

effectively degermed by scrubbing or by application of antiseptics, superficial organisms are eradicated; nevertheless, deep organisms begin coming to the surface.<sup>14</sup> This process may have been accelerated by vigorous stimulation in Phase II. This observation strengthens a time-honored belief that it is not possible to completely eradicate organisms from the skin without destroying it.<sup>14</sup> However, this finding should not discourage the anesthesiologist from preparing the skin before epidural or caudal analgesia, since the purpose is to kill the pathogenic organisms and to reduce the number of saprophytic organisms.

We conclude that anaerobic organisms are present on the skin in the caudal area. However, *all bacterial cultures deep to the skin were negative and infection did not occur with either epidural or caudal technique.* Meticulous care in preparing the skin site and the use of sterile techniques are recommended when using epidural and caudal blocks. Spraying the skin with povidone-iodine and removing the excess of fluid after one minute is adequate; repeating the procedure does not improve the technique.

The authors are grateful to Floyd Taylor, Ph.D., for the statistical analysis of the data and to Ms. Carol Buffenmyer and Mrs. Margaret Faller for assistance in preparing the manuscript.

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Anesthesiology  
53:514-517, 1980

## Dopamine for the Treatment of Spinal Hypotension during Cesarean Section

RICHARD B. CLARK, M.D.,\* AND JOHN A. BRUNNER, III, M.D.†

Despite the use of prophylactic fluid loading<sup>1</sup> and left uterine displacement,<sup>2</sup> hypotension during spinal

anesthesia for cesarean section continues to be a problem.<sup>3</sup> When hypotension occurs despite these maneuvers, a vasopressor such as ephedrine must be administered.<sup>4</sup> Dopamine appears to possess pharmacologic qualities that might be advantageous in this setting. It has a rapid onset and a brief duration of action and lacks alpha-adrenergic activity in low doses. In fact, in very low doses (2 µg/kg/min), dopamine has only dopaminergic action, including vasodilatation of renal and mesenteric vessels.<sup>5</sup> It may also cause vasodilatation and improved perfusion in other splanchnic beds. Intermediate doses (3-12 µg/kg/min) cause primarily beta stimulation, and with more than 12 µg/kg/min, alpha effect may predominate.<sup>6</sup>

\* Professor, Departments of Anesthesiology and Obstetrics and Gynecology.

† Assistant Professor, Department of Anesthesiology.

Received from the Departments of Anesthesiology and Obstetrics and Gynecology, University of Arkansas for Medical Sciences, 4301 West Markham Street, Little Rock, Arkansas 72205. Accepted for publication July 1, 1980. Presented in part at the annual meeting of the American Society of Anesthesiologists, Chicago, October 23, 1978.

Address reprint requests to Dr. Clark.

Key words: Sympathetic nervous system: dopamine; sympathomimetic agents, ephedrine. Anesthesia, obstetric. Complications: hypotension.

However, alpha activity may begin at levels as low as 6  $\mu\text{g}/\text{kg}/\text{min}$ .<sup>7</sup>

Reports of the effects of dopamine on uterine blood flow in animals have been inconsistent. Early studies showed a decrease in uterine blood flow in pregnant sheep.<sup>8-10</sup> Subsequently, other studies in these animals revealed an increase in uterine blood flow.<sup>11-12</sup> Because of the conflict in these reports and because of possible species differences, we decided that a clinical trial in human subjects was indicated. We believed that low doses of dopamine in the pregnant woman would be unlikely to reduce uterine blood flow significantly, and that use of this drug might benefit mother and fetus.

#### MATERIALS AND METHODS

This study was performed on human subjects undergoing repeat cesarean section. None was in labor or had obstetric or medical complications. The protocol was approved by the Human Research Advisory Committee. After informed consent was obtained, the patients received an intravenous infusion of 5 per cent dextrose in lactated Ringer's solution, ‡ 1 liter, during the 30 minutes prior to anesthesia. Then, 5 per cent dextrose in water was slowly infused. No premedication was given. Tetracaine, 8-10 mg without epinephrine, was given for spinal anesthesia, after which left uterine displacement was instituted with a folded blanket beneath the right hip. The dermatome level was sufficient to perform the operation, usually T6 to T4. Blood pressure was measured with a sphygmomanometer by the Riva-Rocci method. The electrocardiogram was monitored continuously. Patients breathed room air throughout.

In the event hypotension (systolic pressure less than 100 torr) occurred, either ephedrine (10-mg increments) or dopamine was given intravenously by random selection. Dopamine was administered through a Harvard Infusion Pump in a dilution of 200  $\mu\text{g}/\text{ml}$  to maintain systolic blood pressure above 100 torr. The initial rate was 2  $\mu\text{g}/\text{kg}/\text{min}$ . If systolic blood pressure did not increase to above 100 torr after one minute, the rate was increased to 5  $\mu\text{g}/\text{kg}/\text{min}$ , then 10  $\mu\text{g}/\text{kg}/\text{min}$ .

Systolic blood pressure and heart rate were measured every 2.5 minutes except during the first 10

minutes (when it was measured every minute) following institution of spinal anesthesia and during the period of vasopressor administration. Urinary output was measured during the induction-delivery interval. At delivery, maternal arterial blood  $\text{Pa}_{\text{O}_2}$ ,  $\text{Pa}_{\text{CO}_2}$ ,  $\text{pH}$ , and base excess were determined. Also, a doubly clamped section of umbilical cord was obtained and umbilical arterial and venous blood  $\text{P}_{\text{O}_2}$ ,  $\text{P}_{\text{CO}_2}$ ,  $\text{pH}$ , and base excess were measured. Uterine blood flow was not measured. One- and five-minute Apgar scores were determined by the pediatricians in attendance, who were unaware of vasopressor administration. The results were analyzed by the analysis of variance and Student's *t* test, with  $P < 0.05$  considered significant.

#### RESULTS

Twenty-seven of the 68 patients received ephedrine, and 26 received dopamine. Fifteen patients did not become hypotensive, and served as the control group. The mean age of the control group was  $21.3 \pm 0.7$  (SE) years, mean weight  $71.2 \pm 2.6$  kg, mean induction-delivery interval  $34.9 \pm 2.1$  minutes, mean urinary output during induction-delivery interval  $139.0 \pm 23.6$  ml. Control maternal arterial blood-gas values at delivery were:  $\text{P}_{\text{O}_2}$   $98.7 \pm 6.3$  torr,  $\text{P}_{\text{CO}_2}$   $34.0 \pm 4.0$  torr,  $\text{pH}$   $7.42 \pm .03$  units, and base excess  $-2.4 \pm 1.9$  mEq/l. Neither the mothers who received ephedrine nor those who received dopamine had significantly different values when these variables were compared with control values.

The mean dose of ephedrine was  $19.1 \pm 1.0$  (SE) mg. Eleven of the 27 patients needed one 10-mg dose to maintain systolic pressure above 100 torr, ten needed two doses, three needed three doses, and three needed four doses. The mean infusion time in the dopamine group was  $23.4 \pm 0.8$  (SE) minutes. Eight patients received a maximal dopamine infusion of 2  $\mu\text{g}/\text{kg}/\text{min}$ , nine received a maximum of 5  $\mu\text{g}/\text{kg}/\text{min}$ , and nine needed 10  $\mu\text{g}/\text{kg}/\text{min}$ . In every instance where a patient received 10  $\mu\text{g}/\text{kg}/\text{min}$ , the rate had to be decreased to 5 or 2  $\mu\text{g}/\text{kg}/\text{min}$  when a systolic pressure of 140 torr was exceeded. Many patients needed repeated alterations in the infusion rates to maintain systolic pressures within the predetermined range. In five of the 26 patients, the infusion was discontinued several minutes prior to delivery because systolic pressure had risen to above 140 torr.

The heart rates of the control and ephedrine-treated mothers at delivery (98.2 and 99.8 beats/min, respectively) were significantly higher than their prespinal levels (87.4 and 93.5 beats/min). Also, these heart rates at delivery were significantly higher than that in the dopamine-treated group (85.4 beats/min).

‡ Lactated Ringer's solution with 5 per cent dextrose was used during this study. Since then, rapid infusion of dextrose solution has been shown to cause neonatal hypoglycemia (Mendlula J, Grylack L, Scanlon J: Influence of intrapartum glucose load on the normal newborn's sugar, insulin and neurobehavioral status, (presented at the annual meeting of the Society of Obstetric Anesthesia and Perinatology, Winston-Salem, North Carolina, April 6, 1979). We now use lactated Ringer's solution to volume-load our patients before cesarean section with spinal or epidural anesthesia.

TABLE 1. Umbilical-artery and Umbilical-vein Blood-gas Values at Delivery (Mean  $\pm$  SE)

	Control	Ephedrine	Dopamine
Umbilical artery			
pH	7.26 $\pm$ 0.03	7.24 $\pm$ 0.01	7.26 $\pm$ 0.02
P <sub>O<sub>2</sub></sub> (torr)	23.3 $\pm$ 4.1	16.4 $\pm$ 1.1*	14.6 $\pm$ 1.0*
P <sub>CO<sub>2</sub></sub> (torr)	46.9 $\pm$ 4.0	48.5 $\pm$ 2.7	49.8 $\pm$ 2.9
Base excess (mEq/l)	-5.4 $\pm$ 1.1	-5.9 $\pm$ 0.9	-6.2 $\pm$ 1.0
Umbilical vein			
pH	7.33 $\pm$ 0.03	7.33 $\pm$ 0.01	7.32 $\pm$ 0.02
P <sub>O<sub>2</sub></sub> (torr)	32.1 $\pm$ 3.4	26.4 $\pm$ 2.1	23.5 $\pm$ 1.2*
P <sub>CO<sub>2</sub></sub> (torr)	44.5 $\pm$ 3.6	42.8 $\pm$ 2.4	42.9 $\pm$ 2.4
Base excess (mEq/l)	-3.0 $\pm$ 1.5	-4.4 $\pm$ 0.7	-4.3 $\pm$ 0.7

\* Significantly different from control,  $P < 0.05$ .

The umbilical arterial and venous blood-gas values of the infants at delivery are given in table 1. The P<sub>O<sub>2</sub></sub> for umbilical arterial blood were significantly lower for the dopamine- and ephedrine-treated infants compared with control. Also, there was a significant difference between P<sub>O<sub>2</sub></sub> for umbilical venous blood of the dopamine-treated group and the control group. There was no correlation between total dose of dopamine or ephedrine and the P<sub>O<sub>2</sub></sub> of blood in the umbilical artery or vein.

There were only two depressed infants: one in the control group and one in the dopamine-treated group. Both infants had 1-minute Apgar scores of 6, and 5-minute scores of 7. The cause for this depression was not apparent.

#### DISCUSSION

We have shown that dopamine restores maternal blood pressure during cesarean section. Though acid-base values and Apgar scores were not significantly different from those of controls, the umbilical arterial and venous blood P<sub>O<sub>2</sub></sub> values were decreased in dopamine-treated neonates compared with controls. However, when compared with the ephedrine-treated group, no difference in blood-gas values could be found. Perhaps maternal hypotension, albeit of short duration, rather than the vasopressors chosen, reduced the P<sub>O<sub>2</sub></sub> values in these infants. Possibly a more exacting evaluation of oxygenation, such as fetal O<sub>2</sub> extraction, might have detected a difference between the results of using these vasopressors. This was not done in this study, but should be considered in future studies, since relatively small differences in oxygen tension within these ranges may make significant differences in oxygen content. Also, a more detailed clinical evaluation of the newborn, such as neuro-behavioral testing, might uncover differences not apparent using Apgar scores.

The incidence of hypotension (78 per cent) in our study was high, but this was not unexpected or un-

usual.<sup>3,13</sup> The selection of an arbitrary systolic pressure of 100 torr as a pressure below which maternal hypotension was diagnosed and treated undoubtedly contributed to this incidence. However, this definition of maternal hypotension has widespread acceptance based on the studies by Hon,<sup>14</sup> Albright,<sup>15</sup> Shnider and Levinson<sup>16</sup> who have defined hypotension as a systolic pressure of less than 100 torr or a fall of 30 per cent from preanesthetic levels. The latter criterion would not apply to our patients, since less than 5 per cent had preanesthetic systolic pressures above 140 torr. Also, the use of a folded blanket under the right hip for left uterine displacement is less effective than is a mechanical device in maintaining maternal brachial arterial pressure, albeit at the possible expense of uterine blood flow secondary to aortic compression.<sup>2</sup> Additional support under the right hip, with or without left lateral table tilt, might have reduced this incidence of hypotension even further.

Eight of the mothers received only the 2  $\mu$ g/kg/min infusion of dopamine, and their systolic pressures returned to 100 torr or higher. In five of these patients, the pressures had decreased only slightly, and might have recovered without dopamine infusion. After induction of anesthesia, the other three had significant decreases in blood pressure, which returned promptly to preanesthetic levels without ancillary maneuvers other than the dopamine infusion. This was unexpected, as dopamine at this dose should not cause a pressure response.<sup>5</sup> Perhaps pregnant patients with expanded blood volumes and nonpregnant patients react differently. Alternatively, this may be an example of biologic variation compounded by the possible error of basing dose on weight, rather than body surface area.

In many ways, dopamine is attractive as a vasopressor in operative delivery. Blood pressure is easy to control. There are less saltatory changes than with ephedrine because dopamine is administered by continuous infusion. Nevertheless, we were unable to detect any improvement in fetal outcome when dopamine was compared with ephedrine. In summary, within the confines of the clinical study, the choice between these two vasopressors made no difference in maternal or fetal condition at birth.

The authors would like to express their appreciation to James Meade, Ph.D., of the Division of Biometry, University of Arkansas for Medical Sciences, for analysis of the data.

The dopamine was supplied as Intropin<sup>®</sup> by Arnar-Stone Laboratories, Mount Prospect, Illinois.

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Anesthesiology  
53:517-520, 1980

## Correlation of Succinylcholine Duration of Action with Plasma Cholinesterase Activity in Subjects with the Genotypically Normal Enzyme

JØRGEN VIBY-MOGENSEN, M.D.\*

In a recent analysis of 225 cases of prolonged apnea following succinylcholine administration reported to the Danish Cholinesterase Research Unit, we found that 14 patients (6.2 per cent) had low plasma cholinesterase activity (cholinesterase: E.C. 3.1.1.8, acetylcholine acylhydrolase) due to an acquired deficiency.<sup>1</sup> The durations of apnea following administration of succinylcholine, 50-250 mg (mean  $\pm$  SE: 102  $\pm$  14.7 mg) in these 14 patients ranged from 15 to 240 min (mean  $\pm$  SE: 82  $\pm$  20.8 min). These figures are not consistent with the generally accepted point of view that even a marked deficiency in enzymatic activity causes only moderate prolongation of the period of apnea following succinylcholine.<sup>2</sup>

Only one of these 14 patients was tested pre- and postoperatively with a nerve stimulator. In some cases, the prolonged apnea may have resulted from other factors, such as hyperventilation and/or residual narcotic

effect. We, therefore, sought to quantify the relationship between duration of succinylcholine-induced neuromuscular blockade and cholinesterase activity in patients with genotypically normal plasma cholinesterase.

### MATERIALS AND METHODS

From November 1977 to December 1978, plasma cholinesterase activity<sup>3</sup> and dibucaine number<sup>4</sup> were determined for 826 patients admitted for elective surgical procedures to our hospital. Patients who had plasma cholinesterase activities less than 680 (normal range: 677-1560 U/l)<sup>5</sup> or dibucaine numbers less than 80 (normal range: 78-86)<sup>5</sup> were further investigated for abnormal cholinesterase genotypes by the following determinations: fluoride number,<sup>6</sup> chloride number,<sup>7</sup> scoline number,<sup>8</sup> and urea number.<sup>9</sup> When the heterozygous occurrence of silent and usual enzymes was suspected, family studies were also conducted. Patients who had abnormal genotypes were excluded. All genotypically normal patients with low ( $n = 23$ ) or high ( $n = 6$ ) plasma cholinesterase activity and 41 patients with normal cholinesterase, selected at random, were included in the study. Thus, the final number of patients studied was 70, 43 women and 27 men of average age 46.3 years (range: 15-86 years).

\* Associate Chairman.

Received from the Department of Anesthesia, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark. Accepted for publication July 8, 1980. Supported by the Danish Medical Research Council.

Address reprint requests to Dr. Viby-Mogensen.

Key words: Enzymes: cholinesterase. Neuromuscular relaxants: succinylcholine. Neuromuscular transmission: stimulator, nerve.