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Screening for critical congenital heart defects with pulse oximetry – medical aspects

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Abstract

The detection of newborn babies with potentially life-threatening, critical congenital heart defects (CCHD) before they collapse or die remains an important clinical challenge. The absence of physical signs and the difficulty assessing mild cyanosis means that the newborn baby check misses up to a third of babies. Fetal anomaly ultrasound scanning identifies an increasing proportion, but this screen is operator-dependent and therefore highly variable; although some units report very high detection rates, overall most babies with CCHD are still missed.

Pulse oximetry screening (POS) is an additional test that meets the criteria for universal screening. POS increases overall detection of CCHD to over 90% and also identifies babies with non-cardiac, hypoxaemic conditions (such as congenital pneumonia, early-onset sepsis and pulmonary hypertension), which are usually included in the false positives.

There is a wealth of published data on POS, both in a research setting and more recently in routine clinical practice, and consideration of POS is becoming increasingly widespread particularly among high-income countries. But a degree of controversy still remains and debate continues regarding the most appropriate time to screen, the most effective screening pathway and screening outside the well-baby nursery. So, should all newborn babies be screened with POS, if so, when and where should screening take place, what saturations are acceptable and which conditions are we trying to identify?

This review will look at the available evidence and try to suggest the way forward for those considering its introduction into their clinical practice.

Critical congenital heart defects

The definition of CCHDs is inconsistent in the literature which makes comparisons difficult.¹ Many authors suggest that lesions which are either duct-dependent (and therefore susceptible to acute collapse or death when the ductus closes) or those causing death or requiring urgent intervention in the neonatal period, should be described as critical (see table 1).¹ The incidence of CCHDs depends on the definition used but is estimated to be between 1-1.8 per 1000 livebirths or 15–25% of all CHDs.^{1,2}

Screening for CCHD

As the majority of CCHDs are amenable to intervention, it is these that are the primary target of screening. Delay in diagnosis may lead to collapse resulting in a worse outcome and so timely diagnosis is an urgent clinical priority.^{1,2} Diagnosis before birth is the ideal solution, allowing for planned delivery and immediate, appropriate intervention but antenatal anomaly ultrasound screening, although improving, has a variable detection rate and still misses most CCHDs.¹ Physical examination screening is also fraught with difficulty as many target conditions do not have murmurs or other physical signs and often appear healthy until imminent collapse.¹ Hypoxaemia or lower oxygen saturations are a feature of the majority of CCHDs but the cyanosis is often mild and clinically undetectable even by experienced clinicians. Pulse oximetry is an accurate, simple, painless method of measuring oxygen saturations which may be used to detect those babies with CCHD and the concept of using this method of screening was first described over 15 years ago. Several recent large European studies³⁻⁶ and one study from China,⁷ have clearly demonstrated the test accuracy of pulse oximetry screening (POS). A systematic review in 2012 reported an overall sensitivity of 76.5% and a specificity of 99.9%.⁸ POS has also been shown to be cost effective⁹ and acceptable to both clinical staff and parents.¹⁰

POS has recently been adopted as national policy in a number of countries (including the USA¹¹ and the Nordic countries¹²) and many others (including the UK) are considering its introduction.

Despite this positive response to the possibility of POS, there remain a number of important issues which still generate debate.^{13,14} The precise screening pathway or algorithm used in studies varies, both in timing of screening and the nature of the saturation data resulting in a positive test. The number of test positive (and false positive) babies identified also varies significantly, raising concern about overwhelming clinical services, particularly paediatric cardiology which may have to deal with increases in echocardiograms for babies identified by screening. Other concerns include the provision of POS for babies born outside hospital and for those born at high altitude where oxygen saturations are naturally lower.

Another interesting and important finding in many studies is that babies with serious, potentially life-threatening, non-cardiac, hypoxaemic condition such as respiratory or infective disorders are also identified by POS.³⁻⁷ These babies are usually classified as false positives, but it is generally accepted that early detection of these babies, before they

become unwell, is a potential advantage and the label of false positive is perhaps a misnomer.

Timing of screening

This is perhaps the most important question arising from different POS studies. The systematic review stated that screening earlier (within 24 hours of age) resulted in a much higher false positive rate than later screening (after 24 hours) – 0.5% vs. 0.05% - a ten-fold difference.⁸ This important finding played a key role in the decision by the USA to recommend later screening.¹¹ However, it is important to understand that in many countries, mothers and babies are discharged before 24 hours and in some, an increasing proportion are born at home which makes later screening challenging.

What is also clear, following careful analysis of the data in studies employing later screening,^{3,4} is that sensitivity seems to be higher with earlier screening¹⁴ and later screening results in babies with CCHD presenting with symptoms *before* screening has taken place. In two studies, 50% of all babies with CCHD presented before screening took place^{3,4} and in one study, 20% of those babies presented with acute collapse³ - which is precisely the situation that screening aims to prevent. In addition, it is clear from the POS research studies³⁻⁷ and from POS in routine clinical practice^{15,16} that in addition to later screening resulting in a reduced number of CCHDs being identified, babies with non-cardiac conditions such as pneumonia and early-onset sepsis usually present within 24 hours and may not be identified before becoming unwell with later screening. Comparison of reports from the UK and the USA (using early and late POS respectively) clearly show the differences that timing of screening make. In the UK cohort of 25 859 babies, nine babies with CCHD were detected and 165 babies had other potentially serious conditions;¹⁵ in the USA cohort of 72 694 babies only three had CCHD and only 17 had other conditions.¹⁶ The false positive rate for the USA cohort was much lower (0.04% vs. 0.8%), however the number of screens required to detect a case of CCHD was much greater (24 231 screens vs. 2 873 screens to detect one CCHD).¹⁵ The detection of significant non-cardiac disease was similarly reduced. So, when considering the timing of POS, it is important to reflect on the available evidence taking timely diagnosis of CCHD and the detection of serious non-cardiac disorders into account rather than just focusing on the false positive rate. As up to 80% of false positives¹⁵ may have a clinically significant alternative condition, the identification of these babies is a potentially

valuable additional benefit of POS. These considerations are becoming increasingly important and were reflected in the POS guidelines recently produced by the Nordic countries which recommended early screening.¹²

Saturation results for a positive test

The majority of POS studies^{4,6,8} used saturations from only one site – the foot, which gives post-ductal saturations. However, more recently, studies^{3,5,7} have employed saturations from two sites – right hand and one foot – giving both pre- and post-ductal saturations. So rather than a single absolute saturation leading to the test result, two individual values and *also* the difference between the two, contributes to the result. Although the systematic review did not identify a significant difference in sensitivity between the two methods, this may be explained by the preponderance of single-measurement studies.⁸ Careful analysis of the raw saturation data shows that post-ductal only measurement would miss a small but significant proportion of babies that dual testing would identify.^{8,13,14} Although a relatively small number, when considering screening national populations, this becomes increasingly important.

In studies using pre- and post-ductal saturations^{3,5,7} there are also subtle differences in the parameters for test positivity. The USA algorithm^{3,11} defines test positives as <95% in both limbs and/or a difference of >3% between the two (see figure 1), whereas the UK definition is <95% in *either* limb and/or a difference of >2% (see figure 2).^{5,15} These differences are small but may result in babies with CCHD being picked up or missed in a very small number of cases.¹⁵

Further collection of raw saturation data will help clarify whether these differences are important for national screening.

A further difference between the two was the number of repeat tests (one for the UK and two for the USA). Although two repeat tests may reduce the number of false positives, it may also increase the delay in establishing a definitive diagnosis. In some cases this delay may lead to compromise.

Investigations following a positive test

In the POS research studies, all test positive babies underwent echocardiography to establish the presence or absence of CCHD. If this were rolled out in clinical practice then

the number of test positives becomes very important, as echo services may be overwhelmed. However, in routine screening it has been reported that echocardiography is unnecessary if an alternative clinical diagnosis (such as a respiratory or infective problem) can be established, reserving echo for those cases where CCHD is strongly suspected or an alternative diagnosis cannot be made.¹³⁻¹⁵ In the UK cohort less than 30% of test positive babies underwent echocardiography.¹⁵ If early screening is performed then a non-cardiac diagnosis is more common and so investigations should be ordered after careful clinical assessment focusing on the most likely condition.¹³⁻¹⁵

Screening outside the hospital

In countries such as the Netherlands, many babies are born at home or in birthing centres and in others such as the UK an increasing proportion are born at home. With homebirths the midwife usually leaves 2 or 3 hours after birth which means that for screening to take place it is required very early or deferred until the following day, potentially leading to a delay. It was a concern that very early screening in the first couple of hours would lead to an unacceptably high false positive rate as more healthy babies with transitional circulation would test positive. Interestingly, recent studies from the Netherlands¹⁷ and the UK¹⁸ have shown the feasibility of screening homebirths as early as one hour after birth without creating a clinically unacceptable number of test positives. The Dutch study algorithm utilised a repeat test on day 2 or 3 whereas the UK study employed day 1 testing only. The benefit of the additional test is as yet unclear but may be clarified with time as more babies are screened in this way.

Screening at altitude

Altitude affects the normal oxygen saturations and this will potentially lead to more false positives. This is felt to be unlikely at mild altitude but becomes more important at moderate to high altitude.¹⁴ At present there are insufficient data to recommend which saturations should be used and more studies are required. Again, a balance between sensitivity and acceptable false positive rate needs to be identified.

False negatives

POS is not a perfect test for CCHD; the overall sensitivity is 75-80%, so 20-25% of babies with CCHD will be missed by this method alone. Coarctation and interruption of the aorta are less likely to cause hypoxaemia and are the commonest defects missed,² although a proportion of these defects are detected by POS.^{2,13} Parents and clinical staff should be made aware of the limitations of the test and appropriate counselling and discharge advice should always be given.

It is important to remember that POS is additional to existing screening and not a replacement. The added value of POS means 92-95% of CCHD are detected.²

Future initiatives

As the evidence for POS becomes stronger, more countries are considering its introduction. In addition to the USA and Nordic countries, other European countries have recommended screening or are engaged in National pilot studies evaluating the feasibility of POS within the individual clinical settings. A workgroup of European and North American clinicians are developing recommendations for an evidence-based universal screening algorithm.¹⁹ As more and more babies are now being routinely screened the collection of raw saturation and outcome data are essential to the refinement of this algorithm.

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