard work training technicians in Cuenca and Mrs. Marta Pizano and Mr. Lewis Grenville for their help in the translation and editing of this article.

REFERENCES

1. Torres Y, Osorio L, Ramos N. Medición de los valores de oximetría de pulso durante sueño, vigilia y succión en neonatos sanos en Bogotá (2640 metros de altura sobre el nivel del mar). *Avances Pediátricos* 1999;1:2-8.
2. Duenas-Meza E, Bazurto MA, Gozal D, González-García M, et al. Overnight polysomnographic characteristics and oxygen saturation of healthy infants, 1 to 18 months of age, born and residing at high altitude (2,640 meters). *Chest* 2015: Epub 2015 Mar 26.
3. Salas AA. Pulse oximetry values in healthy term newborns at high altitude. *Ann Trop Paediatr* 2008;28(4):275-8.
4. Gonzáles GF, Salirrosas A. Arterial oxygen saturation in healthy newborns delivered at term in Cerro de Pasco (4340 m) and Lima (150 m). *Reprod Biol Endocrinol* 2005;3:46.
5. Niermeyer S, Yang P, Shanmina , Drolkar, et al. Arterial oxygen saturation in Tibetan and Han infants born in Lhasa, Tibet. *N Engl J Med* 1995;333(19):1248-52.
6. Niermeyer S, Shaffer EM, Thilo E, Corbin C, et al. Arterial oxygenation and pulmonary arterial pressure in healthy neonates and infants at high altitude. *J Pediatr* 1993;123(5):767-72.
7. Alduncin J, Grañana N, Follett F, Musante G, et al. Problemas respiratorios durante el sueño en lactantes nativos del altiplano argentino. *Arch Argent Pediatr* 2005;103(1):14-22.
8. Pérez A, Rodríguez N, Gil JF, Ramírez GA. Tamaño de la muestra: a computer program to estimate the required sample size and power in clinical research. *J Clin Epidemiol* 1999;52Suppl 1:38S.
9. Berry RB, Brooks R, Gamaldo CE, Harding SM, et al. The AASM Manual for Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, Version 2.0. Darien, IL: American Academy of Sleep Medicine;2012.
10. Schlüter B, Buschatz D, Trowitzsch E. Perzentilkurvenpolysomno graphischer parameter für das erste und zweiteLebensjahr. *Somnologie (Berl)* 2001;5(1):3-16.
11. Kelly DH, Stellwagen LM, Kaitz E, Shannon DC. Apnea and periodic breathing in normal full-term infants during the first twelve months. *Pediatric Pulmonol* 1985;1(4):215-9.
12. Whitelaw W. Mechanisms of sleep apnea at altitude. *AdvExp Med Biol* 2006;588:57-63.
13. Parkins KJ, Poets CF, O´Brien LM, Stebbens VA, et al. Effect of exposure to 15% oxygen on breathing patterns and oxygen saturation in infants: interventional study. *BMJ* 1998;316(7135):887-91.
14. Hoppenbrouwers T,Hodgman JE,Harper RM,Hofmann E, et al.Polygraphic studies of normal infants during the first six months of life: III. Incidence of apnea and periodicbreathing. *Pediatrics*1977;60(4):418-25.
15. Kato I, Franco P, Groswasser J, Kelmanson I, et al. Frequency of obstructive and mixed sleep apnea in 1,023 infants. *Sleep* 2000;23(4):487-92.