Neonatal screening with pulse oximetry

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CHAPTER 4

Pulse oximetry screening for critical congenital heart disease after home birth and early discharge

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ABSTRACT

Objectives: Pulse oximetry (PO) screening for critical congenital heart defects (CCHD) is increasingly implemented worldwide. Feasibility of PO screening in settings with home births and very early discharge is unknown. We assessed this with an adapted protocol in the Netherlands.

Study design: PO screening was performed in the Leiden region in hospitals and by community midwives. Measurements were taken ≥ one hour after birth and on day two or three during the midwife visit. Primary outcome was the percentage of screened infants with parental consent. The time point of screening, oxygen saturation (SpO_2), false positive (FP) screenings, CCHD and other detected pathology were registered.

Results: In a one-year period 3625 eligible infants were born. Parents of 419 infants were not approached for consent and 44 refused the screening. PO screening was performed in 3059/3090 (99%) infants with obtained consent. Median (IQR) time points of the first and second screening were 1.8 (1.3-2.8) and 37 (27-47) hours after birth. In 394 infants with screening within one hour after birth the median pre- and post-ductal SpO_2 were 99% (98-100%) and 99% (97-100%). No CCHD was detected. The FP rate was 1.0% overall (0.6% in the first hours after birth). After referral, significant non-critical cardiac and other non-cardiac pathology was found in 62% of the FP screenings.

Conclusions: PO screening for CCHD is feasible after home births and very early discharge from hospital. Important neonatal pathology was detected at an early stage, potentially increasing the safety of home births and early discharge policy.

INTRODUCTION

Pulse oximetry (PO) as a screening method for critical congenital heart defects (CCHD) in newborns has been assessed in several large studies.[1-7] A systematic review and meta-analysis of studies, which involved approximately 230,000 screened infants, reported a high specificity, moderate sensitivity and low false positive (FP) rate.[8] PO screening is acceptable to both parents and medical staff, and has been shown to be cost effective in the UK and US.[1, 9] Since 2005, routine PO screening for CCHD has been recommended in Switzerland, Poland, the USA and the UK.[7, 10-13] Worldwide, PO screening is now increasingly common, either implemented nationwide or in pilot studies, with the highest coverage in the Nordic European countries.[4, 12, 14-16] The American Academy of Pediatrics now recommends performing PO screening between 24 and 48 hours of age, as the FP is higher if the screening is performed before 24 hours of age (0.5% versus 0.05%).[8, 10] Transition after birth might lead to lower oxygen saturations (SpO_2) when screening is performed in the first hours of life. However, in several countries infants are discharged earlier in case of uncomplicated deliveries, which means that screening <24 hours is preferable. In addition, the more recent large multi-center studies were not included in the meta-analysis and these studies showed a low false positive rate while performing <24 hours after birth.[7, 8, 17] Turska *et al.,* for example, screened at an average of seven hours after birth with a FP rate of 0.026%.[7] Interestingly, there is a secondary catch of significant clinical conditions which are also detected by screening, such as pneumonia, pulmonary hypertension, or sepsis.

Although PO screening is being implemented in several parts in the world, it has not been included in the Dutch universal screening program. The perinatal health care system in the Netherlands is unique due to its high incidence of home births and early discharge after uncomplicated deliveries. In total, 33% of all low risk deliveries are supervised by a community midwife, of which 55% occur at home and 45% at a birthing facility or policlinic.[18] A community midwife leaves approximately three hours after an uncomplicated home birth. After an uncomplicated delivery in hospital, mother and infant are discharged within five hours. In both scenarios, the community midwife will visit the mother and infant at home at the second or third day of life. For this reason it would not be feasible to use the PO screening protocol that is endorsed by the American Academy of Pediatrics.[10]

In order to implement CCHD screening in the Dutch perinatal care system, the protocol would need to be adjusted to coincide with the presence of a healthcare provider, and would thus necessitate screening in the first hours after birth. In addition, all 1850 community midwives would need to be provided with, and trained in the use of a pulse oximeter for screening in home settings. An appropriate logistic system for referrals after positive screenings at home

would also need to be established. Before testing the accuracy and cost effectiveness in a large implementation trial, we assessed the feasibility of PO screening for CCHD in the Dutch perinatal care system, using an adapted protocol.[19]

METHODS

Study design and population

Between October 2013 and October 2014, we performed a prospective study in the Leiden region. The study was conducted in 14 regional community midwifery practices, two regional hospitals (Rijnland Hospital Leiderdorp and Diaconessenhuis Leiden) and one academic hospital (LUMC, Leiden University Medical Centre). In this region, approximately 4,000 infants are born annually. The LUMC has a 24/7 echocardiography service with a paediatric cardiologist on call, and is the regional referral centre for infants with congenital heart defects.

All term infants (gestational age ≥37 weeks) who were not admitted at the paediatric or neonatal department and were not monitored with PO were eligible for this study. Parents were informed of the PO screening prenatally and written informed consent was obtained prior to performing the screening. The study was approved by the Leiden Medical Ethics Committee in September 2013.

Outcome measurements

For this feasibility study, the main outcome was the percentage of infants screened out of all infants with parental consent. PO screening was considered feasible if at least 90% of the infants with parental consent could be screened.

The secondary outcomes were the median SpO_2 values in the first hours after birth, false positive (FP) rate, and CCHD and other significant pathology diagnosed after screening. Defects that are classified as CCHD were hypoplastic left heart syndromes, pulmonary atresia with intact ventricular septum, simple transposition of the great arteries, interruption of the aortic arch, total anomalous pulmonary venous return, or tricuspid atresia; as well as all infants dying or requiring medical interventions within the first 28 days of life, with coarctation of the aorta, aortic valve stenosis, pulmonary stenosis, tetralogy of Fallot, double outlet right ventricle, Ebstein's anomaly, or pulmonary atresia with ventricular septal defect. The median (IQR) time of screening after births was assessed for the first screening moment and the screening moment on day two or three. Day one was defined as the day of birth. For both moments, the median (IQR) time was calculated overall, and also separately for measurements in hospital and for measurements at home, at the policlinic or in a birthing facility. We calculated the FP rate

and assessed the diagnoses that were found as a result of these FP screening tests and needed medical intervention or further monitoring. As a high FP rate could be anticipated when screening in the first hours after birth, we calculated the median (IQR) pre- and post-ductal SpO_2 each hour during the first three hours after birth.

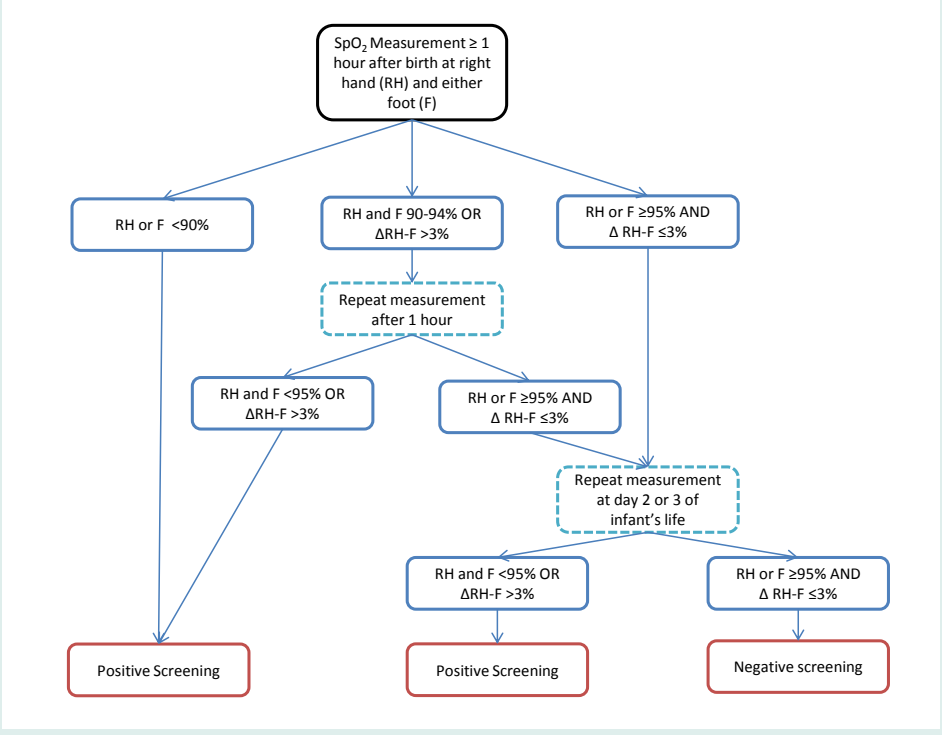
PO measurements

The protocol was adapted to the time of presence of community midwives after birth, so it would fit into the working scheme without the need for extra visits. PO measurements were obtained by a nurse or midwife at least one hour after birth and on day two or three, with the sensor placed on the right hand/wrist and either foot in a non-specified order. All screeners used a Nellcor™ N65 handheld pulse oximeter with reusable sensors and disposable adhesive sensor wraps (Covidien™, Dublin, Ireland).

PO screening was considered positive after one optimal signal quality pre- or post-ductal SpO_2 reading of <90%. The screening was also positive after two repeated measurements, with a one hour interval between them, of either <95% for both limbs or with an absolute difference of >3% between the pre- and post-ductal readings. When SpO_2 readings in the first measurement were normal, the pre- and post-ductal SpO_2 measurements were repeated on day two or three of the infant's life, either at the maternity ward or at home during the follow-up visit of the community midwife. Due to the limited available time during this visit on day two or three, no repeat measurement was performed during this visit after a reading of <95% for both limbs or an absolute difference of >3% (Figure 1).

Infants with positive PO screening were referred to the paediatric department where physical examination was performed by a paediatrician or paediatric resident and pre- and post-ductal PO was repeated. Echocardiography was performed in the LUMC if the SpO_2 readings remained abnormal and no other cause for hypoxaemia was found, or if the examination revealed cardiovascular symptoms.

Figure 1. Flowchart of measurements.



SpO_2: peripheral oxygen saturation; RH: right hand; F: either foot

False negative screenings

Since the LUMC is the regional referral and treatment centre for paediatric cardiology, all infants with false negative (FN) screenings could be detected. Also, mortality registries were consulted to assess for FN screenings. These registries were consulted up to three months after inclusion of the last infant.

Statistical analysis

Results are expressed as percentages, mean (SD) for normally distributed values, or median (IQR) and median (range) for non-normally distributed values. Data were analyzed with SPSS (IBM, version 20.0, 2012, IL, USA).

RESULTS

During the study period, 3,625 eligible infants were born, of which parents of 491 infants (14%) were not approached for consent and 44 (0.4%) were approached but refused the PO screening. Community midwives approached 97% of the parents with eligible infants, while the approach percentage was 89% in the regional hospitals and 70% in the academic hospital. Most reported reasons for not approaching for consent was high workload on the department. Parental consent was obtained for 3,090 infants, and screening was performed in 3,059/3,090 infants (99%).

Thus in 3,059/3,625 (84%) eligible infants PO screening was performed, of which 908 (30%) after home births or policlinical births supervised by a community midwife, and 2151 (70%) were born in hospital under the supervision of clinical midwives or gynaecologists.

The median (IQR) time point of the first PO screening was 1.8 (1.3-2.8) hours after birth, and 37 (27-47) hours after birth for the repeat screening on day two or three. Screening was performed earlier in infants born at home or at the policlinic (first measurement 1.3 (1.0-1.5) hours and late measurement 34 (26-47)) than in hospital (first measurement 2.0 (1.5-3.3) and late measurement 38 (28-47) hours). In 13% (394/3,059) of the infants the first screening was performed within one hour (15-60 minutes) after birth, and in these infants the median (IQR) pre-ductal SpO_2 was 99% (98-100%) and the post-ductal SpO_2 was also 99% (97-100%) (Table 1).

Table 1. SpO_2 values in the first three hours after birth.

Hours after birth	N	Pre-ductal SpO_2, %		Post-ductal SpO_2, %	
		p10	p50 (p25-p75)	p10	p50 (p25-p75)
0-1	394	97	99 (98-100)	96	99 (97-100)
1-2	969	97	99 (98-100)	96	99 (98-100)
2-3	346	96	99 (98-100)	96	99 (98-100)

10^{th} percentile and median (IQR) SpO_2 shown in percentage

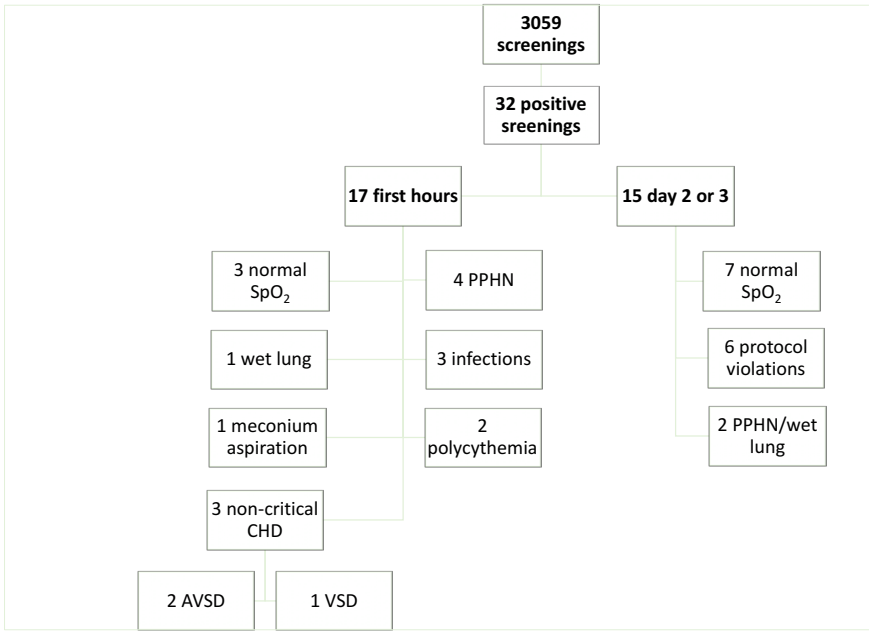
There were no FN screenings or true positive screenings during this study period. No deaths occurred in the cohort of screened infants. No CCHD was detected, nor were any cases missed by PO screening. One infant born in the academic hospital was diagnosed with a CCHD, but the parents were not approached for consent and the infant was not included in the study. The community midwife visited the infant at home for follow-up on day two and was alarmed by the colour of the baby, tachy-dyspnea, and intercostal retractions. The midwife measured a pre-ductal SpO_2 of 98% with the study PO device, but a post-ductal signal could not be detected. An interruption of the aorta was diagnosed after admission to the LUMC.

False positive screenings

PO screening was FP for CCHD in 32/3,059 infants (1.0%), of which 17 were obtained in the first screening and 15 in the second screening moment. Of these, 26/32 infants were referred to the hospital and significant other pathology was diagnosed in 16/26 (62%) infants (14/17 (82%) after the first and 2/9 (22%) after the second screening moment). Non-critical cardiac pathology was detected in 3/26 infants after referral, and in 13/26 infants other significant non-cardiac pathology was diagnosed (persistent pulmonary hypertension of the neonate, infection/sepsis, polycythaemia)(Figure 2). In 10/26 infants physical examination was normal and repeated PO after referral to the hospital showed normal values.

Referral did not take place in 6/32 infants with FP screening. This occurred only in the first half of the study period. In retrospect, the caregivers did not notice these positive screenings and all six infants were healthy at the age of >1 month.

Figure 2. Overview of positive screenings and their findings.



CHD: congenital heart defects; PPHN: persistent pulmonary hypertension of the neonate; SpO^2: oxygen saturation; AVSD: atrioventricular septal defect; VSD: ventricular septal defect.

DISCUSSION

Using an adapted protocol for PO screening, we were able to screen 99% of the infants when parental consent was obtained. There was no difference in FP between the early (≥ one hour after birth) and later (day two or three) measurement time point of the screening. Including a very early time point for screening, in the first hours after birth, did not lead to a high FP rate. Indeed, while screening in the first hours after birth is not recommended, as SpO_2 might not have reached normal values due to transition, we observed a normal range in SpO_2 even within the first 60 minutes after birth.[10] Although we did not detect a CCHD in this feasibility study, PO screening led to early detection of other potentially life-threatening pathology. Early detection of these morbidities is important, especially if infants are at home, and in this way PO screening has the potential to increase the safety of the current perinatal setting in the Netherlands and other countries with home birth or early hospital discharge after birth.
This is the first study with a CCHD screening protocol that is adapted to a setting with home births and early hospital discharge. The Netherlands is unique with 18% of deliveries occurring at home compared to other developed countries where the home birth rate is <2.5%.[18, 20-22] Other groups have assessed out-of-hospital screening,[16, 23] but the PO screening rate in our study was much higher when compared to the previous study of Lhost *et al* (99% vs 37.5%).[23] It demonstrates that the use of PO screening could be easily implemented in the daily routine of midwives attending home births; the rate of successful screening was higher after home births than in the hospitals. The prevalence of true FP screenings (no other morbidity and normal SpO_2 after referral to the hospital) was low: initially one to two per month but this declined after six months to one per two months.

The use of a very early PO screening time point was necessary to fit in the logistics. The time point of screening in our protocol was much earlier than that of previous studies, which demonstrates the feasibility of early screening (median 1.8 hour versus median ≥4 hours after birth).[7, 17] Furthermore, previous studies using early screening were performed in hospital and not at home. Very early screening is not recommended as there is a possibility that SpO_2 may not yet have reached >95% due to adaptation after birth and referral would take place unnecessary.[10] We did not observe a high FP rate, however, and we measured a median pre- and post-ductal SpO_2 of 99% already within one hour after birth. The pre-ductal SpO_2 is ≥95% in 90% of infants after vaginal delivery, which indicates that an infant should be evaluated for pathology even when this is measured within the first hour after birth.[24]

For this study, all infants with positive screening without the existence of a CCHD were classified as FP, since CCHD were defined as the screening target. Significant pathology, including pulmonary hypertension, infection, and non-critical cardiac defects was detected in

the majority of FP screenings, especially after PO screening in the first hours after birth (82%). In most of these cases it is likely that the infants benefit from early detection and treatment. It is well established that if persistent pulmonary hypertension of the neonate (PPHN) is not treated promptly there is risk for sudden deterioration, creating a need of more intensive treatment and an increased risk of an adverse outcome.[25, 26] Also, although most of the wet lungs are usually self-limiting, some of the infants may develop PPHN. For this reason, infants with wet lung should be adequately monitored, which is not possible in the home setting. Infection causes 5% of the perinatal mortality of term infants in the Netherlands.[27] Early detection and treatment of infection and sepsis before development of a full-blown disease, including shock and organ failure, considerably increases the chances of a favourable outcome.[28, 29] Taking into account the importance of the secondary early catch of other significant pathology, one might consider defining PPHN, wet lung, and infection/sepsis as targets for PO screening, and not defining these screenings FP in future studies.

In this study PO screening in the first hours after birth detected three significant septal defects, most likely due to transient right to left shunting shortly after birth. Infants with septal defects could also benefit from early diagnosis, as it would enable early treatment of heart failure and appropriate planning of surgical correction. Therefore, in addition to early detection of CCHD, early detection of other pathologies through PO screening, including non-critical cardiac pathologies, has the potential to increase the safety of early hospital discharge and home births.

Since there was limited time during the midwifery visit on day two or three, no repeat measurement was performed in case of abnormal measurements, and direct referral was recommended. Although our FP rate was no higher than that of previous studies, it is possible that omitting the repeat measurement could have led to a high true FP rate at the time of the second screening. In order to reduce this, a repeat measurement after a shorter time interval will be implemented in the protocol.

This study was carried out at a local level, but has much wider relevance. The Leiden region, is small, but densely populated. Since the Netherlands is small and has a good infrastructure, we predict that the results can be extrapolated to the rest of the country. Moreover, although the Netherlands has the highest home birth rate in the developed world, home births are also performed in other countries.[13, 20, 21] Similarly, there is an increasing tendency towards early discharge after uncomplicated deliveries in hospital. Our study shows that screening infants after home birth and early hospital discharge is both safe and feasible, and the protocol could therefore be applied for these settings in other countries.

Further research remains to be done to test if accuracy will be similar to PO screening in other countries.[1, 3, 4, 8] Previous cost effectiveness studies cannot be applied to this protocol

either, since all community midwives must be provided with a PO device to make sure that all infants receive SpO_2 measurements at both screening times.[9, 30] In order to screen all 33,000 infants that are born at home in the Netherlands annually, all community midwives in (over 1800 in the Netherlands) would need to be provided with a PO device. We are currently performing an implementation trial in the Amsterdam-Haarlem-Leiden region to assess cost-effectiveness and accuracy, aiming to screen at least 20,000 infants with our adapted screening protocol. This study (Pulse Oximetry screening Leiden-Amsterdam Region study) will then provide more insight into the need for implementation of PO screening in the Dutch healthcare system.

CONCLUSION

We have demonstrated that PO screening for CCHD using an adapted protocol is feasible in a perinatal care system with home births and early discharge. The FP rates in the first hours were comparable to other PO screening studies. Importantly, significant pathology- including infections, PPHN, and non-critical cardiac pathology- could be detected at an early stage. A larger implementation study is currently undertaken to assess the accuracy and cost-effectiveness of PO screening using the adapted protocol.

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