Early Detection of Significant Congenital Heart Disease – The Contribution of Fetal Cardiac Ultrasound and Newborn Pulse Oximetry Screening

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Abstract

Fetal cardiac and newborn pulse oximetry screening has greatly facilitated the detection of cardiac abnormalities which may be serious with potentially dire neonatal consequences. The prenatal diagnosis of a serious cardiac abnormality allows the attending obstetrician to organise the much safer in-utero transfer of the fetus for delivery at a tertiary centre particularly if there is evidence of a duct dependent lesion that may require the infusion of Prostaglandin E1 to maintain duct patency pending surgical intervention. Newborn pulse oximetry alerts the paediatrician that the baby may have a significant cardiac abnormality which warrants further elucidation prior to discharge, rather than for the baby to represent unwell a few days later. Despite these advances, serious cardiac abnormalities may be missed on screening. Their detection then falls back onto the clinical acumen of the attending paediatrician/family physician to review the history, carefully elicit and evaluate the clinical signs further aided by whatever investigations that may be available at the birthing hospital frequently less resourced than the tertiary centres.

At the outset a brief synopsis is provided of the clinical findings that may point to a cardiac abnormality. That is followed by a critical review of the accuracy of prenatal and newborn pulse oximetry screening with emphasis on the lesions that may be missed. Suggestions are made as to how to improve the diagnostic accuracy.

Keywords

Congenital heart disease, Fetal/newborn, Prenatal cardiac/pulse oximetry screening

Introduction

Most women are confined away from tertiary centres. The attending paediatrician/family physician caring for the newborn infant may need to diagnose serious congenital cardiac abnormalities which if delayed may cause significant morbidity and/or mortality.

Congenital heart disease (CHD) has an incidence of about 1%[1]. Most defects are minor requiring short/long term review. Ventricular septal defects (VSD) are frequently small, muscular and close spontaneously[2]. Mild pulmonary valve stenosis tends to remain unaltered and may improve with time. Most small atrial septal defects (ASD) or patent ducti close spontaneously. However many newborn cardiac abnormalities may be serious and/or life threatening, warranting an early diagnosis and timely intervention [3]. Paediatric cardiac ultrasound and newborn pulse oximetry have improved the early detection of major CHD, but neither screening method is 100% accurate and serious abnormalities can still be missed.

Clinical Diagnosis of CHD in the Newborn

i. Murmurs

In a well acyanotic newborn, soft cardiac murmurs with little or no radiation, and associated with normal pulses, cardiac impulses and second heart sounds generally are benign and only require clinical review. They include flow murmurs, those arising from turbulence at the site of a small VSD[4], or from transient tricuspid incompetence[5]. Moderately loud or loud murmurs (i.e. with a thrill) that radiate and/or associated with forceful cardiac impulses, differential pulses, loud summated second heart sounds in the pulmonary area with or without cyanosis, and/or increasing tachypnoea and hepatomegaly suggest a significant CHD warranting early

and expert cardiac review[6]. They include obstructive lesions and/or valvular abnormalities with or without associated hypoplasia of one or more ventricles. Murmurs arising from communications between the systemic and pulmonary circulation, even if large, generally take a few days or weeks to develop[7]. So that any newborn requiring for example surgery, warrants a diagnostic echocardiogram[8]. Occasionally murmurs may be heard away from the heart, as for example over the head from a large arteriovenous fistula involving the vein of Galen[9].

ii. Tachypnoea

Tachypneoa on day one or two is generally non-cardiac in origin[10] unless caused by significant aortic runoffs beyond the heart and lungs[9], or resulting from a failing myocardium from a cardiomyopathy[11] or myocarditis[12]. Tachypnoea from substantial left to right shunts, as for example a large VSD or patent duct, takes a week or more to develop and is dependent on how rapidly the pulmonary vascular resistance (PVR) falls[7]. Tachypnoea however may also occur early if there is a left sided obstructive lesion causing pulmonary venous congestion, such as arising from a small left ventricle, mitral stenosis etc., often presenting without a murmur.

iii. Hepatomegaly

Like tachypnoea, hepatomegaly further assessed by percussing the liver span, develops with the onset of right heart failure for example from a left sided obstructive lesion or a large left to right shunt. The enlarged liver has a rounded edge compared to the sharp edge of a liver displaced by hyperexpanded lungs.

iv. Pulses

Assessing the presence and volume of the infant's pulses and checking the prenatal and postductal saturations will provide further important information (see below)[13]. Occasionally even with a tight coarctation or aortic obstruction, with a wide open duct the femoral pulse will be as good if not better than the brachial, though the post ductal saturations will be reduced[13].

v. Cyanosis

Cyanosis generally leads to the early consideration of CHD especially if there is no respiratory distress[14]. A murmur, for example from pulmonary stenosis in Fallot's tetralogy, points to CHD. At times there may be little or no murmurs, for example in transposition of the great arteries (TGA) or pulmonary atresia/intact ventricular septum. Profound or rapidly developing cyanosis suggests cyanotic CHD. It requires urgent cardiology input to avoid the consequences of hypoxia ± acidosis if the abnormality is duct dependent. If such input is unavailable, transfer to a tertiary centre on a prostaglandin E1 (PGE1) infusion to maintain duct patency will be required[15]. Occasionally however, if the duct remains wide open, even for example TGA with a reasonable sized ASD and/or VSD, the diagnosis of a clinically detectable cyanotic CHD may be delayed, especially if there is no murmur[16]. Pulse oximetry if performed, will detect desaturation (see below).

Shinebourne's hyperoxaemic test[17] helps differentiate between a respiratory and cardiac cause for cyanosis. It is especially helpful if a cardiology assessment is unavailable. The baby's pO_2 in air and subsequently in 100% oxygen is measured. Levels in high 20mmHg's and low 30s with only a slight rise is suggestive of TGA, 30s to 40s with a rise of about 10 to 20mmHg is suggestive of RV outflow obstruction or hypoplastic left heart syndrome (HLHS). High 60s reaching the high 90s and low 100s suggest common mixing such as unobstructed TAPVD or truncus arteriosus. Cyanosis from a respiratory cause results in pO_2 levels > 200mmHg when

the infant is in 100% oxygen. Needling of a peripheral artery for blood sampling may drop the pO_2 if the infant cries[17].

vi. Heart Rate

A slow heart rate in the 60s or less warrants an ECG to exclude a complete heart block usually picked up in-utero. Rates above 200bpm also warrant an ECG to diagnose a possible supraventricular tachycardia occasionally present prenatally. An irregular heart rate ± "dropped" beats generally reflect atrial ectopics which tend to disappear with time. A slow heart rate in the 70s to 90s may occur if the baby is cold or may arise from intermittent sinus bradycardia. Rarely it may be a marker for prolonged QT syndrome[18].

vii. Duct Dependent Circulations

a. Duct Dependent Systemic Circulation

A duct dependent systemic circulation[13] may confound or delay the neonatal diagnosis of CHD as the RV through the patent duct assists the systemic circulation if the left ventricle (LV) is small and/or poorly functioning, or where there is aortic obstruction such as from critical aortic valve stenosis, interrupted or hypoplastic aortic arch or a tight coarctation. A murmur for example arising from subaortic stenosis in a baby with an interrupted type B aortic arch, immediately suggests CHD, though differential pulse volumes may be absent if the duct is wide open[13]. Occasionally a loud summated second heart sound in the pulmonary area suggestive of pulmonary hypertension may be the only auscultatory sign[19].

Once the duct begins to close differential pulses may be noted[13]. However that may occur following the infant's discharge as most women in Australia leave hospital on day 2 after a vaginal birth or day 4 after a Caesarean section. Gradual duct closure may make the baby unwell, developing mild tachypnoea, poor feeding, etc. Rapid duct closure may cuase cardiogenic shock with a loss of all pulses and murmur if previously present[3]. Sepsis is commonly considered[20,21] rather than a duct dependent systemic circulation requiring urgent reopening of the duct by PGE1 infusion and circulatory support.

b. Duct Dependent Pulmonary Circulation

A large duct with a substantial left to right shunt may mask the diagnosis of a duct dependent pulmonary circulation as noted above. Rapidly progressive cyanosis may develop in such situations as the duct closes. At times if the cyanosis is mild, the diagnosis may be clinically missed, especially if there is little or no murmur as for example in unobstructed TAPVD[17].

Fetal Cardiac Ultrasound Screening

Fetal ultrasound has greatly facilitated the diagnosis of CHD in the newborn[22] being almost universal within Australia as elsewhere[23]. Indications to study the fetal heart include a family history, maternal risk factor such as diabetes, fetal factors such as an increase in nuchal thickening, presence of other malformations and/or a chromosomal or genetic abnormalities[24]. The converse also applies to search for a malformation and undertake genetic testing if CHD is found. Invasive testing remains controversial for isolated anomalous right subclavian artery or bilateral superior vena cavae particularly with the introduction of fetal cell free DNA analysis[25].

i. What the Fetal Scan Cannot Predict

Detailed fetal echocardiography in designated specialist centres generally recognizes almost all significant CHD as evidenced by our local experience[26-28] but between 15 to 30% if done as a screening service[29]. A recent meta-analysis reported a 45.1% second trimester prenatal detection rate for CHD suggesting overall improvement even for non-specialist centres[30]. Fetal imaging cannot predict following delivery, closure of the ASD which shunts right to left in-utero, or the patent duct which directs almost all the RV blood down the descending aorta with run-off to the placenta. Minor valvular abnormalities are difficult to diagnose prenatally. They become apparent postnatally, for example mild pulmonary[31] or aortic valve stenosis[32]. While most obstructive lesions including valvular stenosis result in a murmur on the first postnatal day, the murmur from mild pulmonary stenosis may be delayed until a fall in the PVR results in a gradient across the valve or pulmonary artery. VSDs may also be missed prenatally if small and not infrequently if at the perimembranous site[33].

Fetal sonographers are trained to acquire and often only do the so-called "four chamber apical view"[24] that displays variations in the size of the chambers, particularly the ventricles. Major discrepancies are obvious as seen in a hypoplastic LV or RV. Minor differences especially if the RV is larger, may point to aortic arch obstruction which may be hard to image (see below)[34]. Of greater difficulty is obtaining the "three vessel view" to determine the great vessel connections and orientations[24] such as in TGA[35] where the four chamber view may be normal as frequently there is no associated malformation. In a local study only 15.6% TGAs were diagnosed prenatally[36]. Difficulties may also be experienced in visualising the aortic arch[32,34] and/or the systemic or pulmonary venous drainage[37]. Aortic obstruction, particularly involving

the aortic isthmus and periductal area may be overshadowed by a large duct shunting right to left in-utero. The diagnosis may be suspected if the RV is enlarged[34]. There may be turbulence at the coarctation site, a smaller transverse or distal arch, or a marginally smaller LV[38]. A left superior vena cava may also be associated with aortic coarctation. Despite these clues the prenatal diagnosis of aortic obstruction remains problematic.

ii. Evolving Cardiac Abnormalities

Some cardiac abnormalities, in contrast to the majority which develop during the early embryological stage, may evolve in the latter part of the pregnancy[22]. The RV's growth may slow and become hypoplastic if there is pulmonary stenosis which occasionally progresses to pulmonary atresia[39,40]. Hypoplasia of the LV and/or the aorta and aortic arch may develop if there is stenosis of the mitral valve, aortic valve, and/or if there is a coarctation of the aorta[41]. Serial fetal ultrasound imaging has revealed that decreased flow across a vessel or a chamber may retard the growth of that particular chamber and/or vessel. A restrictive or absent ASD in the foetus also leads to reduction in the growth of the left sided chambers and vessels evolving into a HLHS[42]. Routine third trimester scans is not the norm but indicated apart from obstetric reasons, if an earlier scan is suspicious or if there is a family history of a left sided cardiac abnormality[22,43].

iii. Maternal Factors and Fetal Position

Improved training, experience and operator skill aided by advances in instrumentation have substantially increased the yield of fetal cardiac diagnoses on routine screening. Even in expert hands, imaging may be limited if the foetus is in a suboptimal position, further compounded if

the mother is obese, or there is gross hydramnios which increases the transducer to fetal heart distance. Distortion of the images may occur from previous abdominal surgery and local scarring[24,44]. If the initial scan is a routine screening without additional risk factors, there may be reluctance to repeat the scan to obtain better images, or to seek the input of a specialised centre. Once fetal cardiac gating is achieved to allow for multiple images taken at the same time in the cardiac cycle, then cardiac magnetic resonance imaging may resolve many of these issues.

In Summary, routine mid second trimester morphological scans pick up many of the serious CHD. Serious abnormalities may be missed depending on the skill of the operator, the nature of the abnormality, the position of the baby and the mother's habitus. That contrasts with the excellent results of specialised centres. Routine third trimester scans are not usually done unless there is an obstetric indication and may therefore miss important evolving cardiac abnormalities occurring late in the pregnancy.

Newborn Pulse Oximetry Screening

Pulse oximetry screening prior to the infant's discharge, compulsory in some countries[45] and increasingly introduced into Australia[46], screens for neonatal hypoxaemia and has been helpful in picking up significant cardiac abnormalities[47], with a specificity of 99%. A negative reading is defined as a saturation at 95% or above, with $\leq 3\%$ absolute difference in oxygen saturations between a preductal and postductal site[48]. Readings on day 1 tend to increase "false positives" as the desaturation may be due to causes other than CHD such as mild respiratory problems or possible infections[47,49]. Very occasionally negative results may occur even in such CHDs as TGA/VSD[15]. "False positives" are more common, reaching almost 0.14%, but that is usually

resolved by clinical assessment and/or echocardiography[46,49]. It will however suggest cardiac abnormalities such as an unobstructed TAPVD where the cyanosis is difficult to recognise clinically[16]. Abnormalities which result in a left to right shunt which increases as the PVR drops do not affect the systemic saturations and are not necessarily detected by pulse oximetry screening. While a systemic duct dependent CHD is uncommon, the lower postductal oxygen saturations compared to the preductal reading caused by the right to left shunt at duct level, may be detected by pulse oximetry screening and help for example in with the diagnosis of a tight coarctation of the aorta. Keeping the duct open by a PGE1 infusion will counter against rapid duct closure which may cause the baby's sudden collapse and possible demise[16,46]. In addition such screening may be helpful even when a murmur is present, for differential saturations suggests the need for early cardiac referral to exclude a duct dependent systemic circulation. If a cardiological review is unavailable then urgent transfer to a tertiary centre on PGE1 to keep the duct open helps maintain the systemic circulation. A previous fetal diagnosis of a duct dependent lesion warrants the much safer in-utero transfer for confinement at a tertiary centre with an established newborn intensive care unit and preferably one with a cardiac surgical centre[50]. Experience with pulse oximetry screening has however shown that it still tends to miss aortic obstructions[16,48]. Differential cyanosis may also help to distinguish between obstructed TAPVD and persistent fetal circulation with a right to left shunt at duct level[51].

In Summary, pulse oximetry screening of the newborn, best done after day 1, has a high specificity – 99%, a low false negative rate, and moderate sensitivity of 75%. From a hypothetical birth cohort of 10000, 5 out of an estimate of 6 with critical CHD will be detected while 14 will have a "false positive" result[47]. The latter may not be an immediate trigger for echocardiography but should prompt expert medical review as many may have non-critical CHD or other pathology such as respiratory illness or infection[46,47]. A British review[52] found a

sensitivity of 75% for critical lesions, 49% for all major lesions but more important 58% for critical CHD and 29% for major lesions where screening altered the postnatal management. This non-invasive relatively easily conducted screening test warrants widespread introduction into all nurseries. It remains relatively insensitive to the detection of aortic arch obstruction despite its main value in picking up duct dependent systemic circulations[16,47].

In Summary, the diagnosis of serious CHD in the newborn is suggested by the presence of a significant murmur, abnormal cardiac impulses, persistent central cyanosis not related to a respiratory cause, the development of tachypnoea and hepatomegaly, and/or differential pulse volumes or saturations. Yet physical examination after birth and at 6 to 8 weeks failed to detect up to 50% of CHD[53]. A prior fetal diagnosis followed by postnatal confirmation allows for interventions to ensure the infant's well-being even before the development of symptoms and/or signs. A further few but important cardiac abnormalities such as a duct dependent systemic circulation, may be picked up by neonatal pulse oximetry screening done prior to the infant's discharge from hospital, preferably carried out after the first postnatal day to reduce the incidence of "false positive" readings. Despite major advances fetal cardiac ultrasound screening may still miss important abnormalities which in addition to those missed by newborn oximetry screening emphasise the importance for careful clinical assessment of any newborn.

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