Non-invasive assessment of pulmonary arterial pressure in healthy neonates

J R Skinner, R J Boys, S Hunter, E N Hey

Abstract
Doppler echocardiograms were carried out on 51 healthy babies three times during the first 72 hours of life to estimate pulmonary arterial systolic pressure by measuring regurgitant tricuspid jet velocity and applying the Bernoulli equation. Tricuspid regurgitation was detected at some stage in all preterm babies and most of those born at full term. Pulmonary arterial pressure could be measured from peak regurgitant velocity in babies with pansystolic regurgitation. The incidence of pansystolic regurgitation among 34 term babies at 0–12, 13–36, and 37–72 hours of age was 22, 27, and 19%, and in 17 preterm babies (within the same age groups) was 53, 50, and 31%, respectively. Estimates of pulmonary artery pressure in the term babies were in accord with known catheter values. Pressure fell rapidly during the first day in all 51 babies. The ratio of pulmonary:systemic arterial pressure was comparable between the two groups throughout. Ductal flow patterns mirrored the fall in this ratio with age—bidirectional flow was associated with a ratio of between 0.88:1 and 1:22:1 and high velocity left to right flow with a ratio of between 0:49:1 and 0:66:1. Both these techniques are non-invasive ways of assessing neonatal pulmonary arterial pressure.

Measurement of cardiac haemodynamics in neonates has always been difficult because it has required invasive techniques. There is, therefore, a paucity of good data particularly about the haemodynamics of the right heart. By applying the modified Bernoulli equation to Doppler ultrasound measurements it is possible to estimate right heart systolic pressures non-invasively. The technique depends on tricuspid regurgitation being detected by Doppler echocardiography and has been validated extensively by simultaneous Doppler cardiac catheterisation studies both in adults and children.1-5

In neonates, clinically detectable tricuspid regurgitation is present in persistent pulmonary hypertension of the newborn and after birth asphyxia.6-8 It can present as a transient pansystolic murmur in healthy newborn infants.9

Tricuspid regurgitation can be detected by Doppler in normal healthy subjects without clinical signs, allowing quantification of right heart systolic pressure in the normal population without resorting to invasive methods.10-12 Tricuspid regurgitation detected by Doppler in the absence of clinical signs, however, may be less common in neonates than in older patients.13

The objectives of this study were:

- To establish the prevalence of tricuspid regurgitation detected by Doppler ultrasound in healthy neonates during the first three days of life.
- To estimate systolic right heart pressures from tricuspid regurgitant jet velocity and the Bernoulli equation.
- To see how changes in ductal flow patterns correlated with estimated pulmonary arterial pressure.

Subjects and methods
Serial Doppler ultrasound examinations were carried out on 34 infants born at full term (birth weight 2615–4659 g) and 17 preterm infants (28–35 weeks' gestation, 1165–2290 g). Each child was examined within 12 hours of birth and daily thereafter for three days unless discharged sooner. All were born in good condition without perinatal asphyxia and none had respiratory distress requiring oxygen. The infants born at full term were recruited antenatally at parentcraft classes, and the preterm infants were enrolled as they arrived in the nursery (provided they were not oxygen dependent after 20 minutes). All but four babies in each group were born vaginally. Parental permission was obtained in all cases and ethical approval for the study was obtained from the district ethics committee.

At the first examination normal intracardiac anatomy was confirmed by cross sectional echocardiography and pulsed wave Doppler studies. Systolic upper limb blood pressure was measured by Doppler sphygmomanometry. Patency of the arterial duct was established using continuous wave Doppler ultrasound (2–2 MHz) by recording flow velocities from the pulmonary artery. Evidence of tricuspid regurgitation was sought, and where it was found the maximal velocities were recorded.

TRICUSPID REGURGITATION AND THE BERNOUlli EQUATION
The Bernoulli equation is a measure of fluid mechanics and relates the pressure drop between two chambers to the velocity of the fluid passing between them.14 The peak velocity of blood is measured using continuous wave Doppler ultrasound which, unlike pulsed wave Doppler, can measure high velocities. The velocity is converted into a pressure drop by application of the modified Bernoulli equation: $P = 4V^2$, where $P$ is the pressure drop (mm Hg) and $V$ is the velocity of blood (metres/second).

The technique was first used clinically to assess mitral or aortic stenosis15-17, and may also
be used to measure the drop in pressure across ventricular septal defects.\(^{18}\)

In the right heart the drop in pressure from the right ventricle to the right atrium in systole can be assessed by applying the Bernoulli equation: right ventricular pressure—right atrial pressure = \(4 \times \text{tricuspid regurgitant jet velocity}^2\).

Systolic pulmonary arterial pressure is equal to right ventricular systolic pressure if there is no pulmonary stenosis. Hence systolic pulmonary arterial pressure is equal to the drop in pressure in systole between the right ventricle and the right atrium plus the right atrial pressure. In neonates shortly after birth right atrial pressure is close to zero\(^{18,21}\); in calculating pulmonary arterial systolic pressure in healthy babies in this paper we have assumed it was zero. Application of the Bernoulli equation to the tricuspid regurgitant jet velocity should therefore estimate systolic pulmonary arterial pressure.

Measurement of the maximal tricuspid regurgitant jet velocity is simple. A blind continuous wave probe (2-2 MHz) was directed towards the tricuspid valve and a Doppler wave form was obtained (fig 1), and babies with any evidence of tricuspid regurgitation were recorded as having ‘detectable tricuspid regurgitation’. In a subgroup of these babies the systolic regurgitant jet was detectable throughout the whole of systole and the maximal velocity was easily seen. These were recorded as having ‘measurable tricuspid regurgitation’, and systolic pulmonary arterial pressure was calculated for these babies. To measure maximal jet velocity accurately the Doppler probe must be in line with the direction of flow. To achieve this a range of apical, subcostal, and lower left sternal edge approaches were tried. The highest velocity recorded was interpreted as being in line with the jet; these values were usually obtained at the lower left sternal edge.

EVALUATION OF DUCTAL FLOW

Ductal flow was assessed by continuous and pulsed wave Doppler. A blind (2-2 MHz) continuous wave probe was placed at the upper left sternal edge and directed posteriorly towards the pulmonary artery. The velocities and flow pattern were recorded. The pulmonary artery and duct were visualised on cross sectional echocardiography, and with a duplex scanner the pulsed wave sample was placed at the pulmonary end of the arterial duct. Care was taken to ensure an angle of incidence of less than 20° to the direction of the arterial duct.

Results

INCIDENCE OF TRICUSPID REGURGITATION

The incidence of tricuspid regurgitation is shown in table 1. Doppler studies were positive in most babies in both groups and at some stage in all preterm babies. Detectable tricuspid regurgitation was more common among the preterm group at all ages and significantly in babies aged 37-72 hours. Measurable tricuspid regurgitation was significantly more common in the preterm group in the first 12 hours than in the term group, the proportion falling significantly with time. Neonates who had measurable tricuspid regurgitation on the third examination were re-examined 24 hours later, but measurable tricuspid regurgitation was found in only two term babies who were still under 72 hours of age. The preterm babies were all re-examined after 72 hours and none had measurable tricuspid regurgitation.

DERIVED SYSTOLIC PULMONARY ARTERIAL PRESSURES

Calculated pressures for the term and preterm groups are plotted in figure 2A and B. The values in the preterm babies are lower than those in the term babies, but they show a similar pattern of change against time. Furthermore,

\(p<0.05 \quad **p<0.02\), Fisher's exact test.

Table 1  Incidence of detectable and measurable tricuspid regurgitation in preterm and term neonates divided into three age groups

<table>
<thead>
<tr>
<th>Term infants</th>
<th>Preterm infants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-12 h (n=32)</td>
</tr>
<tr>
<td>Mean age (hours)</td>
<td>5 25 50</td>
</tr>
<tr>
<td>No (%) in whom tricuspid regurgitation detected</td>
<td>23 (72) 18 (60) 15 (56)**</td>
</tr>
<tr>
<td>No (%) in whom tricuspid regurgitation measurable</td>
<td>7 (22)** 8 (27) 5 (19) 8 (53)* 8 (50) 5 (31)</td>
</tr>
</tbody>
</table>

Figure 1  Examples of Doppler waveforms. Upper: measurable tricuspid regurgitation. The Doppler signal continues throughout the whole of systole and the maximal velocity can easily be seen (numbered 1, 2, and 3). Lower: tricuspid regurgitation detected but not measurable. The signal appears in early systole but is then lost, and the peak velocity cannot be seen. TV, tricuspid valve.
when pulmonary arterial pressure is expressed as a ratio of systemic blood pressure (fig 3) the results from the two groups are almost identical. Differences in the pulmonary: systemic arterial pressure ratios between the preterm and term groups were assessed by relating group and age to the logarithm of the ratio using multiple linear regression. There was no significant difference between the groups (p>0.8). The change with time is partly related to the fall in pulmonary arterial pressure, but it is also related to an increase in systemic blood pressure, which is most obvious in the preterm group. The systemic blood pressure measurements are shown in table 2.

**COMPARISON WITH NEONATAL CARDIAC CATHETERISATION DATA**

The best available data on pulmonary arterial pressures in neonates were obtained in 1964 by Emmanouilides et al who catheterised 51 healthy unsedated term babies. Our data show similar absolute values and similar changes with time (fig 2A). Statistical comparison was made by the same method as we used to compare the term and preterm groups—that is, the logarithm of pulmonary arterial pressure was related to group and age using multiple linear regression. Some babies in our study had serial measurements, but the study of Emmanouilides et al was entirely cross sectional. To permit valid statistical comparison between these two different types of data, one value was selected at random from each of the five babies in our study who had multiple values. The data exhibit considerable variability and this is only partially explained by the regression model. There were no significant differences between the groups overall (p>0.5) or the way in which the pressure fell with time (p>0.8).

**DUCTAL FLOW**

We studied the pattern of ductal flow using continuous and pulsed wave Doppler as described. The flow pattern obtained was compared with the ratio of pulmonary: systemic arterial pressures in those babies with both measurable tricuspid regurgitation and a patent duct. Eleven babies with measurable tricuspid regurgitation had bidirectional flow (forward in systole, backwards in diastole). The ratio of pulmonary to systemic arterial pressure in these babies was between 0.88:1 and 1:22:1. High velocity left to right flow with maximal velocity in late systole was seen in seven babies with measurable tricuspid regurgitation and their arterial pressure ratios ranged from 0.49:1 to 0.66:1. An intermediate type of flow was seen in five babies with continuous low velocity left to right flow, (lowest in systole and highest in diastole); in these the ratios ranged from 0.74:1 to 0.92:1. One baby with a ratio of 0.79:1 had a ductal wave form that varied with respiration from bidirectional to intermediate.

In summary, when derived pulmonary arterial pressure approached systemic pressure, the flow in the pulmonary artery was bidirectional, and conversely low pulmonary arterial pressures were associated with continuous retrograde high velocity flow indicating that calculated pressures do genuinely reflect pulmonary arterial pressure.

Not all babies with bidirectional flow in the pulmonary artery (indicating high pulmonary arterial pressure) had tricuspid regurgitation that was measurable on Doppler. In the term group there were 19 babies with bidirectional flow in the first 12 hours. Only seven of these (37%) had measurable tricuspid regurgitation. In the preterm group five of the seven with bidirectional flow (71%) had measurable tricuspid regurgitation, suggesting that preterm infants          have more likely to have physiological tricuspid regurgitation than term infants if they also have pulmonary hypertension.

The proportion of babies with patent ducts at each examination and the ductal flow patterns seen are shown in table 3. In the first 12 hours 19 of the 30 term babies (63%) and seven of the 16 preterm babies (44%) with patent ducts had

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**Table 2. Mean (SD) systolic upper limb blood pressure (mm Hg) in term and preterm neonates divided into three age groups**

<table>
<thead>
<tr>
<th></th>
<th>0-12 h</th>
<th>13-36 h</th>
<th>37-72 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>49±4 (9±3)**</td>
<td>56±3 (6±4)**</td>
<td>58±0 (9±3) (n=17)</td>
</tr>
<tr>
<td>Term</td>
<td>60±6 (6±3) (n=34)</td>
<td>63±0 (6±0)* (n=31)</td>
<td>71±6 (6±0)* (n=28)</td>
</tr>
</tbody>
</table>

* and ** = p<0.005, paired t test.
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Table 3  Ductal patency and flow velocity patterns among term and preterm neonates divided into three age groups

<table>
<thead>
<tr>
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<th>Preterm infants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-12h</td>
<td>13-36h</td>
</tr>
<tr>
<td></td>
<td>(n=34)</td>
<td>(n=21)</td>
</tr>
<tr>
<td>Flow velocity:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (%) bidirectional</td>
<td>19 (56)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>No (%) intermediate left to right</td>
<td>6 (18)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>No (%) high velocity left to right</td>
<td>5 (15)</td>
<td>11 (35)</td>
</tr>
<tr>
<td>No (%) with patent duct</td>
<td>30 (88)</td>
<td>15 (48)</td>
</tr>
</tbody>
</table>

Figure 3  Systolic pulmonary artery pressure expressed as a ratio of systemic blood pressure in 11 preterm neonates (21 values) (△) and 15 neonates born at term (22 values) (○).

bidirectional flow. The fact that nine of 16 preterm babies (56%) had pure left to right flow during the first 12 hours of life suggests that the pulmonary to systemic arterial pressure ratio falls faster in preterm babies during this time. After 13 hours of age pure left to right flow predominates in both groups and bidirectional flow was seen in only one term baby. At 21 hours, this was the only baby to present with a transient soft systolic heart murmur consistent with tricuspid regurgitation. The data point representing a relatively high pulmonary arterial pressure (pulmonary to systemic arterial pressure ratio 1:1:1) can be seen as an outlier in figure 3.

Discussion
In this study most healthy neonates had Doppler evidence of tricuspid regurgitation without clinical signs, and in an appreciable proportion it was possible to measure the maximal velocity. Systolic pulmonary arterial pressure could be estimated from the right ventricle to right atrial pressure drop (assuming that right atrial pressure approximated to zero). Pulmonary arterial pressure fell quickly in both the premature and the term babies, and the pulmonary to systemic arterial pressure ratio was similar in the two groups. This pattern of change with time was also mirrored by ductal flow patterns. Our finding that the pattern of ductal flow changed as the ratio of pulmonary/systemic arterial pressure changed is consistent with results of the age comparing data on ductal flow velocities with results of simultaneous cardiac catheterisation.23,24

Our observation that pulmonary arterial pressure falls as quickly in the preterm as in the term baby is in conflict with the findings from a recent study by Evans and Archer.25 These authors used a different Doppler technique to monitor circulatory changes in the newborn,26 which quantifies changes in the shape of the velocity wave form at the pulmonary valve by pulsed wave Doppler. The time to peak velocity (acceleration time) is divided by the total ejection time and this ratio is inversely related to pulmonary arterial pressure. This method may be less suitable for neonates because the positioning of the pulsed Doppler sample at the pulmonary valve is critical,27 and the ratio is affected by heart rate and myocardial function,28 and the presence of tricuspid regurgitation.29 Cooper et al found that this method was not reliable in children with ventricular septal defects if they also had pulmonary hypertension,30 and Chan et al, comparing three different Doppler methods of assessing pulmonary hypertension in adults and children, concluded that measurement of tricuspid regurgitant jet velocity was the technique of choice.31

Though the method used in this study has the advantage that it should not be affected either by heart rate or by myocardial performance, a major disadvantage is that we were only able to estimate pulmonary arterial pressure in babies with measurable tricuspid regurgitation. It is possible that babies without tricuspid regurgitation have different pressures; our evidence, however, does not support this. Our results were consistent with previous catheter studies, and ductal flow patterns showed a similar fall of pressure with time in babies with and without tricuspid regurgitation. Furthermore, if the presence of measurable tricuspid regurgitation was dependent merely on pulmonary hypertension then we would not have been able to make sequential measurements in babies as the pulmonary arterial pressure fell. Factors other than pulmonary artery pressure are obviously affecting the competence of the tricuspid valve.29

We have shown that two different Doppler techniques for estimating pulmonary arterial pressure have correlated well and that the calculated pressures were consistent with data from neonatal cardiac catheterisation. The only thing that was not done was to compare direct and indirect measurement in the same baby at the same time. Clearly this is no longer an ethical option in healthy neonates. The technique has been extensively validated at other ages and we can see no reason why the age of the subject should alter the validity of the technique. Nevertheless, this method is the subject of a continuing validating study using data from cardiac catheterisation in infants without right heart disease that will also define limits of variance and error in the technique.
We have found Doppler evidence of tricuspid regurgitation at some stage in most healthy babies during the first three days of life. The detection of tricuspid regurgitation by Doppler cannot therefore be interpreted in isolation as a sign of cardiopulmonary distress at this age. Measurement of the maximal tricuspid regurgitant jet velocity seems to be a useful way of measuring systolic pulmonary arterial pressure non-invasively in a high proportion of babies shortly after birth. The values presented in this paper show how systolic pulmonary arterial pressure changes in relation to systemic pressure over the first 72 hours. The technique may be of practical value in the management of cardiopulmonary distress, as tricuspid regurgitation is a common finding in babies with the respiratory distress syndrome. The method we have described, combined with analysis of ductal flow patterns, seems to be a promising addition to techniques of neonatal intensive care.

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