Anesthesiology
51:36–40, 1979

Dopamine Treatment of Spinal Hypotension Decreases Uterine Blood Flow in the Pregnant Ewe

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In seven pregnant ewes, 3–5 min of hypotension resulting from spinal anesthesia decreased uterine blood flow 17 per cent. Dopamine, in doses sufficient to maintain blood pressure at control values (20–40 μg/kg/min) for 3–5 min, further decreased uterine blood flow to 56 per cent less than control and increased uterine vascular resistance to 50 per cent more than control. Following 30 min of hypotension, 30 min of dopamine administration in doses sufficient to restore blood pressure to control values (5–20 μg/kg/min) similarly decreased uterine blood flow to 29 per cent less than control and increased uterine vascular resistance to 35 per cent more than control. (Key words: Acid–base equilibrium: acidosis, metabolic. Anesthesia, obstetric. Anesthetic techniques, spinal. Blood pressure: hypotension. Sympathetic nervous system: dopamine. Uterus: blood flow.)

HYPOTENSION caused by spinal anesthesia may decrease uterine blood flow and thereby lead to fetal asphyxia.[1,2] Vasopressor therapy may restore blood pressure to normal without increasing uterine blood flow.[1,2] Dopamine increases arterial blood pressure, cardiac output, and splanchnic blood flow in some low-cardiac-output states.[3–6] However, we previously showed that dopamine infusion in the normotensive pregnant ewe increased blood pressure and cardiac output but decreased uterine blood flow.[7] Since many vasopressors act differently in hypotensive and in normotensive states[8] we wished to study further the effects of dopamine used to treat hypotension on uterine blood flow and uterine vascular resistance.

Materials and Methods

Seven pregnant ewes near term (range 126 to 139 days, full term: 147 to 150 days) were studied. The method used has been described,[9] and only the essential steps are mentioned here. During general anesthesia, polyvinyl catheters were placed via groin incisions into a maternal vein for infusion of fluids. Both maternal femoral arteries were catheterized for continuous measurement of blood pressure and intermittent measurement of acid–base status and in conjunction with a right atrial catheter, for the measurement of cardiac output by the cardiogreen dye-dilution technique. Through a midline abdominal incision, a hysterotomy was performed, and a polyvinyl catheter was inserted into a fetal hind-limb artery to measure fetal blood pressure and heart rate continuously and acid–base status intermittently. An additional polyvinyl catheter was placed in the uterus for amniotic fluid pressure measurements. The uterus was closed and the suture line oversewn to prevent leakage of amniotic fluid. A precalibrated electromagnetic flow probe was secured to a branch of the uterine artery to measure continuously uterine blood flow to the uterine horn, which contained the placenta and fetus.

A minimum of 24 hours elapsed between surgical preparation and the conduct of the study. Intra-amniotic fluid pressure was subtracted from the recorded fetal arterial pressure to estimate the true fetal blood pressure. Uterine vascular resistance was estimated from the formula:

$$UVR = \frac{MABP - CVP}{UBF}$$

where UVR is uterine vascular resistance in dynes·sec·cm^{-5}, UBF is uterine blood flow in ml/min, MABP is mean maternal arterial blood pressure in torr, and CVP is central venous pressure in torr.

Experiments were performed with the animal lying on her side breathing supplementary oxygen. Following a 30-min control period, during which maternal and fetal cardiovascular and acid–base variables were stable, hypotension was induced by continuous spinal anesthesia with tetracaine. The sensory level of anesthesia, as determined by lack of response to skin-clamp, was maintained at the mid-thoracic level. After 3–5 min of maternal hypotension, dopamine sufficient to restore maternal mean arterial blood pressure rapidly to control values was infused

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Received from the Departments of Anesthesia, Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, California 94143. Accepted for publication October 31, 1978. Supported in part by USPHS Anesthesia Research Center Grant 5PO1 GM15571 9.

Address reprint requests to Dr. Shnider.

0003-3022/79/0700/0036 $00.75

at a rate of 20–40 μg/kg/min. This dose in normotensive sheep increases maternal blood pressure and cardiac output with no increase in total peripheral resistance. Brief hypotension and immediate therapy simulate the usual clinical situation. After 3–5 min, dopamine infusion was discontinued and maternal blood pressure allowed to return to hypotensive levels for 30 min. We anticipated that fetal asphyxia would occur during this period. Dopamine then was infused and dosage adjusted between 5 and 20 μg/kg/min to maintain blood pressure at control values for 30 min. This time interval was intended to permit observation of the effects of more prolonged infusion of dopamine on mother and fetus. No intravenous fluid other than that used to infuse the dopamine (total 10 ml) was administered during the experiment.

The mean value of six determinations made at 5-min intervals was used as the control value for maternal and fetal blood pressures, heart rates, and uterine blood flow and uterine vascular resistance. Control values for cardiac output, stroke volume, total peripheral resistance and acid–base data were means of two determinations taken at a 15-min interval. At the end of 3–5 min of hypotension and 3–5 min of dopamine therapy, each measurement was repeated. During the periods of prolonged hypotension and dopamine therapy the values for maternal and fetal blood pressures, heart rates, and uterine blood flow and uterine vascular resistance represent means of six determinations taken at 5-min intervals, and the values for cardiac output, stroke volume, total peripheral resistance, and acid–base data represent means of two determinations taken at the beginning and end of a 15-min interval. All cardiovascular values during hypotension and dopamine infusion are given as percentage changes from control. Cardiovascular and acid–base values during dopamine therapy were compared with those obtained during the preceding period of hypotension. Analysis of variance, one-way classification was used to estimate statistical significance. $P < 0.05$ was considered significant.

Results

With spinal anesthesia, mean maternal arterial blood pressure decreased 31 per cent from the control value (table 1; fig. 1). Uterine blood flow concomitantly decreased 17 per cent. Dopamine rapidly restored mean maternal arterial pressure to the control value, but uterine blood flow decreased further to 56 per cent less than control. This brief period of hypotension decreased stroke volume and total peripheral resistance significantly (figs. 2 and 3). Cardiac output was

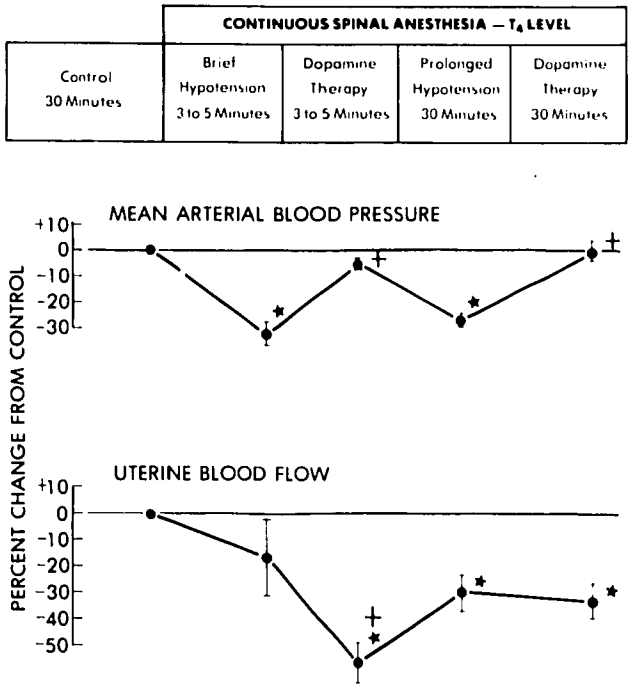

FIG. 1. Percentage changes in mean maternal arterial blood pressure and uterine blood flow during brief and prolonged hypotension and dopamine therapy. *$P < 0.05$ compared with control; †$P < 0.05$ compared with preceding period of hypotension.

unchanged due to an increase in heart rate. Dopamine increased cardiac output by increasing stroke volume. Although dopamine did not alter total peripheral resistance, uterine vascular resistance increased to almost 50 per cent more than control and 190 per cent above the preceding hypotensive value (fig. 3). Neither brief hypotension nor dopamine altered fetal heart rate, fetal blood pressure, or maternal and fetal acid–base status (tables 2 and 3).

With 30 min of prolonged hypotension (blood pressure 26 per cent less than control) uterine blood flow decreased to 29 per cent, cardiac output decreased to 25 per cent, and maternal heart rate decreased to

TABLE 1. Maternal Cardiovascular Values during the Control Period (Mean ± SE)

	Control Value
Mean arterial pressure	101 ± 6 torr
Heart rate	105 ± 6 beats/min
Uterine blood flow	463 ± 73 ml/min
Uterine vascular resistance	368 ± 5 dynes·sec·cm^{-5}
Cardiac output	10 ± 2 l/min
Stroke volume	93 ± 13 ml
Total peripheral resistance	960 ± 174 dynes·sec·cm^{-5}

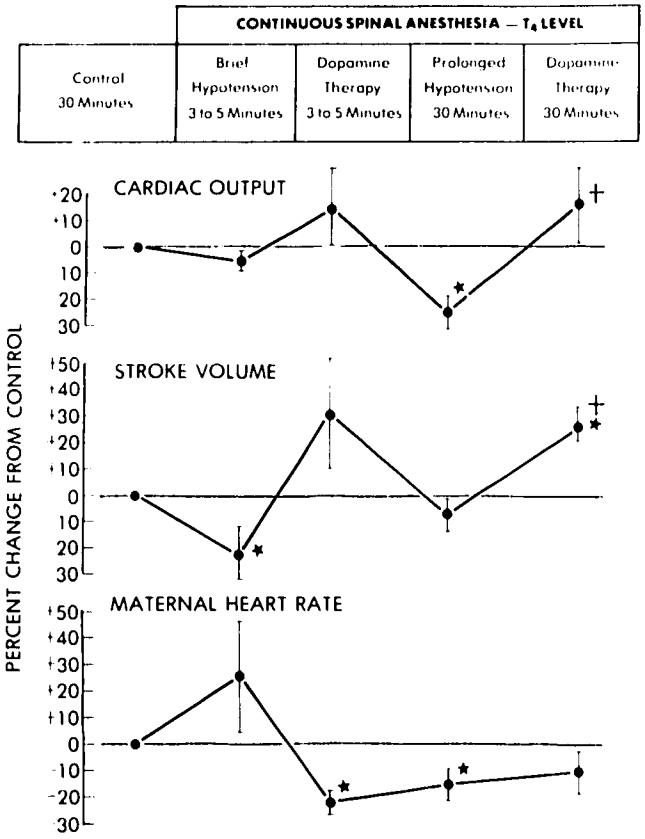

FIG. 2. Percentage changes in cardiac output, stroke volume, and maternal heart rate during brief and prolonged hypotension and dopamine therapy. *$P < 0.05$ compared with control; †$P < 0.05$ compared with preceding period of hypotension.

15 per cent less than corresponding control values (figs. 1–3). Infusion of dopamine for 30 min returned maternal blood pressure to the control value but did not increase uterine blood flow (fig. 1). Uterine vascular resistance increased to almost 35 per cent more than control (fig. 3).

Maternal blood *p*H values decreased from 7.49 to 7.44 with a 30-min infusion of dopamine, primarily because of an increase in Pa_{CO_2} of 6 torr (table 3). Fetal acid–base variables, fetal heart rate, and fetal blood presure did not change significantly (tables 2 and 3).

Discussion

We have shown that either brief or prolonged spinal hypotension decreases uterine blood flow. Dopamine further decreases uterine blood flow by increasing uterine vascular resistance. A similar vasoconstrictive effect on uterine blood vessels has been reported to occur with beta-adrenergic receptor-stimulating drugs such as isoxsuprine,[10] ritodrine,[11] and epinephrine in low doses.[12] The effects of dopamine on the uterine vessels probably represents an increased sensitivity of these vessels to the alpha-adrenergic receptor-stimulating effect of dopamine.

Our results agree with those of Halmagyi *et al.*[13] and Callender *et al.*[7] in normotensive sheep. We observed an increase in cardiac output, a decrease in total peripheral resistance, and an increase in maternal Pa_{CO_2}. In our animals the increase in Pa_{CO_2} was minimal (less than 10 torr) and was not associated with a decrease in Pa_{O_2}.

Our findings with respect to uterine blood flow and uterine vascular resistance differ from those reported by Blanchard *et al.*[14] These investigators found that when dopamine increased blood pressure in normotensive sheep, uterine blood flow increased despite some increase in uterine vascular resistance. However, our findings are consistent with those of Callender *et al.*,[7] who found that uterine blood flow decreased significantly at doses that increased mean maternal blood pressure. We have no explanation for the contradictory findings. We found that treatment with dopamine of hypotension resulting from spinal anesthesia decreased uterine blood flow and increased uterine vascular resistance.

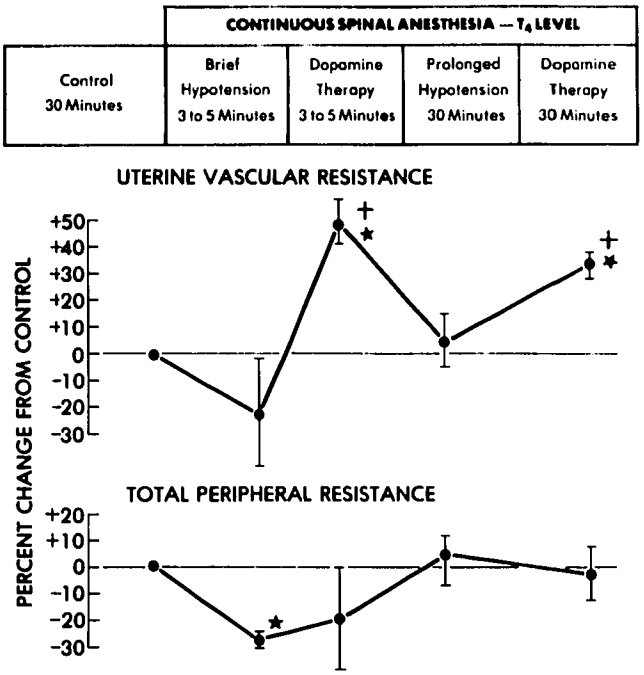

FIG. 3. Percentage changes in uterine vascular resistance and total peripheral resistance during brief and prolonged hypotension and dopamine therapy. *$P < 0.05$ compared with control; †$P < 0.05$ compared with preceding period of hypotension.

TABLE 2. Changes in Fetal Arterial Blood Pressure and Fetal Heart Rate during Control Period, Brief and Prolonged Hypotension, and Dopamine Therapy* (Mean ± SE)

		Continuous Spinal Anesthesia, T4 Level Per Cent Change from Control			
	Control 30 Min	Brief Hypotension 3–5 Min	Dopamine Therapy 3–5 Min	Prolonged Hypotension 30 Min	Dopamine Therapy 30 Min
Fetal mean arterial blood pressure (torr)	50 ± 3	−3 ± 4	6 ± 6	−5 ± 4	0.3 ± 3
Fetal heart rate (beats/min)	158 ± 8	−4 ± 8	−7 ± 8	−10 ± 5	−0.4 ± 4

* No significant difference.

TABLE 3. Changes in Maternal and Fetal Blood-gas and Acid–Base Values during Control Period, Brief and Prolonged Hypotension, and Dopamine Therapy (Mean ± SE)

		Continuous Spinal Anesthesia, T4 Level			
	Control 30 Min	Brief Hypotension 3–5 Min	Dopamine Therapy 3–5 Min	Prolonged Hypotension 30 Min	Dopamine Therapy 30 Min
Maternal					
*p*H	7.49 ± 0.01	7.50 ± 0.01	7.45 ± 0.02	7.50 ± 0.01	7.44 ± 0.02*†
P_{CO_2} (torr)	32 ± 2	27 ± 1	37 ± 5	32 ± 2	38 ± 4
P_{O_2} (torr)	193 ± 29	174 ± 30	225 ± 42	190 ± 23	175 ± 18
Base excess (mEq/l)	1.2 ± 1.2	−0.9 ± 1.0	1.4 ± 1.4	1.7 ± 1.3	1.0 ± 1.2
Fetal					
*p*H	7.31 ± 0.02	7.29 ± 0.03	7.26 ± 0.04	7.27 ± 0.03	7.23 ± 0.05
P_{CO_2} (torr)	44 ± 2	40 ± 3	49 ± 3	47 ± 3	51 ± 4
P_{O_2} (torr)	21 ± 1	17 ± 4	21 ± 3	19 ± 2	22 ± 2
Base excess (mEq/l)	−3.9 ± 1.5	−6.2 ± 2.2	−5.3 ± 2.9	−5.7 ± 2.0	−5.8 ± 3.0

* $P < 0.05$ compared with control.
† $P < 0.05$ compared with preceding hypotension period.

Despite the decrease in uterine blood flow due to spinal hypotension or dopamine administration, fetal hypoxemia, hypercapnia or metabolic acidosis did not occur. Healthy sheep fetuses can obviously tolerate brief periods of decreased placental perfusion. The lack of fetal deterioration in our study in no way suggests that uterine hypoperfusion is benign. Fetuses with uteroplacental insufficiency from other causes may not tolerate even short periods of hypotension or uterine vasoconstriction.[1,2,15,16]

We and other investigators have shown that ephedrine restores uterine blood flow when used to treat spinal hypotension.[2,17] Assuming that our data for dopamine and other vasopressors apply to pregnant women, it would appear that ephedrine is still the drug of choice when a vasopressor agent is necessary in obstetrics.

The halothane (Fluothane) used in this study was donated by Ayerst Laboratories and the dopamine by Arnar-Stone Laboratories.

The authors are grateful to Ms. Judy L. Johnson and Ms. Merrilyn J. Jones for valuable technical assistance.

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