Prime oxygen concentration has no effect on placental vascular resistance for fetal cardiac bypass

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Our laboratory has been investigating fetal bypass for more than a decade because of the possibility that fetal cardiac interventions may prevent the development of certain congenital heart lesions. In many of our studies and much of the past experimental work, the placenta has served as the sole source of oxygenation for fetal bypass because of the long-standing prevailing hypothesis that high oxygen tension (P_{O_2}) causes an increase in placental vascular resistance.^{1,2} However, the effect of prime P_{O_2} concentration on placental vascular resistance and umbilical blood flow in the setting of fetal bypass has not been reported in the literature. Knowledge of the effect of prime P_{O_2} concentration on placental vasculature is required to determine whether unique circuitry is necessary for fetal cardiac bypass. We have found that elevated P_{O_2} concentration of the prime does not have an acute or long-term deleterious effect on placental vascular resistance, umbilical blood flow, or fetal metabolism. These findings suggest that manipulation of the prime P_{O_2} to match fetal P_{O_2} concentrations is not necessary and further supports the potential efficacy of using modern clinical tools used in neonatal practice with fetal bypass.

CLINICAL SUMMARY

All animals received humane care in compliance with the *Guide for the Care and Use of Laboratory Animals* (National Institutes of Health publication No. 85-23; revised 1996). By using standard fetal bypass methods that others and we have previously described,^{3,4} we examined the effect of prime P_{O_2} on the fetal blood lactate and hemodynamic variables on 9 fetal sheep with a mean gestational age of 116 days (term, ~148 days). The placenta served as the sole source of oxygen. The prime P_{O_2} was manipulated with nitrogen to create a range of prime P_{O_2} values, ranging from values corresponding to normal fetal to neonatal environment (arterial oxygen

FIGURE 1. There is not a deleterious effect of prime P_{O_2} concentration on umbilical blood flow and umbilical vascular resistance at 2 minutes after initiation of bypass. There was no correlation between umbilical blood flow and prime P_{O_2} ($R^2 = 0.115$) (A) or between umbilical vascular resistance and prime P_{O_2} ($R^2 = 0.175$) (B). CPB, Cardiopulmonary bypass; P_{O_2} , oxygen tension.

tension, 20-120 mm Hg). Other prime values remained consistent with previously described values.³ All animals underwent 30 minutes of bypass with 90 minutes of off-pump reperfusion. A 4- to 6-mm Doppler flow probe (Transonic Systems, Ithaca, NY) placed on the common umbilical artery measured umbilical blood flow. Placental vascular resistance was calculated as reported previously.⁴ Fetal arterial, prime P_{O_2} , and lactate values were measured with an i-STAT clinical analyzer (i-STAT Corp, Windsor, NJ).

We examined the immediate effect of prime P_{O_2} on umbilical blood flow and umbilical vascular resistance at 2 minutes after initiation of bypass (Figure 1). There was no correlation between umbilical blood flow ($R^2 = 0.115$) and umbilical vascular resistance ($R^2 = 0.175$) according to prime P_{O_2} values. We next evaluated umbilical blood flow, umbilical vascular resistance, and lactate values at the conclusion of 30 minutes of bypass and again found no correlation among umbilical blood flow ($R^2 = 0.012$), umbilical vascular resistance ($R^2 = 0.101$), and serum lactate

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Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication Sept 10, 2013; revisions received Oct 27, 2013; accepted for publication Nov 11, 2013; available ahead of print Dec 27, 2013.

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J Thorac Cardiovasc Surg 2014;147:1107-8

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2013.11.023>

FIGURE 2. There was no correlation between prime Po₂ concentration and umbilical blood flow, umbilical vascular resistance, or fetal lactate at 30 minutes after the initiation of cardiopulmonary or at 90 minutes post-bypass. CPB, Cardiopulmonary bypass; Po₂, oxygen tension.

($R^2 = 0.129$) related to prime oxygen values (Figure 2). Last, we evaluated the long-term effect of prime oxygen on the placental vasculature and fetal lactate at 90 minutes post-bypass and found no correlation among umbilical blood flow ($R^2 = 0.089$), umbilical vascular resistance ($R^2 = 0.122$), and serum lactate ($R^2 = 0.319$) related to prime Po₂ values (Figure 2), but fetal lactate was trending toward an improved value for the animals that had a higher prime Po₂.

DISCUSSION

Our findings indicated that elevated prime Po₂ concentration does not have a deleterious effect on placental vascular resistance, umbilical blood flow, or fetal metabolism. Manipulating the prime oxygen to match fetal oxygen concentration as a therapeutic modality before fetal bypass seems unnecessary, contrary to what was anticipated on the basis of prior obstetrical studies.^{1,2} Furthermore our data suggest that a moderate prime Po₂ (50-80 mm Hg) may be beneficial. Continued research has shown that fetal bypass with ultra-filtration and the ability to modify Po₂, carbon dioxide, pH, and lactate levels can improve fetal hemodynamic parameters during and after bypass.⁵

A minimal circuit cannot ensure that the placenta and other fetal organs receive oxygenated blood during bypass in circumstances in which the placenta itself may be compromised, such as fetal hydrops, which is a real possibility in the clinical setting.

CONCLUSIONS

These findings suggest that experimental fetal bypass and cardiac surgery may be feasible with standard clinical tools currently used in neonatal practice.

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