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Research Article

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Evaluation of Newborn Screening Test for Critical Congenital Heart Disease (Cchd) in a Private Medical Center in Mexico and its Implications for being at 2550 Meters above Sea Level

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Abstract

Pulse oximetry screening test (POT) has been shown to be useful for in early detection of critical congenital heart disease (CCHD). The precise oxygen saturation expected at altitudes above 1500 meters above sea level is unknown, and its usefulness in children born above this height is also unknown.

The target is to describe the results obtained from the POT in 100 apparently healthy newborns in a private hospital at 2550 meters above sea level where most of them were evaluated by one or more fetal-stage ultrasounds for the detection of CCHD among other things. Sex, resuscitation and weeks of gestation did not alter the results.

95 patients had "normal" prenatal ultrasound, of which 32% tested positive POT, and CCHD was also ruled out after clinical follow-up. It was concluded that all the patients with a positive test were healthy. We suggest possibility of modifying the POT parameters in order to avoid false positives is also discussed.

Introduction

Critical congenital heart diseases (CCHD) involve structural malformations of the heart as a result of defects in its formation during the embryogenic period; and are characterized by the presence of hypoxemia related to the anatomical defect of heart disease. Early detection is crucial for long term prognosis, since both morbidity and mortality are increased with a late diagnosis and management. The American Academy of Pediatrics (AAP) and the American Heart Association (AHA) both define CCHD as those heart pathologies present at birth that require either surgical intervention or the use of catheterization in the first year of life in order to survive [1, 2].

CCHD represent approximately one third of all malformation birth defects, with a world prevalence of 9 per 1000 live newborns. It is the second cause of death in children under 1 year of age and the third cause of death in children aged 1 to 4 years [3].

During 2018, Mexico registered 21195 fetal deaths with a death rate of 1.69 per 10,000 inhabitants, of which congenital malformations, deformities and chromosomal abnormalities corresponded to 6.1%.

Patients with CCHD are usually asymptomatic within the first 12-24 hours of life. clinical manifestations are mainly associated with the closure of the ductus arteriosus (DA).

The CCHD with obstructive defects in right heart chambers usually present with severe cyanosis due to hypoxia while left heart chambers obstructions usually manifest with a decreased systemic flow and consequently, cardiovascular collapse.

30% of apparently healthy patients who are discharged from hospital settings have a CCHD with a median age at diagnosis of 6 weeks old. Early screening that detects duct-dependent heart disease is crucial in order to begin medical treatment and improve patient's prognosis [4, 5].

Pulse oximeter screening test (POT) is an easy-to-perform, non-invasive test. It consists in assessing the oxygen saturation (SO2) by pulse oximetry in the circulation located before the DA, which reflects the fraction of saturated hemoglobin with oxygen in relation to the total blood hemoglobin located in the ascending aorta, known as "pre-ductal O2 saturation". Simultaneously, the measurement of the SO2 in the circulation located after the ductus arteriosus is measured afterwards, which reflects the SO2 in the descending aorta "post-ductal O2 saturation".

The Secretariat's Advisory Committee on Hereditary Disorders in Newborns and Children considers seven specific heart diseases as primary detection targets, which are here enlisted: Hypoplasic left heart syndrome; Pulmonary atresia; Fallot´s tetralogy; Total anomalous venous connection; transposition of the great arteries; tricuspid atresia and common arterial trunk [2]. CDC includes 5 secondary cardiovascular pathologies that can be diagnosed by POT which are: Aortic coarctation; right ventricular double outflow; ebstein anomal; interrupted aortic arch and univentricular heart.

Test results are expressed based on the algorithm endorsed by the AAP and AHA, (Figure 1). The accuracy of the test is influenced by the defined saturation objectives, gestational age at which the study was carried out, and prenatal detection of congenital heart disease.

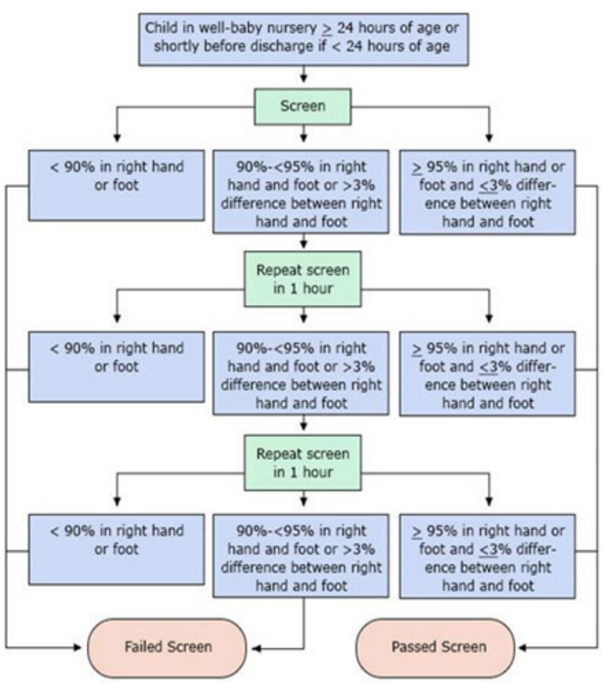


Figure 1: Pulse Oximetry Screening Test Algorithm for CCHD; American Academy of Pediatrics [7].

In 2018, a Cochrane meta-analysis analyzed 21 studies with a sample of 457,202 newborns, finding a study sensitivity of 76.3% (95% CI 69.5-82.0) and a specificity of 99.9% (95% CI 99.7-99.9) with a false positive rate of 0.14% (95% CI 0.07-0.22) and a likelihood ratio of 535.6 (95% CI 280.3-1023.4) and 0.24 (95% CI 0.18-0.31) respectively [5].

Fetal ultrasaound y also usefull in the detection of a CCHD, achieving the visualization at the end of the first trimester (13 weeks of gestation) of the four cardiac chambers in □ 90% of the cases, with a sensitivity of 97.7% and specificity of 88.9% for the detection of CCHD [8, 9].

Historical Background

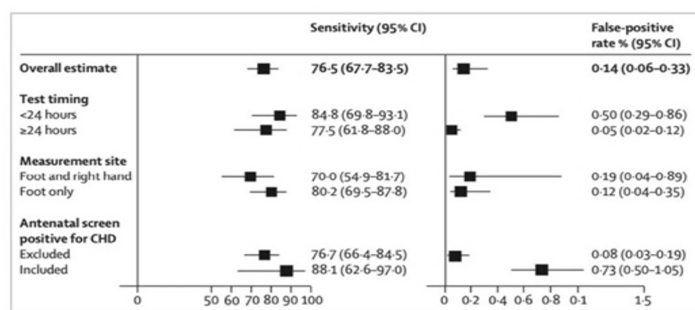
Performing the POT began in the United States of America in 2011, and the first state to legally adopt this screening test was New Jersey; and by 2014, all states except Idaho and Mississippi were conducting the POT as a part of the newborn routine [10].

In Mexico, the state of Baja California Sur was the first to approve the routine use of POT through modifications to the state health law, thanks to the legislative intervention of Deputy María Guadalupe Saldaña Cisneros, with the support of the civil association "Corazón de niño". In 2019, it was proposed to add to the article 61 of the General Health Law the mandatory use of the POT before the newborns´ home discharge, which up until today, it has not been approved by the Congress.

Pot Limitations

Despite the high detection percentages, there are multiple conditions of the newborn and its environment that can result in false positives, such as meconium aspiration syndrome, prematurity, neonatal sepsis, high altitudes, alterations in the upper airway, micrognathia, laryngomalacia, vocal cord alterations, tracheal compression, pneumothorax, pneumonia, cystic adenomatoid malformation and diaphragmatic hernia among others. It is also important to mention that nearly 75% of patients with aortic coarctation and interruption of the aortic arch are not diagnosed through POT.

It has been proved that performing a POT before 24 hours of life increases the false positive percentages up to a 50%, and this percentage decreases as low as 5% when performed after 24 hours of birth.



Graphic 1: POT Accuracy for The Detection of CCHD [11].

In 2016, Julien I.E Hoffman was one of the first researchers to question whether the method and the arterial SO2 cut-off point is applicable to newborns evaluated at high altitudes, defined as greater than 1500 meters above sea level, since in physiological conditions the partial pressure of oxygen is altered in higher altitudes, (Figure 1), as well as a lower arterial SO2 is related with greater variability and a higher percentage of false positives when evaluating healthy newborns, expecting to find an arterial SO2 lower than 95% [11].

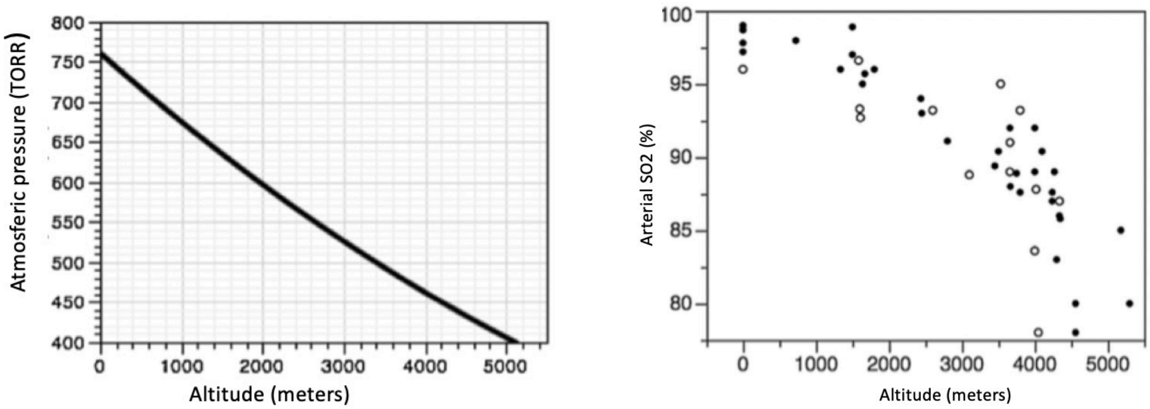


Figure 1-A: Altitude above sea level (expressed in meters) in relation with the Atmosferic pressure (TORR), being the sea level 1 ATM or 760 TORR, one TORR equals 1 mmHg. In some fields, the atmospheric pressure is measured in Kilopascals (kPa), where 1 kPa = 7.5006 TORR, therefore, one ATM equals 101.32 kPa.

B: Altitude (in meters) versus SO2 in newborns, children and adullts (Newborns = uncolored circles in graphic) [11].

Although 74% of the world's population lives at an elevation of ≤ 500 meters above sea level, we know that many cities are at a much higher altitude (Figure 2). Mexico City has an altitude that ranges from 2,250 mt to 2,750 mt above sea level.

It has been demonstrated that some gases have lesser density in high altitudes; so recent studies state the SO2 in different world countries (Table 1).

Table 1: Different Studies that Report the Normal SO2 Levels at Different Altitudes [12].

SO2 in different altitudes above sea level				
Study	**Study**	**Location**	**Altitude (mts)**	**SO2 (%) Mode[a] o medium[b]**
Levesque et al.	24 h	Worcester, MA	Sea level	97.4[b]
De-Wahl Granelli et al.	38 h	West Gotland, Suecia	Sea level	99[b]
Ravert et al.	12-14 h	Provo, UT	1370	96[a]
Thilo et al.	24-48 h	Denver, CO	1609.3	92-93[a]
Lozano et al.	5d-24 m	Bogotá, Colombia	2639.8	93[a]
Niemeyer et al.	24-48 h	Leadville, CO	3094.3	86.7-88.8 [a]
Salas et al.	24 h	La Paz, Bolivia	3649.9	88.2[a]
Gamponia et al.	0-5	El alto Bolivia	4017.8	86.9[a]

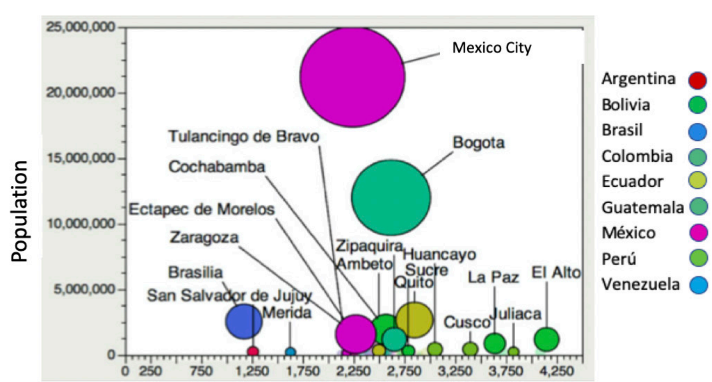


Figure 2: Countries in Central and South America with altitudes greater than 1000 mt above sea level and with over 100,000 habitants.

Based on the above, it was decided to evaluate the usefulness of the POT in a private hospital in the State of Mexico (Angeles Lomas hospital) located at 2550 m above sea level. Most of the patients were evaluated by means of fetal ultrasonography for the detection of CCHD.

Materials and Methods

100 apparently healthy newborns were consecutively included born between the months of June and July 2019, with ages of 35 to 41 weeks of gestation, indistinct sex. Those newborns below 35 weeks of gestation were excluded, as well as those with pulmonary diseases, dysmorphies and added comorbidities. Saturation sensors model LNCS® Neo and 2 Masimo model Rainbow SET® pulse oximetry monitors donated by the Masimo México company were used. The patients underwent POT between 24 and 72 hours of life, and all studies were carried out by previously trained medical personnel. Once the results were obtained, they were captured in the patient's clinical file and, according to the treating physician, pertinent actions were taken.

Results

The demographic data is reported in table 2. The studied variables weren't relevant in the positive tests.

Table 2. Demographic data

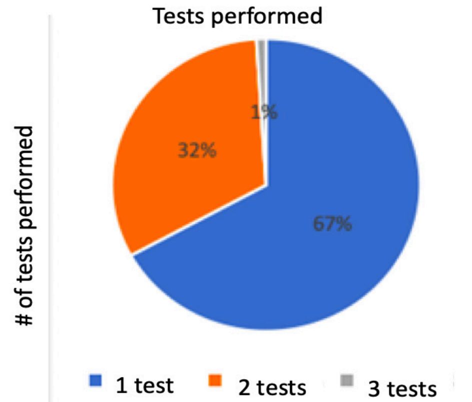
N (total) b	100	
Sex	Male 49% (51 out of 100)	
	Female 51% (49 out of 100)	
Gestational Age (GA)		(35-41 GA, mean 38.7, SD 1.21
	< 37 GA 7%	
	40 GA 28%	
	38.5 GA 13%	
	38 GA 11%	
Weight (kg)		(1.8-4.6 kg) mean 3.0, SD 0.41
# of tests performed		(1-2), mean 1.32, SD 0.49
Pregnancy control	Yes 99% (99 out of 100) No 1% (1 out of 100)	
POT results	Positive 32% (32 out of 100) Negative 68% (69 out of 100)	

The results showed that 5% of the newborns (NBs) (5/100) did not have a history of prenatal ultrasound, 3 out of 5 tested negative and 2 out of 5 tested positive, and the diagnosis of CCHD was ruled out by clinical follow-up.

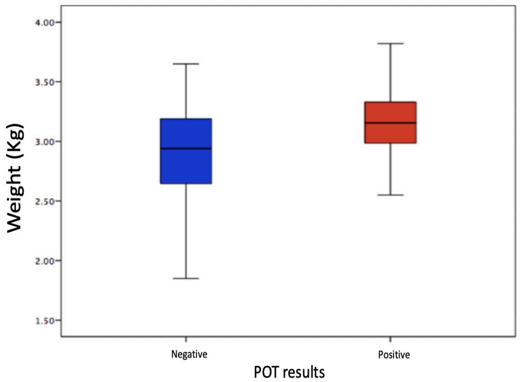
88% (88/100) of the NBs received basic neonatal resuscitation maneuvers (mean 39.1 GA, SD 1.16). The results also showed that 12% of the NBs (12/100) received some type of advanced neonatal resuscitation maneuvers (mean 39.1 GA, SD 1.54), of which 50% (6/12) were positive to the POT, ruling out CCHD in clinical follow-up.

NBs with a negative POT had a mean of 38.5 GA (95% 38.2-38.8, SD 1.24), and those who obtained a positive result had a mean of 39.1 GA (95% 38.8-39-5, SD DSI 1.03).

67% of the patients underwent a single POT, since the results were either positive or negative without a doubt. Only 3 POTs were taken from an NB who had a positive test result (39 GA) (Graph 2).



Graphic 2: Number of POT



Graphic 3: POT Results and its Relation with Birth Weight.

Discussions and Conclusions

The use of the POT in Mexico is increasing both in public and private hospitals; but nevertheless, the high prevalence of CCDH requires a routine implementation of the test be for early detection in order to reduce the morbidity and mortality rate due to CCHD.

The positive results obtained in the POT were false positives, representing 32% of the total sample. There is a huge difference with the report in other studies such as Orozco et all's in Mexico City at a height of 2,240 m above sea level, which reported a false positive rate of 4.6% [13].

At an altitude of 2550 m above sea level, there is a lower atmospheric pressure (550 mmHg) in relation to sea level (760 mmHg), causing a lower percentage of oxygen, a decrease in air density and therefore a lower SO2.

It is suspected under the physiological principle of oxygen saturation at altitudes above 1000 m above sea level, that patients require a lower SO2 cutoff point to determine whether the patient has either a positive or negative test result.

The literature reports adaptations to the current algorithms endorsed by the AAP and AHA, among which the administration of oxygen with an oxygen hood while the test is being carried out stands out, with the aim of replicating the atmospheric oxygen tension at sea level, as well as the delay in the time of completion of the test after 30 hours of life, to allow more time for the cardiopulmonary transition. Neither of them has been approved. [6].

Although the sample in this study is small, it shows that it is necessary to find an effective algorithm for altitudes above 1500 m above sea level, supported by studies that objectively demonstrate the mean oxygen saturation by oximetry at different heights. Having a positive screening test means performing an echocardiogram and further testing. This implies both an increase in the hospital bill as well as discomfort and anxiety in the parents, so it is necessary to carry out more studies with a bigger sample to be able to properly calculate the number of false positives in order to create a new algorithm or modification of the saturation parameters.

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