

190–440 pg/ml. These results correlate with the deficiency of plasma norepinephrine and epinephrine in our patient. In our patient, the ratio of HVA to VMA was 3, whereas the mean ratio for the control group was 1.4.¹⁰ This, again, was probably the result of the low levels of plasma norepinephrine and epinephrine.

In summary, in one patient with CIPA, we found that plasma norepinephrine and epinephrine concentrations were very low, that the urine excretion ratio of HVA to VMA was elevated during enflurane anesthesia, and that an abnormal biosynthesis or catabolism of catecholamines was probably present. Careful management, including premedication to avoid apprehension, light anesthesia, maintenance of body temperature, and avoidance of joint extension, leads to a relatively safe anesthetic. Thus, with careful attention to clinical details as described above, administration of anesthesia should be without problems.

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The Use of Nitroglycerin in Preventing the Hypertensive Response to Tracheal Intubation in Severe Preeclampsia

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Tracheal intubation of the severely preeclamptic patient may provoke life-threatening hypertension.¹ Deep general anesthesia before intubation blunts this response but also increases the risks of aspiration and depresses

the fetus. Intravenous hydralazine and phentolamine also can prevent this response but have a relatively long duration of action, making accurate regulation of blood pressure difficult. Intravenous nitroglycerin (NTG) can control hypertension during cardiac anesthesia,^{2,3} but its use during cesarean section has been limited.⁴ We previously demonstrated the effectiveness of nitroglycerin in counteracting hypertension in gravid ewes.⁵ This study evaluates the maternal and fetal effects of the drug when used during cesarean section in the severely preeclamptic patient.

METHODS

The Human Experimentation Committee approved the protocol, and all patients gave written informed consent. Nineteen severely preeclamptic patients (blood pressure greater than 160/110 mmHg and proteinuria) scheduled for cesarean section under general anesthesia

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TABLE 1. Maternal Variables of the Control and Nitroglycerin Treatment Groups

	Control (n = 10)	NTG (n = 9)
Age (yr)	24.5 ± 2.4	21.0 ± 1.1
Height (cm)	162.0 ± 3.1	158.9 ± 5.1
Weight (kg)	81.9 ± 5.1	75.9 ± 4.7
Gravidity	1.4 ± 0.2	1.6 ± 0.2
Gestation (wk)	32 ± 2	31 ± 1
Baseline BP (mmHg) mean	141 ± 8	127 ± 4
Induction to delivery time (min)	6.9 ± 0.1	7.8 ± 1.0
Uterine incision to delivery time (min)	1.0 ± 0.1	1.7 ± 1.0

Data are mean ± SEM.

No statistical differences between groups.

were randomly placed in either control or NTG treatment groups. All patients received magnesium sulfate before operation. We monitored intraarterial pressure continuously** in all patients. Following acute oxygenation for 5 min, we induced anesthesia rapidly with thiopental, 4 mg/kg and succinylcholine, 1.2 mg/kg intravenously and intubated the trachea while applying cricoid pressure. We maintained anesthesia until delivery of the infant with nitrous oxide/oxygen (60:40) and provided muscle relaxation with a 0.1% succinylcholine infusion. Ten patients served as controls, while in nine patients we administered intravenous NTG (200 µg · ml) during acute oxygenation and lowered mean arterial pressure by approximately 20% before the induction of anesthesia. Following induction and intubation, we continued the infusion and maintained mean arterial pressure near preanesthetic levels until delivery. We recorded maternal pulse and blood pressure every minute until delivery. At delivery, we measured maternal arterial blood gases and umbilical cord blood gases obtained from a doubly clamped section of umbilical cord. A pediatrician blinded as to NTG administration obtained one newborn blood pressure using a neonatal Dinamap® as soon after delivery as possible, but always within the first 10 min, and assigned 1- and 5-min Apgar scores. We also recorded maternal gestation, induction to delivery interval, uterine incision to delivery interval, newborn weight, and time to sustained respiration (TSR). Maternal pulse and blood pressure data were analyzed by multivariate analysis of variance using repeated measures. All paired data were analyzed using the Student's *t* test. We considered a *P* value of less than 0.05 statistically significant.

** Tektronix Model H 414.

RESULTS

Age, height, weight, gravidity, gestation, uterine incision to delivery times, and baseline blood pressures were similar in the control and treatment groups (table 1).

Mean maternal heart rates were similar in both groups throughout the study period. Maximal maternal heart rate occurred 2 min following intubation in both groups. Figure 1 shows the changes in blood pressure in the control and NTG treatment groups. NTG infusion significantly reduced mean arterial pressure from 127 ± 4 mmHg to 103 ± 6 mmHg (SEM) before induction of anesthesia (*P* < 0.01). Tracheal intubation increased blood pressure significantly in both groups (*P* < 0.05). Maximal levels occurred 2 min after intubation. Mean maternal arterial pressure increased to 155 ± 4 mmHg in the control group and to 119 ± 7 mmHg in the NTG treatment group. This difference in maximal blood pressure between the two groups was statistically significant (*P* < 0.001). Maternal arterial blood gases at delivery were similar (table 2).

Table 3 illustrates that newborn weight, blood pressure, heart rate, and Apgar scores were similar in the two groups, as were umbilical cord blood gases (table 2).

DISCUSSION

Patients with severe preeclampsia have blood pressures greater than 160/110 mmHg. Aggravation of severe hypertension by tracheal intubation can cause intracerebral hemorrhage and left ventricular failure.^{1,6} In contrast, excessive reductions in blood pressure in the parturient can decrease uterine blood flow and threaten the fetus. Since placental degeneration and placental abruption occur frequently in severe preeclampsia, compromised placental function increases the susceptibility

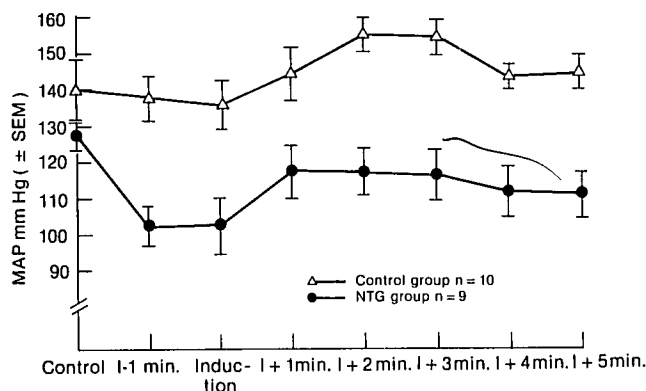


FIG. 1. Changes in maternal blood pressure in the control and NTG treatment groups. The individual points represent mean ± SEM.

of the fetus to the hazards of hypotension. Thus, severe preeclampsia requires close control of blood pressure during anesthesia for cesarean section for maternal and fetal well being.

The relatively slow onset and long duration of action of hydralazine and phentolamine prevent rapid adjustment of blood pressure. Trimethaphan, sodium nitroprusside, and NTG act rapidly and have a short duration of action. Unfortunately, the ganglionic blocker, trimethaphan, can prolong paralysis following succinylcholine administration.⁷ Other potential undesirable side effects of trimethaphan include histamine release, splanchnic blood flow reductions, and reductions in cardiac output.⁸ Nitroglycerin and nitroprusside effectively counteract norepinephrine-induced uterine vasoconstriction in gravid ewes and significantly improve uterine blood flow.⁵ Naulty *et al.* reported fetal cyanide toxicity with the use of nitroprusside in pregnant ewes.⁹ However, their protocol involved significant, sustained maternal hypotension and required the administration of large doses of SNP. We selected nitroglycerin infusion for this study because of this drug's attractive properties: direct vasodilation, rapid metabolism, effectiveness in countering hypertension and decreased uterine blood flow in sheep rendered hypertensive by norepinephrine, and an apparent absence of maternal or fetal toxic effects.⁵

Nitroglycerin infusion smoothly and gradually reduced mean maternal blood pressure by approximately 20% of control within 10 min. This smooth, gradual reduction mitigated the risk of unintentional hypotension. The 20% reduction in blood pressure buffered the increase in blood pressure following tracheal intubation. The lower peak blood pressure lessened the risk of significant hypertensive morbidity. Although NTG directly relaxes smooth muscle, the smooth-muscle cells still responded to catecholamine stimulation, as shown by the residual hypertensive responses.¹⁰

Compensatory tachycardia occurs during antihypertensive therapy and has been reported in anesthetized patients during nitroprusside-induced hypotension.¹¹ However, Fahmy¹² lowered mean blood pressure with NTG by 25% during general anesthesia without causing significant increases in heart rate. Our stable maternal heart rate during NTG infusion supports his results.

Arterial oxygenation may decrease during NTG-induced hypotension during general anesthesia.¹² In theory, inhibition of normal hypoxic pulmonary vasoconstriction may increase V/Q mismatch, increase pulmonary shunt, and decrease arterial oxygenation. We did not observe this. We lowered blood pressure for only a few minutes and then maintained blood pressures near preanesthetic control levels. In contrast, Fahmy¹² reduced mean blood pressure to as low as 60 mmHg and

TABLE 2. Maternal Arterial and Umbilical Cord Blood Gas Values at the Time of Delivery in the Control and NTG Treatment Groups

	Control (n = 10)	NTG (n = 9)
Maternal pH	7.40 ± 0.02	7.40 ± 0.01
Maternal PaO ₂ (mmHg)	119 ± 15	118 ± 19
Maternal PaCO ₂ (mmHg)	34.0 ± 2.8	34.1 ± 1.2
Maternal HCO ₃ (meq/l)	22.6 ± 1.4	20.3 ± 0.7
Umbilical artery pH	7.29 ± 0.02	7.26 ± 0.02
Umbilical artery PaO ₂ (mmHg)	12.8 ± 2.2	8.0 ± 1.8
Umbilical artery PaCO ₂ (mmHg)	52.2 ± 2.1	55.1 ± 1.1
Umbilical artery HCO ₃ (mEq/l)	24.7 ± 0.4	24.7 ± 0.4
Umbilical vein pH	7.33 ± 0.02	7.30 ± 0.02
Umbilical vein PaO ₂ (mmHg)	24.0 ± 2.3	18.1 ± 3.0
Umbilical vein PaCO ₂ (mmHg)	46.4 ± 1.7	48.7 ± 1.7
Umbilical vein HCO ₃ (mEq/l)	23.4 ± 0.6	23.6 ± 0.4

Data are mean ± SEM.
No statistical differences between groups.

maintained this degree of hypotension for approximately 112 min. We used NTG to prevent hypertension rather than to produce hypotension, and this may explain our normal arterial oxygenation.

Nitroglycerin's low molecular weight (227) and uncharged state should facilitate transplacental passage. However, Rosayro *et al.*¹³ found a fetal to maternal nitroglycerin arterial ratio of only 0.04. Reduced glutathione rapidly metabolized NTG in animal and human liver,¹⁴ and NTG has a plasma half-life of approximately 12 s.¹⁵ Rapid metabolism of nitroglycerin probably accounts for the lack of significant clinical effects in our infants. This rapid metabolism of NTG makes it a useful antihypertensive agent during induction of anesthesia

TABLE 3. Newborn Variables in Control and Nitroglycerin Treatment Groups

	Control (n = 10)	NTG (n = 9)
Newborn BP, mean (mmHg)	28 ± 3	32 ± 2
Newborn HR, mean (beats/min)	137 ± 5	134 ± 7
1 min Apgar < 7	6	6
5 min Apgar < 7	3	2
Newborn weight (kg)	1,688 ± 326	1,231 ± 151

Data are mean ± SEM.
No statistical differences between groups.

and overweighs the theoretic criticism of its low molecular weight and probable rapid placental transfer.¹⁶ Trimethaphan, although it has a larger molecular weight with less possibility of transference across the placenta, has the problem of acting too rapidly and strongly, thus may cause precipitous hypotension. Normal umbilical artery and vein blood gases emphasize the fetal safety of maternally administered NTG.

Severe preeclampsia may affect multiple organ systems. These effects may call for different anesthetic techniques, depending on the particular organs affected. Cerebral hemorrhage represents the most frequent cause of death of severe preeclampsics,¹⁷ and endotracheal intubation in the severely hypertensive patient has caused sudden left ventricular failure and pulmonary edema.^{1,6} Close control of blood pressure is essential. Cerebral edema also occurs in severely preeclamptic patients. Sudden increases in mean arterial pressure increases intracranial pressure. Nitroglycerin dilates cerebral vasculature and may increase intracranial pressure.^{18,19.}†† Whether prior nitroglycerin administration ameliorates or aggravates the potential increases in intracranial pressure with increasing blood pressure is unknown. The anesthesiologist must assess each individual patient's potential risk. The known risks of increasing intracranial pressure during intubation, the potential risks of cerebral hemorrhage and left ventricular failure may outweigh the hazard of potentially elevated intracranial pressure accompanying NTG treatment of severe hypertension.

In summary, nitroglycerin successfully blunted the hypertensive response to endotracheal intubation in this study. We did not observe adverse maternal or fetal effects. We conclude that intravenous nitroglycerin safely and effectively attenuates the hypertensive response to tracheal intubation in the severely preeclamptic patient without compromising the fetus or newborn. However, particular caution must be exercised and the relative risks of nitroglycerin administration carefully weighed in eclamptic patients who may have elevated intracranial pressure as well as in any patient who exhibits symptoms of cerebral edema.

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