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Pulse Oximetry as a Screening Test for Critical Congenital Heart Disease in Term Newborns

Guadalupe Gómez-Rodríguez[1], Anaí Quezada-Herrera[1], Norma Amador-Licona[2]*, Deyanira Carballo-Magdaleno[1], Evaldo Jesús Rodríguez-Mejía[1] and Juan Manuel Guízar-Mendoza[3]

[1]Department of Neonatology, UMAE 48-Instituto Mexicano del Seguro Social (IMSS), León, Gto., Mexico; [2]Department of Education and Research, UMAE HE 1-IMSS, León, Gto., Mexico; [3]De LaSalle University, León, Gto., Mexico

ABSTRACT

Background: Pulse oximetry has been suggested as a screening test for congenital heart disease (CHD) in asymptomatic newborns. However, most newborns in Mexico are discharged from the hospital without this evaluation. **Objective**: To evaluate pulse oximetry as a screening test for critical congenital heart disease (CCHD) in term newborns. **Methods**: We conducted a cross-sectional study in term newborns between July 2010 and April 2011. Pulse oximetry was determined before hospital discharge; in case of post-ductal oxygen saturation < 95%, a Doppler echocardiogram was performed. **Results:** From 1,037 newborns screened, two had CCHD, one had pulmonary atresia and ventricular septal defect, and one Ebstein´s anomaly. Minor CHD was present in 10 babies. The overall prevalence of CHD was 11.5 per 1000 live births, and the prevalence of CCHD was 3.9 per 1000 live births. For those with critical disease, pulse oximetry had a sensitivity of 100%, specificity 98.8%, positive predictive value 14.2%, negative predictive value 100%, and positive likelihood ratio of 86.2. In regression analysis, oxygen saturation, respiratory frequency, and postnatal age were related with CCHD. **Conclusions:** Pulse oximetry had a good sensitivity and specificity for the identification of critical congenital heart disease in term newborns. Low oxygen saturation, higher respiratory frequency, and early postnatal age were related with congenital heart disease. (REV INVES CLIN. 2015;67:130-4)
Corresponding author: Norma Amador-Licona, norma.amador@imss.gob.mx

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BACKGROUND

Congenital heart disease (CHD) is the most common class of birth defects. From 1998 to 2005, the overall prevalence of CHD in the USA was 81.4/10,000 births[1]. In Latin America, the reported prevalence is 2.3/1000 live newborns[2]. Clinical examination is usually the initial method for diagnosis of heart disease, particularly in the presence of a heart murmur. However, the presence of heart murmurs in newborns in the first week of life varies from 0.6 to 77.4%, and most murmurs are known to be related to the circulatory

Corresponding author:
*Norma Amador-Licona
Department of Education and Research
UMAE HE 1-IMSS
López Mateos e Insurgentes, s/n
Col. Parisos, León, Gto., México
E-mail: norma.amador@imss.gob.mx

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changes occurring after birth[3,4]. Also, their detection may depend on the experience of the examiner, postnatal age, and the study population[3-6].

The American Heart Association, American Academy of Pediatrics, and clinical studies suggest performing pulse oximetry as a routine test to detect CHD in asymptomatic newborns, combined with clinical examination[7-9]. Pulse oximetry offers a reliable, noninvasive method for continuous assessment of arterial oxygen pressure (PaO2) and heart rate[10,11], based on the physiological principle that oxygenated and deoxygenated hemoglobin have different absorption spectra[9,12]. In some studies, a saturation difference between right upper extremity (ductal) and lower extremity (post-ductal) of ≥ 7% in the first six hours of life or a lower extremity saturation of < 92% are considered abnormal[13]. In Mexico, performing pulse oximetry is not a universal policy for newborn screening, although early detection of CHD is crucial for survival in these newborns. Thus, the aim of this study was to evaluate pulse oximetry as a screening test for critical congenital heart disease (CCHD) in term neonates.

METHODS

Study design and population

The study was approved by the research and ethics committees of the hospital. In July 2010 to April, 2011 we conducted a prospective, cross-sectional study of newborns of > 6 hours of age. The study included consecutive infants born at our hospital, irrespective of mode of delivery, in whom no CHD was suspected and who were available during the working hours of the investigators. We excluded newborns with lung diseases or whose parent or guardian did not sign the informed consent. Due to a policy of early discharge in our hospital, the mean age at pulse oximetry screening was 12 hours. The clinical records of all newborns were reviewed at six months of age to identify whether any heart disease was diagnosed after hospital discharge.

Pulse oximetry screening

Saturation of peripheral oxygen (SpO2) was measured using a portable Rad-5™ handheld pulse oximeter with multisite sensor that prevents the pulse wave from changing with the neonate's movements. This pulse oximeter signal is obtained by subtraction, making it more reliable than other equipment (Nellcor N-395, Novametrix MARS, and Philips Viridia 24C Rev BO), and has higher sensitivity and specificity[14]. The measurement was taken during two minutes in the left lower extremity (post-ductal) until the reading remained the same in two determinations; the measurement was performed under physiological sleep and by only one member of the study team.

Echocardiography

In case the SpO2 was < 95%, Doppler echocardiography was performed in the Pediatric Cardiology Department to detect a probable CHD. Patients with CCHD were admitted to the neonatal intensive care unit and were followed until discharge from the hospital. We included a control group of 28 healthy newborns with normal clinical examination and SpO2 > 95% for evaluation by Doppler echocardiography.

STATISTICAL ANALYSIS

We used descriptive statistics and analysis of quality of statistical test: sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio. A logistic regression analysis was performed to identify variables related with all CHD and CCHD. Statistical analyses were performed using Statistica 6.0 software.

RESULTS

We evaluated 1,037 neonates, of whom 42.1% were delivered by caesarean section. Mean birth weight was 3,000 g, and mean age at pulse oximetry screening was 12 hours (range, 6-48) (Table 1).

Fourteen (1.35%) patients were referred to pediatric cardiology because of a SpO2 < 95%. These newborns also had a heart murmur at auscultation. Only 12 were true positives; of them, two had CCHD: one had pulmonary atresia and a ventricular septal defect, and the other one had Ebstein's anomaly. The remaining 10 babies had mild CHD: five had patent ductus arteriosus (PDA) and foramen ovale (FO), two had PDA + FO + pulmonary hypertension (PH), one had PDA + PH + mild mitral insufficiency, and two had an atrial septal

Table 1. General characteristics of 1,037 term newborns screened by pulse oximetry

Variable*	
Sex, *n* (female/male)	490/547
Gestational age (weeks)	38.9 ± 1.1
Birth weight (g)	3,080 ± 182.2
Postnatal age at discharged (hours)	12.0 (8.2-15.8)
Apgar scores	
– 1 min	8 (6-9)
– 5 min	9 (7-9)
Mode of delivery, *n* (%)	
– Cesarean section	437 (42.14)
– Vaginal birth	600 (57.86)
SpO2 (%)	96.02 ± 3.15
Postnatal age at evaluation (hours)	12.0 (17.7-15.8)

*Variables are shown as mean ± standard deviation, median (range) or median (95% CI) according to their distribution.

defect > 3.5 mm (Table 2). There were no differences in frequency or severity of CHD when comparing mode of delivery. The global prevalence of CHD was 11.5 per 1000 live births, 3.9 per 1000 live births considering only CCHD + atrial septal defect, and 1.9 per 1000 live births for CCHD.

From the 14 neonates with a murmur at auscultation, 12 had CHD and in eight of them (all with PDA) this abnormality was detected in their pulses. Two babies had cyanosis, one with pulmonary atresia and one with Ebstein´s anomaly.

Of the 12 patients with CHD, two (16.6%) underwent surgery, eight (66.6%) received follow-up in pediatric cardiology, and two (16.6%) were admitted to the neonatal intensive care unit, but there were no deaths.

As the purpose of the study was early diagnosis of CCHD, minor CHD in 10 children was classified as false positive for screening by pulse oximetry, thus obtaining a very good sensitivity, specificity, and negative predictive value, but low positive predictive value for this procedure in CCHD. However, these values increased when we considered screening for all CHD (Table 3).

In logistic regression analysis we found that oxygen saturation, respiratory frequency, and temperature were associated with all CHD, while oxygen saturation, respiratory frequency, and postnatal age were the variables associated with CCHD (Table 4).

DISCUSSION

Pulse oximetry proved to be a useful screening tool for the identification of congenital heart disease in the first hours after birth, as other studies have reported[15-17].

Table 2. Clinical characteristics of newborns with congenital heart diseases

No.	Sex	Postnatal age (hours)	Oxygen saturation %	Diagnosis by echocardiography	Femoral pulses	Cyanosis
1	M	8	92	PDA 2.5 mm, FO 3 mm, LVEF 73%	Abnormal	-
2	M	16	93	PDA 1.5 mm, FO 2 mm, LVEF 65%	Normal	-
3	F	48	92	ASD 6 mm, LVEF 60%, mild PS	Normal	-
4	F	22	92	PDA 2.1 mm, FO 2 mm, LVEF 77%,	Abnormal	-
5	M	14	94	PDA 2.5 mm, FO 3 mm, LVEF 74%, PH 40 mmHg	Abnormal	-
6	M	46	91	PDA 3 mm, ASD 4 mm, LVEF 68%, mild TI, mild MI	Abnormal	-
7	M	7	75	PDA 2 mm, FO 3mm PH 45 mmHg, LVEF 60%, mild TI	Abnormal	-
8	F	19	93	PDA 3 mm, FO 3 mm	Abnormal	-
9	M	8	90	PDA 2.7 mm, FO 2.8 mm	Abnormal	-
10	M	12	88	PDA 2 mm, mild-moderate MI, LVEF 68%, PH 40 mmHg	Abnormal	-
11*	M	6	85	PA, severe VSD	normal	+
12*	M	8	88	Ebstein´s anomaly	normal	+

*Critical congenital heart disease.
PDA: patent ductus arteriosus; FO: foramen ovale; LVEF: left ventricular ejection fraction; ASD: atrial septal defect; PS: pulmonary stenosis; PH: pulmonary hypertension; TI: tricuspid insufficiency; MI: mitral insufficiency; PA: pulmonary atresia; VSD: ventricular septal defect.

Table 3. Pulse oximetry screening for the detection of congenital heart disease in term newborns

	Values for all congenital heart diseases	Values for critical congenital heart diseases
Sensitivity (%)	100 (73.5-100)	100 (15.8-100)
Specificity (%)	99.8 (99.3-99.9)	97.9 (98.2-99.4)
Likelihood ratio	512 (128-2,046)	86.2 (49.1-151.3)
Positive predictive value (%)	85.7 (57.1-98.2)	14.2 (1.7-42.8)
Negative predictive value (%)	100 (99.6-100)	100 (99.6-100)

Values are shown as mean (95% CI).

The prevalence of all CHD (11.5 per 1000 live births) was similar to other populations[18-20] and PDA was the single most common defect, followed by atrial septal defect.

There were no deaths from CCHD in this cohort. Although false positives of pulse oximetry represented 0.19%, similar to the results of Granelli, et al., who reported 0.17%[21], this screening test proved essential because mortality in early versus late detection of CCHD could be as different as 0.9 and 14.8%, respectively[10,13,22,23]. A delayed diagnosis has been estimated between 13.8 and 29.5% of live-born infants with nonsyndromic CCHD who could have benefited from routine screening at birth hospitals[24,25].

Newborns with CCHD had an oxygen saturation of < 95%. This is consistent with data from Tapia-Rombo, et al.[15], who reported that oxygen saturation of term infants at sea level is 97-100%, and in preterm infants, it is 95-100%; oxygen saturation below these values is considered abnormal in the first 24 hours of life[25]. De-Wahl Granelli, et al., in a study of 39,530 patients, reported similar sensitivity and specificity values after including non-cyanogenic CHD[21].

In regression analysis, we found that low oxygen saturation and low temperature, but high respiratory frequency, were related to all CHD. High respiratory frequency could be related to peripheral airway obstruction that occurs in children with pulmonary hypertension associated to CHD[26]. Furthermore, in children with CHD, even after surgical repair of the malformations, pulmonary function is often abnormal and there is ventilatory limitation to exercise[27]. We do not have a clear explanation of the high body temperature found in this study because it was related with all CHD but not with CCHD alone when these were analyzed separately. Finally, low oxygen saturation, high respiratory frequency, and early postnatal age were the variables associated with CCHD, demonstrating the accuracy of pulse oximetry in this diagnosis.

Table 4. Factors related with all or critical congenital heart disease in term newborns

Variable	β	p
All congenital diseases		
– Oxygen saturation (%)	–0.42	< 0.0001
– Respiratory frequency	0.09	0.004
– Temperature (°C)	–0.08	0.03
Intercept 1.07, SE 0.52; p= 0.001 for the model		
Critical congenital diseases		
– Oxygen saturation (%)	–0.25	< 0.0001
– Postnatal age (hours)	–0.06	0.04
– Respiratory frequency	0.11	0.002
Intercept 0.61, SE 0.08; p= 0.01 for the model		

Limitations of our study are that we performed only post-ductal measurement, and we did not perform Doppler echocardiography on all newborns. However, this study included a large sample size, and all patients were followed for six months to allow for detection of CCHD that may have been diagnosed after the screening test. Another advantage of our study is that the pulse oximeter used in this study precluded changes in oxygen saturation readings caused by the neonate´s movements. Furthermore, other studies have also performed only post-ductal measurement[28].

Although many studies have shown that pulse oximetry is useful in the diagnosis of CHD[29-32], few studies

have been conducted in Latin American populations[15,25]. According to our results, we consider that pulse oximetry must be implemented as a routine screening test in all newborns, as proposed by the American Heart Association and the American Academy of Pediatrics[8].

REFERENCES

1. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. J Pediatr. 2008;153:807-13.
2. Castilla EE, Orioli IM. ECLAMC: the Latin-American collaborative study of congenital malformations. Community Genet. 2004; 7:76-94.
3. Ainsworth S, Wyllie J, Wren C. Prevalence and clinical significance of cardiac murmurs in neonates. Arch Dis Child-Fetal Neonatal. 1999;80:43-5.
4. Hallidie-Smith KA. Some auscultatory and phonocardiographic findings observed in early infancy. BMJ. 1960;i:756-9.
5. Arlettaz R, Archer N, Wilkinson AR. Natural history of innocent heart murmurs in newborn babies: controlled echocardiographic study. Arch Dis Child-Fetal Neonatal. 1998;78:F166-70.
6. Attenhofer Jost CH. [Heart murmur-auscultation or echocardiography in the diagnostic assessment of congenital or valvular heart disease?]. Ther Umsch. 2006;63:463-70.
7. Kamlin CO, Dawson JA, O'Donnell CP, et al. Accuracy of pulse oximetry measurement of heart rate of newborn infants in the delivery room. J Pediatr. 2008;152:756-60.
8. Rabi Y, Yee W, Yue Chen S, Singhal N. Oxygen saturation trends immediately after birth. J Pediatr. 2006;148:590-4.
9. Mahle WT, Newburger JW, Matherne GP, et al. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the American Heart Association and American Academy of Pediatrics. Circulation. 2009;120:447-58.
10. Richmond S, Reay G, Abu HM. Routine pulse oximetry in the asymptomatic newborn. Arch Dis Child Fetal Neonatal. 2002;87:83-8.
11. Rabi Y, Yee W, Yue Chen S, Singhal N. Oxygen saturation trends immediately after birth. J Pediatr. 2006;148:590-4.
12. Jubran A. Pulse oximetry. Intensive Care Med. 2004;30:2017-20.
13. Hoke TR, Donohue PK, Bawa PK, et al. Oxygen saturation as a screening test for critical congenital heart disease: a preliminary study. Pediatr Cardiol. 2002;23:403-9.
14. Saugstad OD. Oxygen saturations immediately after birth. J Pediatr. 2006;148:569-70.
15. Tapia-Rombo CA, Rosales-Cervantes MG, Saucedo-Zavala VJ, Ballesteros-del Olmo JC, Sánchez-García L, Santos-Vera I. Peripheral oxygen saturation using pulse oximetry among healthy term newborns at Mexico City's altitude (2240 m). Gac Med Mex. 2008;144:207-12.
16. de-Wahl Granelli A, Mellander M, Sunnegardh J, Sandberg K, Östman-Smith I. Screening for duct-dependent congenital heart disease with pulse oximetry: a critical evaluation of strategies to maximize sensitivity. Acta Paediatr. 2005;94:1590-6.
17. Reich JD, Miller S, Brogdon B, et al. The use of pulse oximetry to detect congenital heart disease. J Pediatr. 2003;142:268-72.
18. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39:1890-900.
19. Sipek A, Gregor V, Sipek A Jr. Incidence of congenital heart defects in the Czech Republic-current data. Cska Gynekol. 2010;75:221-42.
20. Maroto-Monedero C, Camino-López M, Girona-Comas JM, Malo-Concepción P. Clinical practice guidelines of the Spanish Society of Cardiology in congenital heart disease in newborns. Rev Esp Cardiol. 2001;54:49-66.
21. de-Wahl Granelli A, Wennergren M, Sandberg K, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39 821 newborns. BMJ. 2009;338:a3037.
22. Arlettaz R, Bauschatz AS, Monkhoff M, Essers B, Bauersfeld U. The contribution of pulse oximetry to the early detection of congenital heart disease in newborns. Eur J Pediatr. 2006;165:94-8.
23. Koppel RI, Druschel CM, Carter T, et al. Effectiveness of pulse oximetry screening for congenital heart disease in asymptomatic newborns. Pediatrics. 2003;111:451-5.
24. Peterson C, Ailes E, Riehle-Colarusso T, et al. Late detection of critical congenital heart disease among US infants: Estimation of the potential impact of proposed universal screening using pulse oximetry FREE. JAMA Pediatr. 2014;168:361-70.
25. Liberman RF, Getz KD, Lin AE, et al. Delayed diagnosis of critical congenital heart defects: Trends and associated factors. Pediatrics. 2014;134:e373-81.
26. Niederbacher-Velásquez J, García-Niño M, Gómez-Moya G. [Reference values of arterial oxygen saturation by pulse oximetry in healthy children from Bucaramanga]. MedUNAB. 2003;6:63-9.
27. Jing ZC, Xu XQ, Badesch DB, et al. Pulmonary function testing in patients with pulmonary arterial hypertension. Respir Med. 2009;103:1136-42.
28. Pianosi PT, Johnson JN, Turchetta A, Johnson BD. Pulmonary function and ventilatory limitation to exercise in congenital heart disease. Congenit Heart Dis. 2009;4:2-11.
29. Meberg A, Brügmann-Pieper S, Due R, et al. First day of life pulse oximetry screening to detect congenital heart defects. J Pediatr. 2008;152:761-5.
30. Frank LH, Bradshaw E, Beekiman R, Mahle WT, Martin GR. Critical congenital heart disease screening using pulse oximetry. J Pediatr. 2013;162:445-53.
31. Ewer AK, Middleton LJ, Furmston AT, et al. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. Lancet. 2011;378:785-94.
32. Ewer AK, Furmton AT, Middleton LJ, et al. Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness. Health Technol Assess. 2012;16:v-xiii 1-184.