New Zealand should introduce nationwide pulse oximetry screening for the detection of critical congenital heart disease and other hypoxaemic conditions in the newborn

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ABSTRACT

The mortality risk for infants with critical congenital heart disease (CCHD) unrecognised at the time of birth is high. Pulse oximetry has been utilised as a screening tool for the detection of these anomalies in the newborn as the majority will have a degree of hypoxaemia. This screening strategy has a moderate sensitivity and excellent specificity for the detection of CCHD, and a low false-positive rate. Respiratory and infective diseases are responsible for a large number of positive test results. The early recognition of these diseases can also improve health outcomes. Different approaches have been taken to introduce screening, ranging from hospital-led initiatives to mandatory state-wide policies. A study conducted in New Zealand demonstrated that sector-led screening initiatives are unlikely to result in equitable outcomes. In this midwifery-led maternity setting a nationwide pulse oximetry screening programme with adequate human and material resources should be introduced.

In the last decade, advances in antenatal screening have been made leading to improvement in the detection of critical congenital heart disease (CCHD) in the fetus.[1,2] Furthermore, new developments in the field of interventional cardiology continue to offer those affected by cardiac disease a better chance of survival and an improved quality of life.[3,4] Antenatal detection of a severe cardiac anomaly enables physicians and parents to plan and prepare for the birth and to discuss subsequent management pathways if they wish to continue with the pregnancy. Birth at a centre capable of providing cardiac intervention provides the affected infant with the best chance of survival.[5]

The mortality risk for those with severe cardiac anomalies that are unrecognised at the time of birth do, however, remain high as survival often depends on the patency of the ductus arteriosus that enables the mixing of oxygenated blood with deoxygenated blood. This vessel starts to constrict shortly after birth as a result of the rise in blood oxygen content and will generally close within 24–48 hours after birth. Time is therefore of the essence, as unrecognised cardiac disease can result in sudden cardiovascular compromise and death.

The newborn physical examination is a screening assessment that can potentially identify infants with an underlying

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cardiac anomaly. However, even in the most experienced hands the sensitivity of this examination for the detection of cardiac disease is modest.[6] In New Zealand this assessment is done on the first day after birth by the lead maternity carer, who is most often a midwife. Cardiac disease may not cause visible cyanosis, but a degree of hypoxaemia will be present in the majority of infants with severe anomalies. This has led to the logical conclusion that pulse oximeters (devices measuring oxygen saturation levels) can be utilised as a screening tool for the detection of CCHD in newborns.

The first research in this field emerged in the early 2000s[7,8] and now, nearly 20 years later, the value of pulse oximetry as a screening tool for CCHD has been firmly established. A Cochrane systematic review of 21 studies that included 457,202 participants was published in 2018.[9] Pulse oximetry was found to be highly specific (99.9%; 95% confidence interval [CI] 99.7% to 99.9%) and moderately sensitive (76.3%; 95% CI 69.5% to 82.0%) for the detection of critical cardiac disease with a very low false-positive rate (0.14%). This review showed that six out of 10,000 apparently healthy late preterm and term infants will have CCHD and that pulse oximetry screening can detect five of them. The reviewers therefore concluded that current evidence supports the introduction of routine pulse oximetry screening for CCHD.

Importantly, there is also evidence to show that pulse oximetry screening improves survival for infants with congenital cardiac disease. Abouk et al reported a 33.4% (95% CI, 10.6–50.3%) decline in cardiac-related deaths in American states with mandatory screening policies between 2007 and 2013.[10]

As a result of the mounting evidence in favour of universal pulse oximetry screening, several developed countries have formulated a consensus statement in favour of its implementation. Perhaps the most widely cited is the recommendation made by the United States Secretary of Health and Human Services in 2011 to add pulse oximetry screening to the country's Recommended Uniform Screening Panel.[11] More recently statements have been published by a European workgroup,[12] and in Canada,[13] Spain[14] and Nordic countries.[15] Research has also been conducted in developing countries to investigate the feasibility and unique challenges associated with introducing pulse oximetry screening in those settings.[16–18]

An ideal screening test has a high sensitivity, a high specificity and a low false-positive rate. In pulse oximetry screening, both the timing of screening and the site(s) used to do the test can impact on the accuracy of the test. The Cochrane review on pulse oximetry screening found greater variability in sensitivity than specificity across studies, but could not find an explanation for this heterogeneity in sensitivity.[9] No significant difference in test accuracy was found when comparing measurements obtained from the foot alone (post-ductal) with measurements taken from both the foot and the right hand (post- and pre-ductal). Nonetheless, there are many advocates for two-limb testing as there are reports in the literature of infants diagnosed with coarctation of the aorta or interrupted aortic arch based solely on a difference between pre- and post-ductal oxygen saturation.[19,20] This difference, when present, is produced by right to left shunting across the ductus arteriosus as a result of the pressure gradient between the pulmonary circulation and the aortic arch beyond the level of obstruction. This is an important consideration in the New Zealand context where fewer than 40% of the 15 infants born each year with either coarctation of the aorta or an interrupted arch are diagnosed before birth.[21]

The incidence of specific cardiac anomalies among population groups and its relationship to the sensitivity of pulse oximetry has not been investigated yet. It is well understood that cardiac anomalies produce varying degrees of hypoxaemia depending on the anatomy of the defect with, for instance, aortic arch anomalies less likely to produce hypoxaemia in the first few days after birth than transposition of the great arteries.[22] The incidence of left heart obstructive lesions is significantly higher in the New Zealand European population compared with all other ethnic groups in the country.[23] The ethnic composition of communities and its relationship with disease incidence may therefore contribute to the variation in the test's sensitivity that has been reported.

Furthermore, test accuracy may be influenced by human error.[24,25] Computer-based tools have been shown to result in improved accuracy compared with manual interpretation of screening algorithms. Oster et al reported that 81.6% of mock screening scenarios (using a two-limb strategy) were manually correctly interpreted compared with 98.3% when using a computer-based tool. This difference was most pronounced for "fail" scenarios (65.4% manual vs 96.1% computer).[25] A single-limb screening strategy was used in the New Zealand feasibility study.[26] The simplicity of performing the test on one limb was an important consideration in this setting where significant concerns were raised about the impact of the test on the workload of midwives. This factor, combined with the lack of evidence suggesting a higher sensitivity when using a two-limb strategy and in the absence of a computer-based programme that can store and interpret the test results, resulted in a decision by the Steering Committee that a single-limb strategy was most appropriate for the New Zealand setting.

Test accuracy studies have also investigated the impact of the timing of the test, with screening conducted <24 hours after birth reportedly resulting in higher false-positive rates, but with no significant impact on sensitivity or specificity.[9] We have demonstrated a relationship between the false-positive rate and not only the timing of the test, but also infant activity. Infants tested <4 hours of age were significantly more likely to have a low oxygen saturation level in the absence of pathology (2.8%) compared with 1.9% that were tested after 24 hours (p=0.005).[26] It is generally recommended that pulse oximetry should be conducted on infants that are calm and alert, but the relationship between infant activity and oxygen saturation levels has not previously been investigated. Our research showed that conducting the test while infants are unsettled or asleep will result in a significantly higher proportion of low oxygen saturation levels in the context of no underlying pathology when compared to tests conducted when infants are awake and settled. We were the first to demonstrate that breastfeeding does not result in a higher false-positive rate. This finding demonstrates that the bonding between a mother and infant does not have to be interrupted in order to perform the test. When pulse oximetry screening is conducted in the first 24 hours after birth, the number of false-positive results can be limited if the test is conducted after four hours and while infants are settled or breastfeeding.[26] This is an important finding as infant activity is a variable that can be adjusted more easily than the timing of the test, which is often dictated by the setting in which screening is undertaken. Jurisdictions characterised by early postnatal discharges have to conform to an early screening strategy.[26,27]

False-positive test results are to a large extent attributed to conditions such as respiratory or infective diseases that can also produce hypoxaemia. Early screening in particular presents an opportunity to detect and treat these conditions. The study we undertook showed that 33 of 48 (69%) infants with a positive screening result had a respiratory or infectious disease.[26] This is in keeping with others that reported that pneumonia, septicaemia and transient tachypnoea are some of the most common causes of low oxygen saturations on the first day of life.[28,29] Detecting these 'false-positives' is of benefit to the affected infants as some of these conditions are potentially life-threatening if treatment is delayed. Undertaking pulse oximetry screening before discharging newborns home can also avert the morbidity, cost and anxiety associated with later urgent transfer. During the course of our study, pulse oximetry screening prevented the discharge of several infants with congenital pneumonia and sepsis, and an infant with supraventricular tachycardia.[26] Clinicians are in agreement that no newborn with unexplained persistent hypoxaemia should be discharged home.[30] It is therefore surprising that the UK National Screening Committee recently decided against routine pulse oximetry screening in the UK due to, among other reasons, concerns about potential overdiagnosis and treatment of infants with false-positive test results.[31] A pilot study conducted in the UK found that seven out of every 1,000 infants that are screened will be healthy despite failing to reach target saturations on the first day. Contrary to this up to 80% of infants that are admitted to a neonatal unit following a positive test

have a non-cardiac condition that requires treatment.[32]

In the last decade New Zealand has made significant improvement in the antenatal detection of cardiac anomalies with >70% of fetuses with critical anomalies currently diagnosed during pregnancy.[21] The yield from pulse oximetry screening may therefore be less than in other jurisdictions with lower antenatal detection rates. However, even with high-quality antenatal screening there will always be infants born with CCHD who have not had an antenatal diagnosis either because the lesion was not detected or because of lack of access to appropriate ultrasound investigation. We have estimated that five previously undiagnosed infants with CCHD can be identified each year if pulse oximetry screening is offered in New Zealand.[21] Different approaches have been used globally to introduce screening, ranging from hospital-led initiatives to mandatory state-wide policies.[10,15,16,33] New Zealand has a midwifery-led model of maternity care and women can choose whether to give birth at home, a primary maternity unit or a hospital. Women who birth in a hospital are frequently discharged either home or to a primary unit within hours of the birth. Ensuring that pulse oximetry is offered to all, regardless of the chosen place of birth, will be an important determinant of the success of a screening programme.

Midwives' central role in the care of mothers and babies on the first day postpartum place them in the ideal position to perform pulse oximetry screening. Consultation with New Zealand midwives revealed concerns over the impact on workload and additional resource requirements.[34] The New Zealand College of Midwives and Ministry of Health are working jointly to address the current midwifery workforce shortage and its impact on maternity services. The parties recently agreed to a process for the co-design of a new funding model and contracting of community Lead Maternity Carer midwives.[35] The recognition of the value of midwives' work has also been stressed by the Midwifery Employee Representation and Advisory Services in their advocacy for pay equity for midwives.[36]

Staffing and resource constraints are likely to detract from equitable service delivery. We found significant ethnic and regional disparities in the delivery of pulse oximetry screening in a research setting. Screening rates were lowest among Māori and Pacific infants from the most deprived areas. Furthermore, only 6% of infants born at home were tested. There was also an association between the type of maternity carer and screening rates, with the lowest rates recorded for infants whose mothers failed to register with a carer.[37] The additional demands placed on midwives by a screening programme and the resource requirements therefore require careful consideration.

Reassuringly, there is no evidence to suggest that positive test results will place excessive pressure on child health services in New Zealand. Referral pathways are already in place to ensure that any infant suspected of cardiac or other diseases are assessed and treated appropriately. In our study, 48 of 16,644 (0.28%) infants that underwent pulse oximetry screening had a positive result. Eleven (23%) of those were found to have no underlying pathology. Four (36%) of these infants were admitted to a neonatal unit for investigations and/or observation. The median (range) duration of these admissions was one day (0–2). Over the course of the study 11 echocardiograms were performed, of which four may be considered unnecessary. These four scans were performed by paediatricians and neonatologists and did not impact on cardiac services.[26]

Conclusion

Pulse oximetry is a safe, easy-to-use and effective tool that can identify serious diseases in the newborn before the onset of symptoms. The research conducted in New Zealand supports the introduction of a national screening programme. Such a programme should be adequately resourced, with both equipment, consumables and funded time in order to perform the screening test. The programme should be subjected to monitoring in order to identify deficiencies and to enable quality improvement and equitable access to the test. Uniform guidelines and educational

material should be developed to guide screening practices and to raise awareness among consumers and healthcare professionals. As such, the programme should be governed by the Ministry of Health's National Screening Unit. The best outcomes will be achieved if antenatal ultrasound, the newborn physical examination and pulse oximetry are all offered as screening tests. There must be ongoing efforts to improve the quality of each of these screening tests.

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