Comparison of effects of 95% and 90% oxygen saturations in respiratory distress syndrome

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Abstract

Aims—To determine if decreasing arterial blood saturation from 95% to 90% could cause vasoconstriction of the pulmonary vasculature and dilatation of a patent ductus arteriosus in preterm newborn infants with respiratory distress syndrome (RDS).

Methods—Doppler echocardiographic studies were compared at 95% and 90% pulse oxygen saturation (SpO_2) in 13 preterm infants aged 61.7 (4.3) hours with RDS and Doppler echocardiographic evidence of tricuspid regurgitation.

Results—The mean (SD) Doppler echocardiographic indices determined at 95% were heart rate (146 (3.60) beats per minute), acceleration time of the velocity wave forms of the pulmonary artery (PAAT) (51.8 (2.5) milliseconds), ratio of PAAT to right ventricular ejection time (ET) (0.26 (0.02)), diameter of the ductus arteriosus (2.6 (0.6) mm), pulmonary blood flow (0.33 (0.03) l/minute) and the left ventricular shortening fraction (SF) (0.4 (0.02)%). The ascending aorta flow velocity wave form was used for the calculation of pulmonary blood flow. The right ventricular to right atrial systolic pressure gradient calculated using the peak velocity of the tricuspid regurgitation jet was 26.7 (7.4) mm Hg.

Conclusions—A decrease from 95% to 90% SpO_2 did not have any effect on the pulmonary circulatory haemodynamics nor the ductus arteriosus.

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Very low birthweight infants (VLBW) are sensitive to oxygen toxicity and have a high incidence of retinopathy of prematurity as well as bronchopulmonary dysplasia. The management of oxygen treatment for an unstable VLBW infant with respiratory distress syndrome (RDS) can be difficult due to the lack of data and the ambiguity that exists defining adequate oxygenation.^{1,2} In a recent study³ it was shown that for VLBW infants, because of the fetal nature of their oxygen dissociation curve, an arterial partial pressure of oxygen (PaO_2) of 41 mm Hg (5.5 kPa) was adequate enough to saturate 90% of their haemoglobin at a physiological pH. But an important question must be addressed. Could the PaO_2

that results in a saturation of 90% at a physiological pH be low enough to cause vasoconstriction of the pulmonary artery vasculature, leading to an increase in pulmonary artery pressure, as well as dilatation of the ductus arteriosus?¹ This concern is based on the fact that one of the most important factors affecting pulmonary vascular resistance in the postnatal period are decreases in oxygen tension.⁴ One of the few human studies carried out in the postnatal period concerning the affect of lowering PaO_2 was in normal term newborn infants three decades ago, when it was shown that a substantial lowering of the PaO_2 during a short period of time (10-30 minutes) caused a rise in pulmonary arterial pressure.⁵ The response to acute hypoxia with increases in pulmonary artery pressure and vascular resistance is a response shared by all species in which it has been studied. The response begins within seconds and reaches a maximum within minutes.⁶

In an attempt to solve this potential problem, a Doppler echocardiographic study was planned to determine if there would be differences in cardiopulmonary haemodynamics in preterm newborn infants with respiratory distress syndrome (RDS) receiving oxygen treatment at a level that maintains arterial saturation at 90% compared with those having the level maintained at 95%. Doppler echocardiographic techniques are a valid, non-invasive, indirect way of assessing pulmonary artery pressure when tricuspid regurgitation exists.⁷

Methods

Thirteen preterm newborn infants with RDS, free of any congenital abnormalities, requiring oxygen treatment and assisted ventilation, were studied. Their gestational age was ≤ 34 weeks (mean (SD) 28.9 (0.9) weeks), with a mean birthweight 1284 (120) g and mean age at the time of study of 61.7 (4.3) hours. The gestational age was determined by menstrual history and ultrasound scan performed at 18-20 weeks of gestation and confirmed by medical examination at birth. To be included in this study, all infants had to show colour Doppler echocardiographic evidence of tricuspid regurgitation.

The infants were monitored by pre-ductal pulse oximetry and arterial blood gas measurements. Because of highly significant and rapid correlations with changes in arterial saturation, pulse oximetry has become the standard method of monitoring blood oxygenation in newborn infants.⁸ The pulse oximeter used in

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these investigations was the Ohmeda BIOX 3700 pulse oximeter (Ohmeda Louisville Co). The concentration of inspired oxygen (FIO_2) was adjusted to maintain two steady states of SpO_2 at 95% and then at 90%. The Doppler echocardiographic studies were carried out after 20 minutes at each level of saturation. The ultrasound studies were performed with a Hewlett Packard echocardiographic machine (model Sonos 1000, 770-30A) with a 7.5 MHz transducer (Hewlett-Packard Co., Palo Alto, California, USA).

Measurements of left ventricular end diastolic diameter (LVED) and left ventricular end systolic diameter (LVES) were made from M-mode echocardiograms taken from the parasternal short axis view, according to the recommendations of the American Society of Echocardiography.⁹ From these measurements, the shortening fraction (SF), an index of systolic ejection phase function, was derived as follows: $(\text{LVED}-\text{LVES})/\text{LVED}$. The peak velocity of the tricuspid regurgitation jet was obtained using continuous wave Doppler recording. The peak velocity (V) of the tricuspid regurgitation jet was used to calculate the pressure drop from the right ventricle to the right atrium (RV-RA, mm Hg) by the application of the modified Bernoulli equation $((\text{RV}-\text{RA}=4V^2))$.¹⁰ The pressure gradient obtained was considered (for the purposes of this investigation) as equivalent to the systolic right ventricular or pulmonary artery pressure. The blood flow velocity wave form through the pulmonary valve was also recorded after identification of the right ventricular outflow tract and the pulmonary valve on the high left parasternal short axis view. Pulsed Doppler was used with the sample volume placed just above the pulmonary artery valve where the best velocity envelope could be obtained. This recording permitted measurement of the acceleration time during the ejection phase (PAAT, msec) from the beginning to the peak of the flow velocity envelope, and the ejection time (ET) from the beginning to the end of the velocity wave form.

The PAAT and PAAT:ET ratio decrease in the presence of a rise in pulmonary artery pressure.¹¹ From the same high left parasternal approach, the presence of a patent ductus arteriosus was also established using the colour Doppler technique. The gain was adjusted to obtain the colour jet through the ductus with the sharpest contour. At least three measurements at the site of maximum constriction were used to determine ductal diameter. The same settings were applied for the recordings taken at the two arterial oxygen saturation levels. The echocardiographer that carried out the Doppler echocardiographic index measurements was not aware of the purpose of the study.

Pulsed Doppler flow velocity wave forms recorded above the aortic valve were used for the calculation of the pulmonary flow, applying the standard Doppler equation: stroke volume = flow velocity time integrals multiplied by $\pi(D/2)^2$ (where D is the diameter of the artery at the site of the Doppler sampling.) For this purpose, the outflow tract of the left ventricle

Table 1 Blood gas monitoring (mean (SEM) values)

SpO_2	95%	90%
PaO_2 (kPa)*	11.6 (0.7)	7.5 (0.4)
pH	7.29 (0.01)	7.28 (0.01)
pCO_2 (kPa)	5.9 (0.1)	6.0 (0.2)
FIO_2 (%)**	51.3 (5.5)	33.5 (1.8)

* $P < 0.001$.

** $P < 0.005$.

Table 2 Doppler echocardiographic indices (mean (SEM) values)

SpO_2	95%	90%
Heart rate (bpm)	146 (3.6)	145.2 (3.4)
PAAT (ms)	51.8 (2.5)	50.2 (3.3)
PAAT:ET	0.26 (0.01)	0.25 (0.01)
SF (%)	0.4 (0.02)	0.4 (0.01)
RV-RA (mm Hg)	26.7 (2.1)	27.2 (2.9)
Ductus arteriosus size (mm)	2.6 (0.3)	2.7 (0.3)
Pulmonary blood flow (l/minute)	0.33 (0.03)	0.34 (0.03)

was visualised from the apical four chamber view. Using this approach, the ultrasound beam was in line with the direction of the blood flow.

Data were expressed as mean and standard error of the mean and analysed by Student's *t* test for paired measurements. Parental informed consent was obtained in accordance with the institution's human investigation committee.

Results

Blood gas values are shown in table 1. Saturations of 95% and 90% corresponded to a mean PaO_2 of 11.6 (0.7) kPa (range 7.7-15.2) and 7.5 (0.4) kPa (range 5.7-9.3), respectively in the infants studied. Table 2 compares the Doppler echocardiographic indices at 95% and 90% saturations. There was no difference in heart rate, PAAT, PAAT:ET, SF or systolic pulmonary artery pressure. No changes were observed in the diameter of the ductus arteriosus or pulmonary blood flow at SpO_2 90% compared with 95%.

The FIO_2 required to maintain a 90% saturation was 33 (2)% compared with 51.3 (6)% for a 95% saturation. At the higher saturation there were four infants whose PaO_2 was greater than 13.3 kPa (range 13.5 to 15.2 kPa). At the lower saturation there were four infants whose PaO_2 was less than 6.6 kPa (range 5.7 to 6.5 kPa). There was no difference between the mean values of these two extreme groups of PaO_2 ($\text{PaO}_2 < 6.7$ kPa and $\text{PaO}_2 > 13.3$ kPa) in any of the Doppler echocardiographic indices studied; in the infants with the lowest PaO_2 there was no evidence of vasoconstriction of the pulmonary vasculature or vasodilatation of the ductus arteriosus.

Discussion

In this study indirect evaluation of pressures in the pulmonary circulation were based on the peak velocity of tricuspid regurgitation, the PAAT, and the ratio of PAAT over the right ventricular ET. With the application of the Bernoulli equation, the tricuspid regurgitation permitted an estimation of right heart systolic

pressure. Systolic pulmonary arterial pressure is therefore equal to the gradient in systole between right ventricle and right atrium assessed by the Bernoulli equation, plus the right atrial pressure. Pulmonary arterial pressure has been calculated by some authors by adding 5 mm Hg to the RV-RA difference when the patients were ventilated.¹² In this study each infant served as its own control, so no allowance was deemed necessary for right atrial pressure within the time scale of the echocardiographic exams. The pulmonary artery acceleration time was an additional method for evaluating pulmonary artery pressure, because shortening of the time interval occurs in the presence of pulmonary hypertension. In the present study the SaO₂ changes did not affect heart rate, pulmonary artery acceleration time, myocardial contractility or the PAAT:ET.

The fact that there was no change in apparent pulmonary systolic pressure was reassuring, as a raised pulmonary artery pressure would be expected if ductal dilatation and pulmonary arteriolar vasoconstriction occurred during the period of lower saturation. It can still be argued that the absence of change in systolic pulmonary artery pressure does not necessarily indicate a stable pulmonary vascular resistance. A fall in pulmonary vascular resistance to accommodate an increase in pulmonary artery blood flow, caused by a rise in the left to right shunting through the ductus, could indeed occur without a significant modification of systolic pulmonary pressure. However, the fact that there were no changes in ductal diameter or in the actual volume of blood flow through the lungs adds more evidence to the concept of a stable pulmonary artery resistance. These results could help achieve the optimal oxygen levels during the management of oxygen treatment for preterm infants. On the one hand, adequate tissue oxygenation must be provided at the lowest concentration of oxygen to diminish the risk of retinopathy and bronchopulmonary dysplasia; on the other hand, the concentration of oxygen should be high enough to avoid adverse cardiac and pulmonary haemodynamic changes. Short periods of hypoxia have a significant effect on the pulmonary vasculature,^{4,5} but the present

study shows that the level of PaO₂ which provides an arterial oxygen saturation of 90% does not result in an increase in pulmonary artery pressure or ductal vasodilatation. The use of SpO₂ in the 90% range, should it be considered safe during oxygen monitoring, could possibly decrease the incidence of retinal vascular injury and other forms of oxygen toxicity in preterm infants. Moreover, due to the shape of the HbO₂ dissociation curve, the higher FIO₂ values required to maintain an SaO₂ of 95% cause a very significant increase in PaO₂ for an arterial O₂ content which is not much different from that which occurs at an SaO₂ of 90%.

The findings in this study were observed over a short period of time and further investigation may be necessary to evaluate the effects of lower saturations over a more prolonged period.

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