

line-induced apnea, which eliminates the possibility of coughing and laryngospasm.

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## Prophylactic Ephedrine Preceding Spinal Analgesia for Cesarean Section

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Hypotension frequently occurs in parturients undergoing cesarean section with high subarachnoid block, due to decreased cardiac output from inferior vena caval compression by the gravid uterus, compounded by vasodilatation and bradycardia.<sup>1</sup> In normotensive parturients systolic blood pressures below 100 torr are associated with fetal bradycardia, indicating fetal distress *in utero*<sup>2</sup> as well as indicating neonatal depression at birth.<sup>3</sup>

Prophylaxis of spinal hypotension has included im administration of ephedrine,<sup>2,4</sup> rapid iv hydration with balanced salt solutions,<sup>5</sup> and left uterine displacement.<sup>6,7</sup> Prophylactic ephedrine, 50 mg, im, alone, was effective in preventing hypotension (maintaining systolic blood pressure above 100 torr) in less than 50 per cent of parturients.<sup>2</sup> The efficacy and safety of im ephedrine given combined with rapid iv hydration and left uterine displacement as prophylaxis against hypotension have re-

ceived little attention. The purpose of this study was to determine the need for and effects of prophylactic im administration of ephedrine when both left uterine displacement and maternal hydration are employed. Results indicated that left uterine displacement and maternal hydration alone were not sufficient, and that addition of prophylactic im administration of ephedrine was efficacious.

## METHODS

Seventeen patients (gestation 38 weeks or more) in good health (ASA Class I or II) undergoing elective repeat cesarean section with high subarachnoid block (T<sub>5</sub>-T<sub>7</sub> sensory level) were studied. High sensory levels were purposely sought to decrease maternal discomfort and to obviate the need for analgesic drugs before birth. Eight to 25 minutes preceding subarachnoid injection, the unpremedicated patients received balanced salt solution iv (Plasmalyte<sup>®</sup> or Normosol-R<sup>®</sup>, 844 ml, SE 34.8). Five to 23 minutes prior to subarachnoid injection, eight study patients received 50 mg ephedrine im, and 20 mg procaine in 2-ml volume by deep im injection in the deltoid, while nine patients received only procaine, 20 mg in 2 ml. A double-blind

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TABLE 1. Systolic Blood Pressures in the 17 Patients Studied (Mean  $\pm$  SE)

	Control—Measured on Arrival in O.R.	Following Ephedrine or Placebo Immediately Preceding Subarachnoid Injection	Lowest Pressure after Subarachnoid Injection	Immediately after Birth
Placebo (9 patients)	126 $\pm$ 5.2	134 $\pm$ 3.9	87 $\pm$ 2.5	114 $\pm$ 7.1
Ephedrine (8 patients)	121 $\pm$ 5.0	141 $\pm$ 4.7	109 $\pm$ 5.8	135 $\pm$ 4.7

Unpaired *t* tests between placebo and ephedrine groups showed  $P < 0.01$  for lowest pressure after subarachnoid injection,  $P < 0.05$  immediately after birth, and no significant difference in control values or immediately preceding subarachnoid injection.

Paired *t* tests of differences within the placebo group showed  $P < 0.01$  for lowest pressure after subarachnoid injection,  $P < 0.05$  immediately after birth, and no significant difference immediately preceding subarachnoid injection, compared with control. Paired *t* tests of differences within the ephedrine group showed  $P < 0.01$  immediately preceding subarachnoid injection,  $P < 0.01$  immediately after birth, and  $P < 0.05$  after subarachnoid injection, compared with control.

technique was used. With the patient in the right lateral decubitus position, tetracaine, 9 or 10 mg in 1.8 or 2.0 ml of 5 per cent dextrose solution, respectively, was injected into the subarachnoid space with a 25-gauge needle. Following injection the patient was placed supine, then immediately positioned with 5–10-degree left lateral tilt and 5-degree Trendelenberg. The uterus was displaced manually to the left. Oxygen, 5 l/min, was administered through nasal prongs until delivery. Three to five minutes after subarachnoid injection, the level at which the patient perceived cold from an alcohol-dampened sponge was determined. With levels of less than  $T_4$  the degree of head-down tilt was increased, and the patient was instructed to cough until there was a  $T_4$  sensory level or no further increase of analgesia.

Blood pressures were recorded on arrival at the operating theater with left uterine displacement, just prior to subarachnoid injection (patient in right lateral decubitus position with spinal needle in place), every minute thereafter for ten minutes or until delivery, and immediately following birth of the newborn. When systolic blood pressure fell below 100 torr, iv fluid infusion and left lateral tilt were increased. If these measures failed to restore systolic blood pressure to 100 torr within one minute, ephedrine, 10–20 mg, iv, was given as needed to maintain systolic blood pressure at a minimum of 100 torr. No other medication was given until the birth of the newborn.

From a double-clamped segment of umbilical cord obtained at birth before neonatal respirations were established, venous blood was obtained for  $P_{O_2}$ ,  $P_{CO_2}$  and pH analysis. One- and five-minute Apgar scores and time to sustained respiration were determined by a pediatrician, who was unaware of the study.

## RESULTS

Analysis of patients receiving placebo and those receiving ephedrine showed no statistically significant difference in maternal ages, weights, heights, levels of sensory blocks, initial blood pressures, amounts of hydration fluid administered before subarachnoid injection, or times between injection of ephedrine or placebo and subarachnoid injection.

Table 1 summarizes mean systolic blood pressures of both groups on arrival in the operating room, just before subarachnoid injection, the lowest pressures obtained before delivery, and the blood pressures immediately following delivery before the injection of an oxytocic drug. The unpaired *t* test revealed that the patients receiving placebo had significantly lower systolic pressures before delivery ( $P < 0.01$ ) and immediately following delivery ( $P < 0.05$ ). There was no significant difference in systolic blood pressures between the ephedrine- and placebo-treated groups in the control period or immediately prior to subarachnoid injection. A paired *t* test of blood pressure changes from control within each group showed both had increases in systolic pressure prior to subarachnoid injection.

tion (ephedrine  $P < 0.01$ , placebo  $P < 0.05$ ). Patients in both groups also experienced significant reductions in systolic pressure after subarachnoid injection, with the decreases being significantly greater in the placebo patients. Immediately following birth only ephedrine-treated patients had significantly higher systolic pressures ( $P < 0.01$ ) compared with control values. No patient developed significant hypertension at any time. The highest systolic pressure was 160 torr, compared with 135 torr before ephedrine.

The systolic blood pressures of all nine placebo-treated patients decreased to less than 100 torr, and all needed iv ephedrine (12.5–50 mg, mean 25, SE 4.6). Two of the eight ephedrine-treated patients had systolic pressure reductions to less than 100 torr; one responded within one minute to further left uterine displacement and iv fluid; the other needed ephedrine, 10 mg, iv, in addition. Chi-square analysis of the numbers of patients who had systolic pressure reductions to less than 100 torr yielded a highly significant difference between the two groups ( $P < 0.01$ ). Six of nine placebo-treated patients experienced nausea and/or vomiting before delivery, while this was seen in only one ephedrine-treated patient ( $P < 0.05$ ,  $\chi^2$  analysis).

There was no significant difference in mean or median one- and five-minute Apgar scores between the two groups. No newborn scored less than 7 at one minute or less than 8 at five minutes. The mean times to neonatal sustained respiration were 14 sec, SE 4.0 sec, for ephedrine-treated patients and 31 sec, SE 6.1 sec, for placebo-treated patients ( $P < 0.01$ ). Umbilical venous blood obtained at birth showed no significant difference in  $P_{O_2}$ ,  $P_{CO_2}$ , or pH values.

#### DISCUSSION

Our results indicated that left uterine displacement and rapid iv hydration alone were not adequate prophylaxis to prevent maternal hypotension in healthy parturients undergoing cesarean section with high subarachnoid block. The addition of prophylactic ephedrine, 50 mg im, reduced the incidence of maternal hypotension, as well as nausea and vomiting, with its possible dangers. Prophylactic ephedrine had no adverse effect on

either mother or newborn. It should not, however, be concluded that im administration of ephedrine obviates the need for left uterine displacement and maternal hydration. All three factors were present in the group in which blood pressures were adequate.

Our results are contrary to those of Marx and co-workers,<sup>5,6</sup> who felt that left uterine displacement and rapid iv hydration were adequate prophylaxis against maternal hypotension following spinal analgesia. Several factors may account for those differences. The sensory levels obtained in this study were generally higher than those in the Marx study. However, Moya and Smith<sup>3</sup> found that once a T8 sensory level was obtained, higher levels of analgesia were not associated with a significantly higher incidence of hypotension. The volume of hydrating solution in this study (mean 844 ml) was slightly smaller than that used by Marx (1,000 ml). Finster<sup>9</sup> also found that left uterine displacement and prehydration with 1,000 ml of lactated Ringer's solution alone was not reliable prophylaxis.

A major difference of the Marx studies compared with that of Finster and ours was the hydrating solution. Our study and the Finster study used isotonic or slightly hypotonic hydrating solution, while Marx used a hypertonic solution, 5 per cent dextrose in lactated Ringer's solution. Such a hypertonic solution might temporarily expand the intravascular volume more by causing a translocation of body fluids into the intravascular compartment.

While not conclusive, the decreased time to sustained neonatal respirations in the ephedrine-treated patients of this study support the contention of Marx<sup>6</sup> that it is better from the fetal standpoint to prevent maternal hypotension than to treat it rapidly.

One argument against the prophylactic use of ephedrine is that maternal hypertension following vasopressor-induced vasoconstriction may cause decreased uteroplacental perfusion, which results in deterioration of the fetus in both ewe and primate.<sup>11–13</sup> Studies in normotensive gravid primates<sup>4</sup> and ewes<sup>10</sup> not subjected to hypotension have shown that ephedrine increases uterine blood flow even in the presence of a 50 per cent increased maternal systolic blood pressure. Other in-

investigators have shown ephedrine is effective in partially restoring uterine blood flow and in improving the acid-base status of fetal lambs of ewes rendered hypotensive by spinal analgesia.<sup>11,12</sup>

Another argument against prophylactic im administration of ephedrine is that it may act synergistically with oxytocics to cause severe maternal hypertension. Cassidy *et al.*<sup>10</sup> reported that the combination of a vasopressor and an oxytocic could result in severe maternal hypertension. The majority of their patients received the potent vasoconstrictor, methoxamine, and an ergot alkaloid. Three patients received the older pituitary extract of Pitocin<sup>®</sup>, known to have vasopressor activity due to contamination with vasopressin.<sup>16</sup> Unless given in an iv bolus, which results in transient hypotension secondary to maternal vasodilatation, synthetic oxytocin has minimal cardiovascular activity and is not contraindicated in conjunction with a vasopressor. The use of prophylactic im administration of ephedrine might, however, be contraindicated in essential hypertension or hypertension secondary to toxemia of pregnancy.

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