Neonatal screening with pulse oximetry

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SUMMARY

Pulse oximetry (PO) screening for critical congenital heart defects (CCHD) was proven to be an effective, acceptable and cost-effective screening method in hospital setting. For this reason, the screening has been implemented in many countries across the world. However, these factors are currently unknown for the Dutch perinatal care system with a high home birth rate and early discharge from hospital after uncomplicated deliveries.

The general aim of this thesis was to assess the feasibility, accuracy, acceptability and costs of PO screening for CCHD with a protocol that is adapted to the Dutch perinatal care system. We also aimed to assess the rate of detection of other pathologies by PO screening, such as infections and respiratory pathology.

Chapter 2 provides an overview of all aspects of PO screening that need to be considered before implementing it in a specific setting. In this narrative review we concluded that the screening is effective, simple, quick, reliable, cost-effective, and does not lead to extra burden for parents and caregivers. However, test accuracy is influenced by several factors. For example, early timing of screening is accompanied with an increase in false positive (FP) screenings, but has the advantage to detect pathology in an earlier stage, preventing worse outcome. Furthermore, in 35-74% of the FP screenings significant non-CCHD pathology is diagnosed. When a pre-ductal measurement is added more cases of CCHD will be identified when compared to measuring post-ductal SpO_2 only. More FP screenings are obtained at higher altitudes when using the same cut-off values as used at (near) sea level. It is feasible to screen newborns at Neonatal Intensive Care Units and newborns born out-of-hospital, but the accuracy in these settings should be further investigated. The quality of PO screening for CCHD can be optimised by training caregivers, simplifying the algorithm, and using computer-based interpretation tools.

It is important to consider all the above-mentioned aspects when choosing an optimal screening protocol for implementation in a specific setting.

In **Chapter 3** we describe our protocol for PO screening for CCHD that was adapted to the Dutch perinatal care setting, with home births and early postnatal discharge. International screening protocols were adjusted to fit the working schema of community midwives.
Two time points for pre- and post-ductal SpO_2 measurements were used: at least one hour after birth and on day two or three. If the pre- or post-ductal SpO_2 at the measurement one hour after birth is <90%, the screening test is considered positive. In case of a repeated measurement with one hour interval with pre- and post-ductal SpO_2 <95% or a difference between

pre- and post-ductal SpO_2 of >3%, the screening test is also considered positive. If the pre- or post-ductal SpO_2 is ≥ 95% and the difference between pre- and post-ductal SpO_2 is ≤ 3%, the screening test will be repeated on day two or three. The screening test on day two or three of life is considered positive if the pre- and post-ductal SpO_2 are <95% or if the difference between pre- and post-ductal SpO_2 is >3%. Newborns with positive screenings are referred for paediatric assessment and an echocardiogram is performed in case of persistent abnormal SpO_2 values. The protocol we provided might also be useful for other countries with home births or early discharge from hospital.

Chapter 4 reports the results of a pilot study of the adapted protocol described in chapter 3, performed in the Leiden region. Primary outcome in this feasibility study was the percentage of screened newborns with parental consent. We also registered the time point of screening, distribution of SpO_2, FP screenings, and detection of CCHD and other pathology. With the adapted protocol PO screening was performed in 3,059/3,090 (99%) newborns for whom parental consent was obtained. Median (IQR) time points of the first and second screening were 1.8 (1.3-2.8) and 37 (27-47) hours after birth. We observed that the median (IQR) pre- and post-ductal SpO_2 in the 394 newborns with screening within one hour after birth were 99% (98-100%) and 99% (97-100%). No CCHD was detected or missed. The FP rate was 1.0% overall (0.6% in the first hours after birth), but significant non-CCHD pathology, such as non-critical CHD, infections and respiratory pathology, was found in 62% of the FP screenings. We concluded that PO screening for CCHD with this adapted protocol is feasible after home births and early postnatal discharge from hospital. The screening detected important neonatal pathology at an early stage, which has the potential to increase the safety of home births and early discharge policy after delivery in hospital.

After demonstrating the feasibility, the objective of the study described in **Chapter 5** was to assess the accuracy of PO screening in the Dutch perinatal care setting in a larger implementation study. In order to reduce the FP rate on day two or three, a repeat measurement was added to this screening moment if the pre- and post-ductal SpO_2 were <95% and/or if there was a pre-post-ductal difference of >3%. Also, an echocardiogram was only indicated in case of persistent abnormal SpO_2 values in the absence of a non-cardiac explanation.

We analysed two cohorts: the first cohort also included newborns with a prenatal diagnosis of CCHD and with symptoms of CCHD before screening took place. In this cohort of 23,996 newborns PO screening detected CCHD with a sensitivity of 70.2% (95%CI 56.0-81.4) and specificity of 99.1% (95%CI 99.0-99.2). The prenatal detection rate of CCHD was 73%. In cohort two these prenatal detected cases as well as symptomatic CCHD were excluded. In this

second cohort 23,959 newborns were screened. The sensitivity of PO screening for CCHD in this second cohort was 50.0% (95%CI 23.7-76.3), with a specificity of 99.1% (95%CI 99.0-99.2). The screening was FP for CCHD in 221 newborns, of which 61% had other serious illnesses, including infections and respiratory pathology.

Our findings implicate that PO screening with an adapted protocol for home births and early postnatal hospital discharge detects CCHD, but the sensitivity was moderate because of a high prenatal detection in our study. The early detection of other significant pathology in newborns enables early treatment and can reduce morbidity and mortality in newborns as well.

In **Chapter 6** we presented the results of the cost-effective analysis of PO screening for CCHD in the Dutch perinatal care setting using the adapted protocol. We used the data from the implementation study as well as input from other sources. The screening costs €14,71 per newborn or €139,000 per timely detected CCHD with PO screening, in comparison with the current practice of fetal anomaly scan and postnatal physical examination. PO screening in the Dutch care setting would be cost-effective if considerable savings in lifetime treatment and, or substantial gains in Quality Adjusted Life Years would be obtained per newborn timely diagnosed with PO screening. Additional studies on treatment costs, life expectancy and quality of life of children with CCHD are needed to conclude whether addition of PO screening is cost-effective in the Netherlands.

The maternal acceptability of PO screening in home setting was described in **Chapter 7**. The acceptability of the screening was already demonstrated in hospital setting, but we assessed this for screenings performed at home by community midwives in the Leiden pilot study by sending out an online questionnaire. The questionnaire included questions based on satisfaction, general feelings and perceptions of PO screening and was responded by 77% of approached mothers.

Overall, mothers were happy with the performance of the test (95%), thought their baby was comfortable during the screening (90%) and did not feel stressed while the screening was performed (92%). Most mothers would recommend the test to others (93%) and considered the test important for all babies (93%). We therefore concluded that PO screening performed at home is acceptable to mothers.

The objective of **Chapter 8** was to assess the differences of SpO_2 and heart rate between measurements with and without system messages at PO, and if reference ranges would change with inclusion of data with system messages. We observed that system messages occurred frequently (46% of 28,477 data points) in the first 10 minutes after birth and almost all (99.9%)

were caused by a low signal quality. Mean SpO_2 with system messages was lower ($p<0.001$), while SD of SpO_2 was similar to data without system messages. With system messages included, centile charts of SpO_2 are approximately 2% lower, but not more dispersed. Mean heart rate was also lower ($p<0.001$) and more dispersed ($p<0.001$) when system messages occurred. Centile charts of heart rate are lower and have increased variability when including system messages.

We concluded that during PO in term newborns at birth system messages occurred frequently. The findings implicate that SpO_2 measurements with low signal quality are reliable for monitoring a newborn's clinical condition. However, heart rate measurements with low signal quality might underestimate a newborn's heart rate.

Finally, in **Chapter 9** we discuss the results of our studies, draw general conclusions based on these results, and also discuss perspectives for future research. Based on the studies in this thesis we have shown that PO screening for CCHD after home births and early postnatal discharge with an adapted protocol is feasible and acceptable for mothers. The sensitivity was moderate, probably due to a high prenatal detection, with a high specificity. PO screening also detects other significant neonatal pathology in an early stage, such as infections and respiratory morbidity. This can be of extra importance for newborns who are at home already on the first day of life and could decrease infant mortality and morbidity. The screening is likely to be cost-effective in the Dutch perinatal care setting.

We conclude that PO screening in the Dutch perinatal care setting complies to the Wilson and Jungner screening criteria and we recommend that PO screening should be implemented as a universal screening in the Netherlands.