Fetal Endoscopic ('Fetendo') Surgery: The Relationship Between Insufflating Pressure and the Fetoplacental Circulation

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• Application of video-endoscopic surgery to the gravid uterus provides a new treatment option for the fetus with a correctable congenital anomaly. "Fetendo" surgery requires temporary enlargement of the uterine cavity to create a working space. Volume expansion of the amniotic space raises intrauterine pressure, which could increase placental vascular resistance and thereby reduce placental blood flow. To test this hypothesis, the authors developed a fetal sheep model to examine the relationship between insufflating pressure and flow in the placental circulation. Fetoplacental blood flow was measured via ultrasonic flow probes placed around the fetal common umbilical artery and the maternal uterine artery in five anesthetized 120-day-gestation ewes. Invasive feto-maternal monitoring permitted synchronous measurement of fetal mean arterial pressure, fetal central venous pressure, maternal mean arterial pressure, amniotic pressure, and fetal oxygen saturation, with calculated values for fetal and maternal placental vascular resistance. Amniotic pressure was raised from 10 mm Hg to 40 mm Hg in 5-mm Hg increments by a combination of saline amnioinfusion and external uterine compression. At amniotic pressures of 20 mm Hg or less, placental blood flow was preserved; however, elevation of amniotic pressure above 20 mm Hg resulted in a significant decrease in placental flow, with concomitant fetal hypoxia. The authors conclude that the relationship between intrauterine pressure, flow in the placental circulation, and fetal oxygen delivery must be considered when selecting intrauterine insufflation pressures for hysteroscopic intervention.

INDEX WORDS: Fetal surgery, video-endoscopy, amnioinfusion, amniotic pressure, placental blood flow.

THE OPTION of in utero surgical therapy now exists for a number of life-threatening congenital fetal defects, including congenital diaphragmatic hernia (CDH),[1] congenital cystic lung disease,[2] obstructive uropathy,[3] and sacrococcygeal teratoma (SCT).[4] Although fetal surgery has had many refinements since its inception, postoperative preterm labor—related to the hysterotomy necessary for fetal exposure—remains a persistent problem.[5] One potential solution to postoperative preterm labour is to eliminate the need for a hysterotomy by adapting currently available, minimally invasive surgical techniques to the gravid uterus to achieve fetal endohysteroscopic or "fetendoscopic" intervention.[6,7]

Just as abdominal cavity insufflation with carbon dioxide is a primary requirement for laparoscopic surgical procedures, volume expansion of the uterus is necessary to create a "working space" for fetendoscopic intervention. Increasing the volume of the amniotic space raises intrauterine pressure, which may have adverse hemodynamic effects on the fetus and the placental circulation.[8] This study examines the relationship between intrauterine pressure and fetoplacental circulation in a fetal sheep model.

MATERIALS AND METHODS

Five time-mated ewes (Torrel Farms, Ukiah, CA) underwent laparotomy under halothane anesthesia at 120 to 130 days' gestation (full term, 145 days). The uterus was exposed, "baseline" intrauterine pressure was measured with a transuterine catheter, and a hysterotomy was performed, exposing the left fetal flank. Through a left retroperitoneal approach, the fetal aortic trifurcation (into right and left common iliac arteries and the common umbilical artery) was identified, and the common umbilical artery was encircled with a 6-mm ultrasonic flow probe (Transonic Systems Inc, Ithaca, NY) to permit measurement of total umbilical flow. Through a left hind limb vascular cutdown, polyvinyl catheters (internal diameter, 0.76 mm) were advanced into the descending aorta and vena cava for arterial and central venous pressure monitoring and arterial blood gas sampling. The fetal head was delivered through a second hysterotomy, and a specially calibrated pulse oximetry sensor (Nellcor Inc, Pleasanton, CA) was bonded to the shaved skin surface between the mandibular rami with liquid adhesive and elastic wrapping. Two amniotic catheters (an 8F feeding tube for uterine infusion, and a 1.3-mm [internal diameter] polyvinyl catheter for amniotic pressure transduction) were placed, and after exteriorization of all catheters and cables, both hysterotomies were closed.

Placental blood flow from the maternal side was measured via a 4-mm flow probe placed around the uterine artery near its origin from the internal iliac artery, on the side of the gravid uterine horn. Maternal blood pressure was measured via a 1.3-mm polyvinyl hind limb arterial catheter. All fetal and maternal catheters were connected to calibrated-strain gauge transducers. A schematic summary of the surgical preparation appears in Fig 1.

The following variables were recorded synchronously and continuously via an on-line strip chart recorder (Astro-Med Instruments Inc, Minneapolis, MN): fetal mean arterial (fMAP) and central venous (fCVP) pressures, maternal mean arterial pressure (mMAP), amniotic pressure (P_{amn}), total umbilical artery (Q_{umb}) and uterine artery ($Q_{uterine}$) blood flow, and fetal oxygen saturation (O_{2sat}). Fetal arterial pressures were corrected for elevations in amniotic pressure for the purpose of data analysis. Using the above

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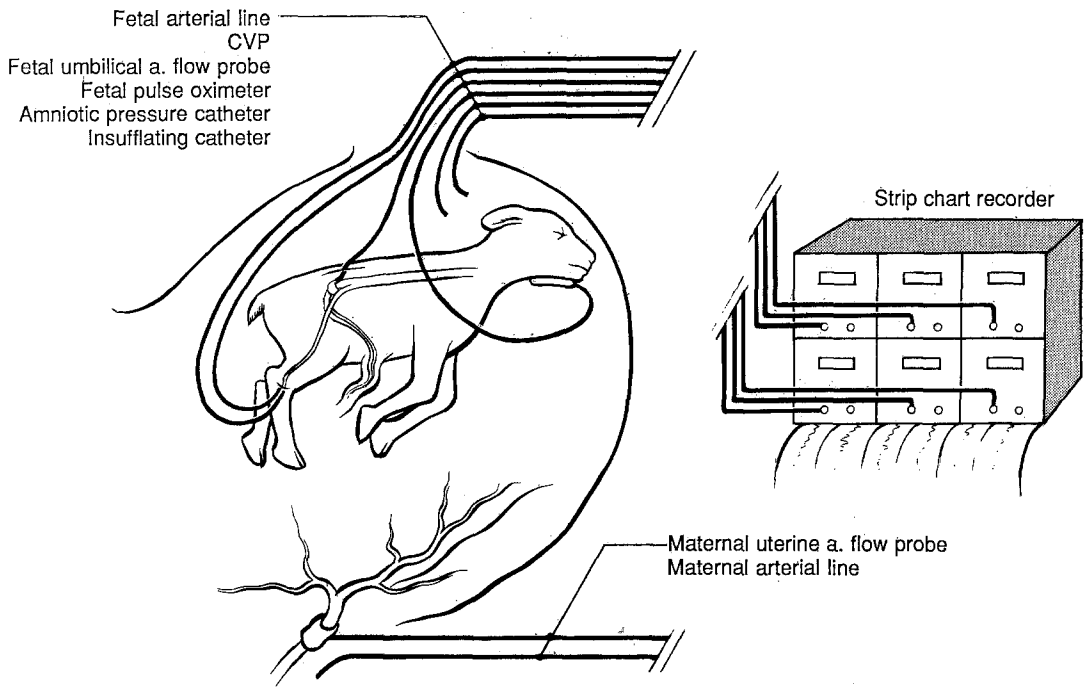

Fig 1. Experimental model for the study of the relationship between intrauterine pressure and blood flow in the fetoplacental circulation.

variables, placental vascular resistance (PVR) was calculated on both the fetal and maternal sides of the placenta as follows: Fetal PVR (mm Hg · min · kg · mL^{-1}) = $fMAP/Q_{umb}$; Maternal PVR (mm Hg · min · mL^{-1}) = $mMAP/Q_{uterine}$.

Intrauterine pressure was increased to 40 mm Hg in 5-mm Hg increments by a combination of volume expansion with warm saline and external uterine compression. Amniotic pressure was maintained at each measuring point for 5 minutes to ensure flow and pressure stabilization. To assess the effects of sustained amniotic pressure elevation on placental blood flow and fetal hemodynamics, amniotic pressure was maintained at 20 mm Hg for 30 minutes.

Data were expressed as mean values ± one standard deviation, and were analyzed using single-factor analysis of variance (ANOVA).

RESULTS

Baseline amniotic pressure measured 10 ± 2 mm Hg. Instillation of 1,000 mL of saline raised amniotic pressure to 13 ± 2 mm Hg. Subsequent elevations in amniotic pressure were achieved by manual external compression. At amniotic pressures less than 20 mm Hg, flow on both the fetal and maternal sides of the placenta remained unchanged; however, at amniotic pressures above 20 mm Hg, there was a pronounced reduction in total umbilical artery and maternal uterine artery flow, coincident with prompt fetal oxygen desaturation (Fig 2). These changes were immediately reversed by returning to the baseline amniotic pressure. Despite changes in placental blood flow associated with amniotic pressure elevation, both fetus and mother demonstrated hemodynamic stability over the range of amniotic pressures studied. The calculated values of fetal and maternal PVR are shown in Fig 3.

Sustained elevation of amniotic pressure at 20 mm Hg over a 30-minute period did not cause a significant change in fetal or maternal hemodynamics or PVR, nor did it significantly alter fetal oxygen saturation.

DISCUSSION

This study illustrates the relationship between intrauterine pressure and PVR, as estimated from

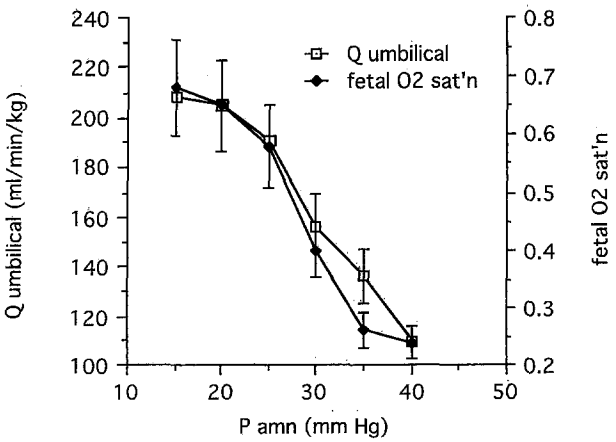

Fig 2. The relationship between amniotic pressure (P amn), total fetal umbilical artery flow (Q umbilical) and fetal oxygen saturation (O_2 sat'n). This relationship is statistically significant at amniotic pressures greater than 20 mm Hg (single-factor ANOVA, $P < .05$).

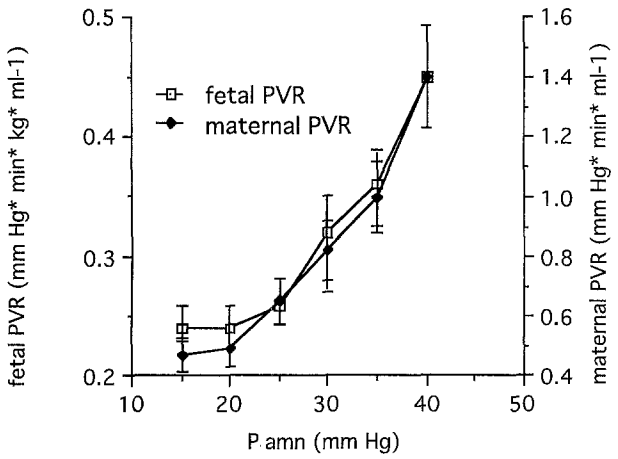

Fig 3. The relationship between amniotic pressure (P amn) and maternal and fetal placental vascular resistance (PVR). This relationship is statistically significant at amniotic pressures greater than 20 mm Hg (single-factor ANOVA, $P < .05$).

blood flow measurements taken from the fetal (common umbilical artery) and maternal (uterine artery) sides of the placenta. This pressure/flow relationship has important implications for minimally invasive fetal surgery, because volume expansion (and hence, pressure elevation) of the amniotic cavity is necessary to create a "working space" for intrauterine instrumentation with videoscopic equipment. In this study, we found that increased amniotic pressure, above 20 mm Hg, caused an acute elevation in feto-maternal PVR, resulting in fetal hypoxia. In contrast, amniotic pressures of less than 20 mm Hg did not significantly alter PVR or fetal oxygen saturation. In an attempt to simulate a clinical "insufflation" scenario, we maintained intrauterine pressure at 20 mm Hg (a level deemed to be safe over a 5-minute study period) for 30 minutes, and found that this did not significantly alter feto-maternal hemodynamics, PVR, or fetal oxygen saturation.

An important consideration in interpreting the relevance of these data to human hysteroscopic intervention is uterine wall compliance. Under deep halothane anesthesia, the highly compliant sheep uterus has an incremental amniotic pressure elevation of only 3 mm Hg in response to 1,000 cm^3 of volume expansion. The amniotic working space generated by volume expansion to a "safe" level of amniotic pressure should vary in direct relation to uterine wall compliance. Similar studies performed on the halothane-anesthetized gravid rhesus monkey showed an increase in amniotic pressure, from a baseline of 10 mm Hg to 20 mm Hg in response to a gradual amnioinfusion with 500 mL of fluid (unpublished data). Anecdotal information regarding the compliance of the gravid human uterus can be derived from case reports describing saline amnioinfusion in the treatment of repetitive variable fetal decelerations. In one report,[8] intrauterine pressure increased from a baseline of 10 mm Hg to 20 mm Hg after gradual infusion of 3,300 mL of warm sterile saline. Infusion of an additional 1,000 mL of saline increased the intrauterine pressure to 50 mm Hg, and the persistent bradycardia developed in the fetus, which was relieved by reducing the amniotic pressure to 15 to 20 mm Hg by fluid withdrawal.

Another important safety issue not assessed by this study is the ability of the gravid uterus to tolerate first an amnioinfusion (necessary for creation of a hysteroscopic working space) and then amniocentesis to restore the uterus to its preintervention state. This acute reversible "polyhydramnios" could contribute to postoperative preterm labour, and in addition the amniochorionic shearing forces resulting from acute uterine volume expansion and contraction could potentiate a postoperative amniotic fluid leak or placental abruption.[9] Preliminary observations in a preterm-labor rhesus monkey model suggest that postoperative labor is likely to be of greater magnitude if the uterus is first subjected to acute amniotic volume expansion before hysterotomy (unpublished data).

We have chosen to use fluid rather than gas as the insufflating medium in our recent experimental models of Fetendo surgery. In our experience, amniotic fluid permits satisfactory hysteroscopic visualization provided that the fluid is continuously exchanged with fresh saline. By avoiding gas insufflation within the uterus, we maintain the fetus in a physiological fluid environment and prevent the potential fatal complication of air embolism within the placental circulation. Carbon dioxide (CO_2), the primary gas used to create pneumoperitoneum for laparoscopic surgery, causes respiratory acidosis in humans from both impaired ventilation and transperitoneal gas absorption.[10] A recent study performed in fetal lambs showed that intrauterine CO_2 insufflation at pressures equal to the resting amniotic pressure causes severe fetal hypercapnea and acidosis.[11] By avoiding intrauterine CO_2 insufflation, we prevent the potentially deleterious fetal systemic and placental vascular resistance effects that might result from local CO_2 absorption.

Fetendo surgery will likely play an important role in the treatment of fetuses with life-threatening congenital anomalies especially if it reduces the postoperative fetal and maternal morbidity associated with preterm labor. Recognition of the limitations imposed by basic fetoplacental physiology on

the application of new video-endoscopic technology to the gravid uterus will assist in the development of safe, new, minimally invasive in utero techniques. As demonstrated by this study, the relationship between intrauterine pressure, flow in the placental circulation, and fetal oxygen delivery must be considered when selecting intrauterine insufflation pressures for hysteroscopic intervention.

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