

Does Magnesium Sulfate Alter the Maternal Cardiovascular Response to Vasopressor Agents in Gravid Ewes?

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Magnesium sulfate ($MgSO_4$) attenuates the maternal compensatory response to hemorrhage in gravid ewes, perhaps by decreasing the response to endogenous vasopressors. The purpose of this study was to determine whether $MgSO_4$ alters the cardiovascular response of gravid ewes to vasopressor agents. Sixteen gravid ewes underwent a series of experiments consisting of administration of two exogenous and two endogenous vasopressors, each with and without a concurrent $MgSO_4$ infusion. Dose-response curves were constructed for phenylephrine (an α_1 -adrenergic agonist), ST-91 (an α_2 -adrenergic agonist), angiotensin II, and arginine vasopressin (AVP). $MgSO_4$ significantly attenuated the increase in maternal mean arterial pressure and systemic vascular resistance and the decrease in cardiac output during ST-91 infusion but not during phenylephrine, angiotensin II, or AVP infusions. $MgSO_4$ significantly attenuated the increase in uterine vascular resistance during phenylephrine, ST-91, and angiotensin II infusions and the decrease in uterine blood flow during phenylephrine and angiotensin II infusions. $MgSO_4$ also appeared to attenuate the decrease in uterine blood flow during ST-91 infusion ($P = 0.067$). The present study suggests that $MgSO_4$ antagonizes the effects of α_1 -adrenergic agonists, α_2 -adrenergic agonists, and angiotensin II on the uterine vasculature, thus providing a level of protection for the fetus in situations of maternal stress. (Key words: α -adrenergic agonists: phenylephrine; ST-91. Anesthesia: obstetric. Electrolytes, ions: magnesium. Pharmacology: angiotensin II. Pregnancy: hypertension; preterm labor. Tocolytic agents: Magnesium sulfate. Vasopressin.)

OBSTETRICIANS give magnesium sulfate ($MgSO_4$) to preeclamptic women for seizure prophylaxis. In many centers, $MgSO_4$ is also the tocolytic agent of choice, especially in women at increased risk for hemorrhage.¹ However, Chestnut *et al.*² observed that $MgSO_4$ worsened maternal hypotension during hemorrhage in gravid ewes. Subsequently, they reported³ that indomethacin did not

attenuate the hypotensive response to $MgSO_4$ infusion and hemorrhage, suggesting that cyclooxygenase products were not responsible for the worsening of maternal hypotension. Vincent *et al.*⁴ observed that $MgSO_4$ decreased maternal blood pressure but not uterine blood flow (UBF) during epidural anesthesia in gravid ewes.

Hemorrhage results in increased concentrations of catecholamines, angiotensin II, and vasopressin.⁵⁻⁹ Each helps to maintain perfusion of vital organs. Lee *et al.*¹⁰ noted that $MgSO_4$ decreased the hypertensive response to angiotensin II and norepinephrine (NE) in a dose-dependent fashion in gravid rabbits. We speculated that $MgSO_4$ attenuates the maternal compensatory response to hemorrhage or sympathectomy by decreasing the maternal response to endogenous vasopressors. The purpose of the present study was to determine whether $MgSO_4$ alters the maternal cardiovascular response to vasopressor agents in gravid ewes.

Materials and Methods

MATERNAL/FETAL INSTRUMENTATION AND POSTSURGICAL CARE

The protocol was approved by the University of Iowa Animal Care Committee. Mixed breed ewes were obtained from a commercial breeder at approximately 118 days of timed gestation (term = 145 days). Each animal was fasted for 36 h before surgery. At 120 days of gestation, induction of general anesthesia was accomplished with sodium thiopental (8-12 mg/kg). After tracheal intubation anesthesia was maintained with 50% nitrous oxide, 50% oxygen, and 1-1.5% halothane. Mechanical ventilation was maintained throughout surgery. Using sterile technique, a laparotomy and hysterotomy were performed, and catheters (polyethylene-90) were inserted into the fetal descending aorta *via* each femoral artery. Fenestrated high pressure tubing (MX 566, Medex, Hilliard, OH) was secured to the fetal hind limb to monitor intraamniotic pressure. After the hysterotomy and laparotomy incisions were closed, a left paramedian incision was made. The left uterine artery was isolated *via* a retroperitoneal approach, and an electromagnetic flow probe (Dienco, Los Angeles, CA) was placed around the artery. Catheters (polyethylene-240) were then inserted into the maternal descending aorta and inferior vena cava *via* the left mammary artery and vein, respectively. All catheters

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were tunneled subcutaneously and exteriorized through a small incision in the left flank. Finally, an 8.5-Fr introducer (AK09800, Arrow, Reading, PA) was placed percutaneously into the right jugular vein.

After surgery, each animal was kept in an approved cage in a restricted area, fed a balanced diet, and allowed a recovery period of at least four days. Procaine and benzathine penicillin G (Dual-Pen[®], Tech America, Kansas City, MO) 600,000 U or procaine penicillin G 300,000 U and dihydrostreptomycin 375 mg (Distracyllin[®], Solray Veterinary, Princeton, NJ) were given to the mother intramuscularly before surgery and daily for 3 days after surgery. Gentamicin 80 mg was given to the mother intravenously during surgery and after the experiment each day, and gentamicin 40 mg was given *via* the amniotic catheter during surgery and after the experiment each day. Nalbuphine hydrochloride 5 mg was given as needed for postoperative analgesia on the day of surgery.

EXPERIMENTAL MEASUREMENTS AND DATA ACQUISITION

Each experiment was performed with the animal standing, supported by a canvas sling, within an approved transport cart. The canvas sling allowed the animals to remain upright at all times.

Before the first experiment in each animal, a pulmonary artery catheter (93A-131H-7F or 93A-831H-7.5F, American Edwards Laboratories, Santa Ana, CA) was inserted through the jugular vein introducer. At the end of each experiment, the catheter was withdrawn into the superior vena cava. Sterility was maintained with an 80-cm sheath. Maternal arterial blood pressure, central venous pressure, pulmonary artery pressure, and fetal arterial blood pressure were measured continuously *via* disposable strain gauge pressure transducers (46951-02, Abbott Critical Care Systems, North Chicago, IL) and transducer couplers (572-25, Coulbourn Instruments, Lehigh Valley, PA). Fetal pressures were corrected by subtraction of simultaneous intraamniotic pressure. Mean arterial blood pressure was computed arithmetically. The maternal and fetal heart rates were computed from the arterial waveforms. UBF was measured continuously with a quantitative electromagnetic flowmeter (RF-2500, Dienco). Arterial and venous pressures, heart rates, and UBF were recorded at 10-s intervals using a computer-based system and customized data acquisition software (Alternatives Unlimited, Des Moines, IA).

Cardiac output measurements were made in triplicate with 10 ml iced saline and a thermodilution cardiac output computer (9520A, Edwards Laboratories). Maternal and fetal arterial blood gas and pH values were determined using an Instrumentation Laboratory (1302, Leighton, MA) blood gas analyzer. All values were corrected for

temperature (39.5° C). Serum magnesium concentrations were measured using a spectrophotometric technique (Lancer Magnesium Rapid Stat Diagnostic Kit, Sherwood Medical, St. Louis, MO).

EXPERIMENTAL PROTOCOL

Four vasopressors were chosen for these experiments: phenylephrine (an α_1 -adrenergic agonist), ST-91 (an α_2 -adrenergic agonist), angiotensin II, and arginine vasopressin (AVP).

The experimental sequence included the following:

1. One hour for initial baseline measurements.
2. Time zero: intravenous administration of MgSO₄ 4 g or normal saline over 5 min. The total volume of crystalloid was 50 ml in each group.
3. At 5 min, intravenous infusion of MgSO₄ 4 g/h or normal saline for the duration of the experiment. The total rate of crystalloid infusion was 100 ml/h in each group.
4. At 90 min, the initial vasopressor dose was given intravenously over 5 min.
5. The second, third, fourth, and fifth doses of each vasopressor were given 40 min after the preceding dose. (Because of the longer half-life of ST-91, 4 h separated each dose of ST-91 in order to allow maternal cardiovascular measurements to return to baseline. Each animal received only two active doses of ST-91 each day.)

The infusion rates of each vasopressor were as follows: 1) phenylephrine: 0, 1, 2, 4, and 8 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; 2) ST-91: 0, 1, 2, 4, and 8 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; 3) angiotensin II: 0, 0.01, 0.02, 0.04, and 0.08 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; and 4) AVP: 0, 0.002, 0.004, 0.008, and 0.016 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

There were four groups of experiments: 1) phenylephrine, with and without MgSO₄ (n = 8); 2) ST-91, with and without MgSO₄ (n = 8); 3) angiotensin II, with and without MgSO₄ (n = 8); and AVP, with and without MgSO₄ (n = 8). We used a total of 16 animals for these experiments. Only one set of vasopressor doses (either with or without MgSO₄) was given per day, and each animal rested at least overnight before undergoing the alternate experiment. (Each complete set of ST-91 doses [with or without MgSO₄] required 2 days to complete.) Experiments were performed and doses given in random order.

Dose-response curves were constructed using hemodynamic measurements obtained during the last 2 min of the 5-min vasopressor infusion. Each measurement represents the mean of 12 observations made at 10-s intervals over the 2-min measurement period. Baseline measurements for each individual vasopressor dose were defined as the mean of 12 measurements obtained over 2 min just before infusion of that dose of vasopressor. Blood gas

TABLE 1. Initial Baseline Maternal and Fetal Hemodynamic, Blood Gas, and Acid-Base Measurements

| | Phenylephrine | | ST-91 | | Angiotensin II | | Vasopressin | |
|--|-------------------|--------------|-------------------|---------------|-------------------|-------------|-------------------|--------------|
| | MgSO ₄ | Control | MgSO ₄ | Control | MgSO ₄ | Control | MgSO ₄ | Control |
| Maternal | | | | | | | | |
| Heart rate (beats per min) | 125 ± 3 | 129 ± 3 | 111 ± 4 | 113 ± 4 | 120 ± 3 | 117 ± 3 | 118 ± 4 | 114 ± 4 |
| Mean arterial pressure (mmHg) | 95 ± 3 | 95 ± 3 | 89 ± 4 | 88 ± 4 | 94 ± 2 | 94 ± 2 | 92 ± 1 | 90 ± 1 |
| Cardiac output (l/min) | 9.2 ± 0.4 | 9.7 ± 0.4 | 10.2 ± 0.4 | 9.9 ± 0.4 | 9.4 ± 0.3 | 10.0 ± 0.3 | 8.7 ± 0.3 | 8.9 ± 0.3 |
| Systemic vascular resistance (dyne · s · cm ⁻⁵) | 940 ± 88 | 749 ± 88 | 661 ± 97 | 700 ± 97 | 719 ± 35 | 725 ± 38 | 814 ± 50 | 777 ± 53 |
| Uterine blood flow (ml/min) | 630 ± 57 | 543 ± 49 | 589 ± 43 | 532 ± 43 | 700 ± 40 | 656 ± 37 | 558 ± 39 | 562 ± 39 |
| Uterine vascular resistance (dyne · s · cm ⁻⁵) | 15493 ± 6323 | 16946 ± 5476 | 10970 ± 12998 | 13173 ± 12998 | 10757 ± 868 | 12036 ± 868 | 13349 ± 1170 | 11653 ± 1308 |
| pH | 7.44 ± 0.01 | 7.45 ± 0.01 | 7.42 ± 0.01 | 7.46 ± 0.01 | 7.45 ± 0.01 | 7.43 ± 0.01 | 7.45 ± 0.01 | 7.44 ± 0.01 |
| P _{O₂} (mmHg) | 108 ± 3 | 112 ± 3 | 111 ± 5 | 104 ± 5 | 113 ± 2 | 109 ± 2 | 113 ± 2 | 114 ± 2 |
| P _{CO₂} (mmHg) | 38 ± 1 | 38 ± 1 | 36 ± 1 | 38 ± 1 | 37 ± 1 | 38 ± 1 | 38 ± 1 | 37 ± 1 |
| Fetal | | | | | | | | |
| Heart rate (beats per min) | 161 ± 6 | 164 ± 6 | 177 ± 5 | 178 ± 6 | 170 ± 4 | 167 ± 4 | 172 ± 4 | 165 ± 4 |
| pH | 7.33 ± 0.01 | 7.32 ± 0.01 | 7.34 ± 0.01 | 7.35 ± 0.01 | 7.30 ± 0.01 | 7.32 ± 0.01 | 7.30 ± 0.01 | 7.30 ± 0.01 |
| P _{O₂} (mmHg) | 20 ± 1 | 20 ± 1 | 21 ± 1 | 22 ± 1 | 20 ± 1.5 | 19 ± 1 | 19 ± 1 | 19 ± 1 |
| P _{CO₂} (mmHg) | 50 ± 1 | 50 ± 1 | 48 ± 1 | 49 ± 1 | 50 ± 1 | 50 ± 1 | 48 ± 1 | 50 ± 1 |

All values are mean ± SEM.

There were no significant differences between the MgSO₄ and control groups for any of the measurements in the four sets of experiments.

and acid-base measurements were obtained 5 min after the completion of the vasopressor infusion.

Initial baseline hemodynamic measurements, and all blood gas and acid-base measurements and MgSO₄ concentrations are reported as mean (± standard error of the mean). Hemodynamic changes are presented as mean (± standard error of the mean) percent of baseline for that dose of vasopressor. Statistical analysis was performed by repeated-measures analysis of variance for overall differences between the dose-response curves with and without MgSO₄. Linear regression analyses were performed for each hemodynamic variable versus dose to determine the presence of dose-dependency. *P* < 0.05 was considered significant.

Results

The mean (± standard error of the mean) weight of the animals was 58 ± 2 kg. Initial baseline maternal and fetal hemodynamic, acid-base, and blood gas measurements were similar before MgSO₄ and control (normal saline) experiments for each of the four vasopressor groups (table 1). No values had changed significantly at 90 min after starting the infusion of MgSO₄ or normal saline-control (data not shown). Mean serum magnesium concentrations at time zero, at 90 min, and before the final vasopressor dose for each experiment day are listed in table 2. (These concentrations were within the therapeutic range for pregnant women.^{11,12})

Each of the four vasopressors tested produced a dose-dependent increase in maternal mean arterial blood pressure and systemic vascular resistance and a dose-dependent decrease in cardiac output (figs. 1-3). All vasopressors decreased UBF (fig. 4), but the decrease was dose-dependent only during infusion of phenylephrine and ST-91. All vasopressors increased uterine vascular resistance (UVR) (fig. 5). The increase in UVR was dose-dependent for all vasopressors except AVP. MgSO₄ significantly attenuated the increase in mean arterial blood pressure (*P* = 0.01) and systemic vascular resistance (*P* = 0.002) and the decrease in cardiac output (*P* = 0.003) during ST-91 infusion, but not during phenylephrine, angiotensin II, or AVP infusions (figs. 1-3).

MgSO₄ significantly attenuated the decrease in UBF due to phenylephrine (*P* = 0.004) and angiotensin II (*P* = 0.0001) but had no effect on UBF during AVP infusion (fig. 4). There was a trend toward attenuation of the ST-91-induced decrease in UBF during MgSO₄ infusion (*P* < 0.07). MgSO₄ significantly attenuated the increase in UVR in response to phenylephrine, ST-91, and angiotensin II but not AVP infusion (fig. 5).

Maternal pH decreased significantly from baseline only in the ST-91 MgSO₄ group (from 7.46 ± 0.01 to 7.41 ± 0.01, *P* = 0.04) and the ST-91 control group (from

7.43 ± 0.01 to 7.39 ± 0.01, *P* = 0.007). The decreases observed for the two groups were not significantly different from each other. Fetal arterial pH decreased significantly (from 7.32 ± 0.01 to 7.28 ± 0.01 in the MgSO₄ group and from 7.35 ± 0.01 to 7.29 ± 0.01 in the control group) during ST-91 infusion only. Fetal arterial carbon dioxide tension also increased significantly (from 52 ± 1 to 56 ± 1 mmHg in the MgSO₄ group and from 50 ± 1 to 55 ± 1 mmHg in the control group) during ST-91 infusion only. These changes did not significantly differ between the MgSO₄ and control groups. Maternal arterial carbon dioxide tension and oxygen tension and fetal arterial oxygen tension did not change significantly during any vasopressor infusion, with or without MgSO₄.

Discussion

Magnesium has several known effects on vascular smooth muscle cells and neurotransmitter release that may explain the observed attenuation of specific vasopressor effects during MgSO₄ infusion. First, magnesium interferes with multiple cellular mechanisms involving calcium binding and transport. In smooth muscle cells, magnesium blocks transmembranous influx of calcium across calcium channels, competes intracellularly with calcium at non-specific binding sites on troponin-C and myosin, and inhibits calcium release from the sarcoplasmic reticulum.¹³⁻¹⁶ Second, magnesium interferes with neurotransmitter release at the adrenergic nerve terminal. *In vitro* magnesium facilitates NE uptake into nerve granules while inhibiting its release.¹⁷ In contrast, calcium enhances NE release from these granules.¹⁷ The work of Weaver *et al.*¹⁸ supports the premise that MgSO₄ alters NE reuptake at adrenergic nerve endings. These authors reported that

TABLE 2. Serum Magnesium Concentrations (mg/dl)

| | Baseline | 90 Min | Before Final Vasopressor Dose for the Day |
|-------------------|-----------|------------|---|
| Phenylephrine | | | |
| MgSO ₄ | 2.3 ± 0.2 | 5.8 ± 0.2* | 6.0 ± 0.2* |
| Control | 2.2 ± 0.2 | 2.3 ± 0.2 | 2.2 ± 0.2 |
| ST-91 | | | |
| MgSO ₄ | 2.2 ± 0.1 | 6.4 ± 0.1* | 7.7 ± 0.1† |
| Control | 2.2 ± 0.1 | 2.4 ± 0.1 | 2.4 ± 0.1 |
| Angiotensin II | | | |
| MgSO ₄ | 2.2 ± 0.2 | 5.4 ± 0.2* | 5.9 ± 0.2† |
| Control | 2.2 ± 0.2 | 2.0 ± 0.2 | 2.1 ± 0.2 |
| Vasopressin | | | |
| MgSO ₄ | 2.1 ± 0.2 | 5.7 ± 0.2* | 5.8 ± 0.2* |
| Control | 2.2 ± 0.2 | 2.3 ± 0.2 | 2.1 ± 0.2 |

Values are reported as mean ± SEM.

* Significantly different from baseline only.

† Significantly different from both the baseline and the 90-min values.

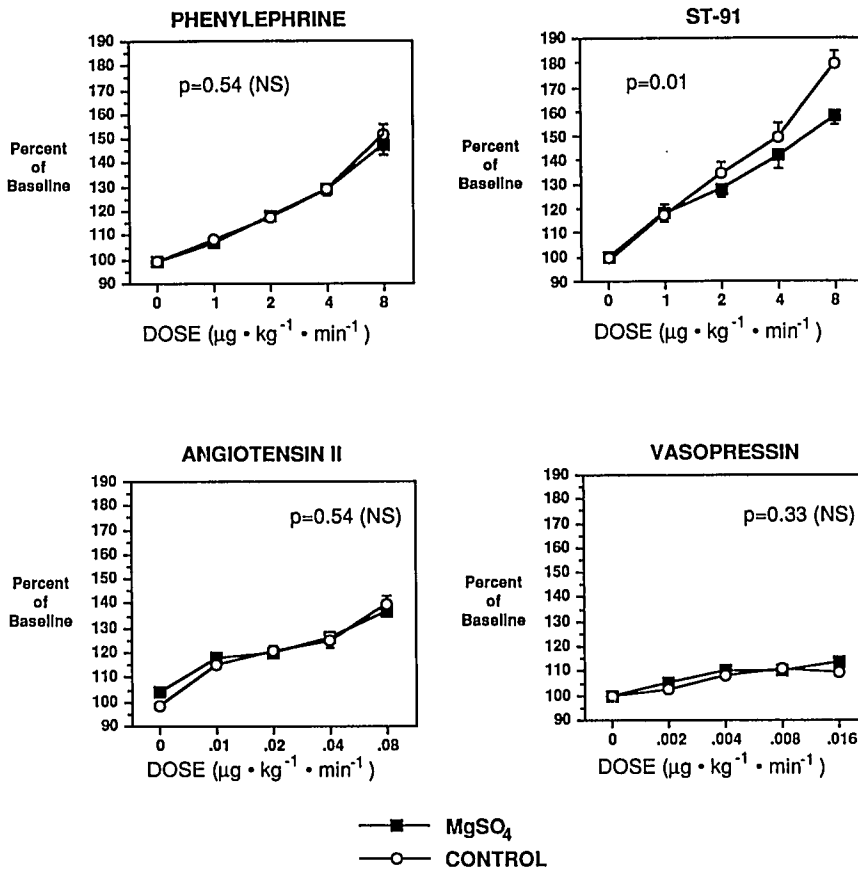


FIG. 1. Maternal mean arterial pressure dose-response curves for each vasopressor, with and without MgSO₄. Each response is expressed as mean (\pm SEM) percent of the baseline for that dose of vasopressor. Standard error bars, if not shown, are included within the height of the squares or circles for each data point. *P* values are reported for the overall difference between the MgSO₄ and control groups.

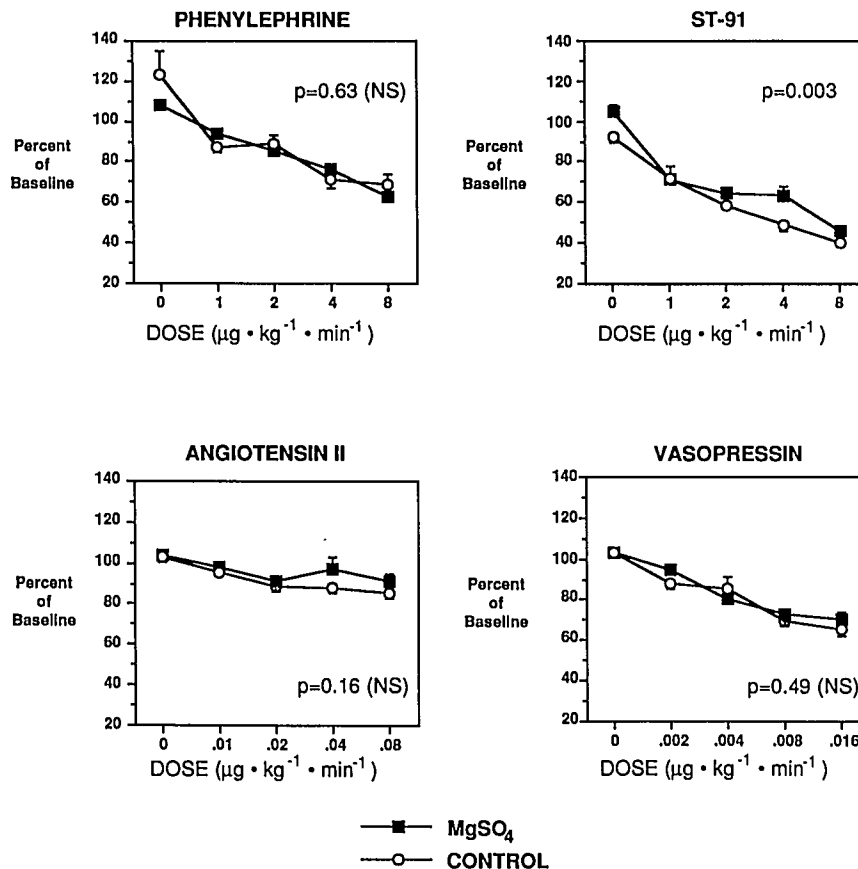


FIG. 2. Maternal cardiac output dose-response curves for each vasopressor, with and without MgSO₄. Each response is expressed as mean (\pm SEM) percent of the baseline for that dose of vasopressor. Standard error bars, if not shown, are included within the height of the squares or circles for each data point. *P* values are reported for the overall difference between the MgSO₄ and control groups.

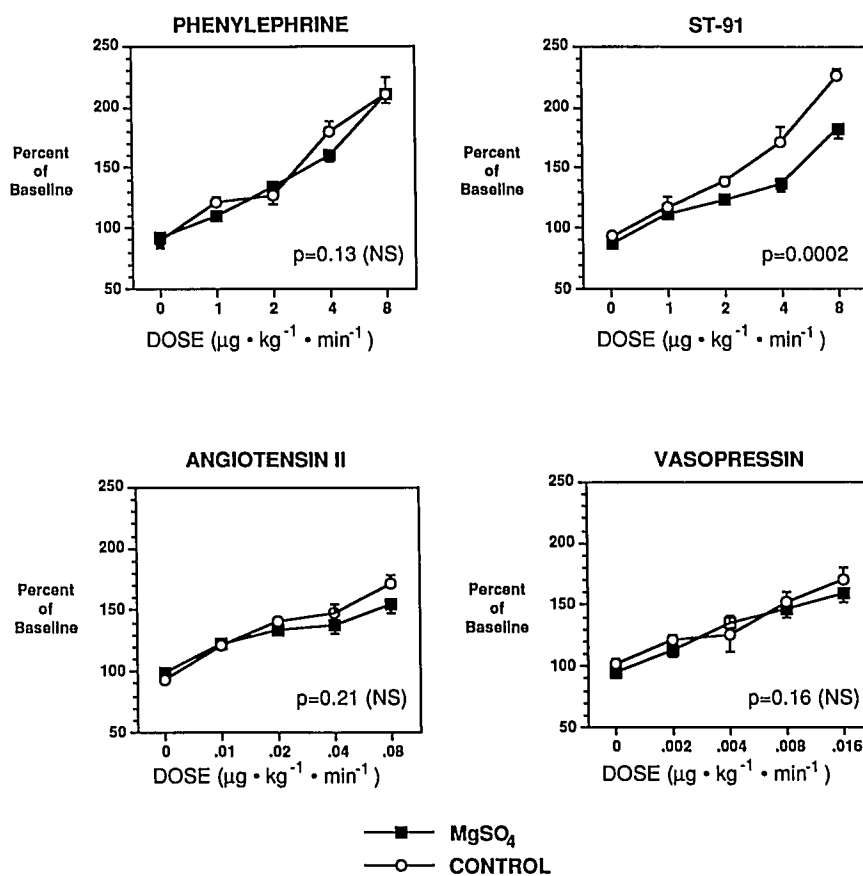


FIG. 3. Maternal systemic vascular resistance dose-response curves for each vasopressor, with and without MgSO₄. Each response is expressed as mean (\pm SEM) percent of the baseline for that dose of vasopressor. Standard error bars, if not shown, are included within the height of the squares or circles for each data point. *P* values are reported for the overall difference between the MgSO₄ and control groups.

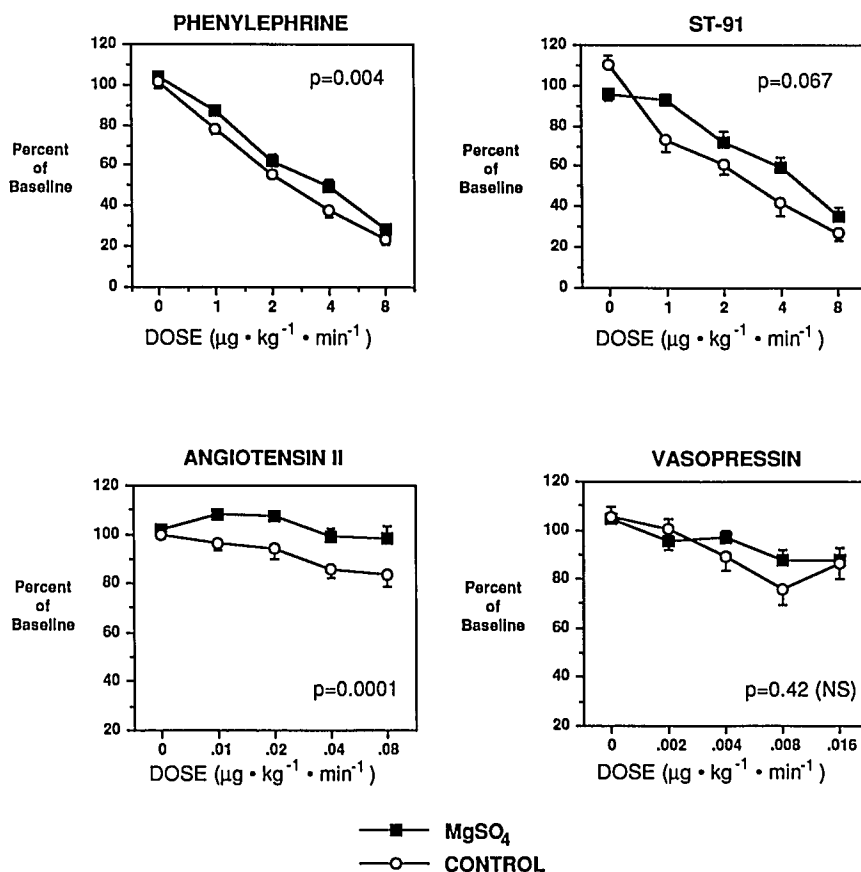


FIG. 4. Uterine blood flow dose-response curves for each vasopressor, with and without MgSO₄. Each response is expressed as mean (\pm SEM) percent of the baseline for that dose of vasopressor. Standard error bars, if not shown, are included within the height of the squares or circles for each data point. *P* values are reported for the overall difference between the MgSO₄ and control groups.

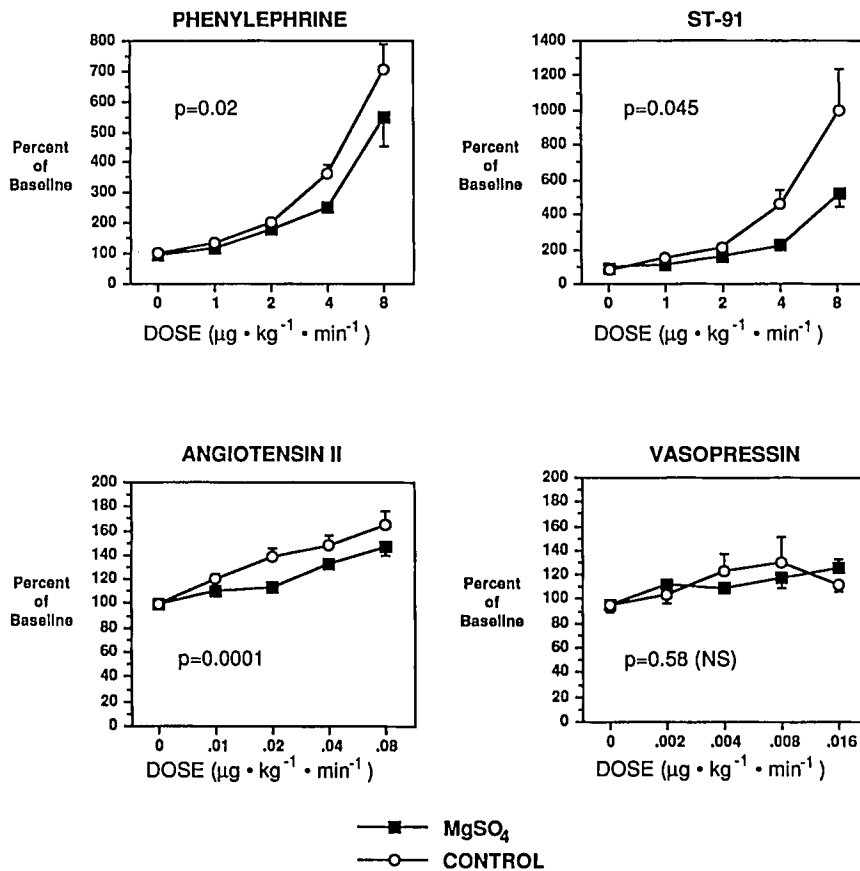


FIG. 5. Uterine vascular resistance dose-response curves for each vasopressor, with and without MgSO₄. Each response is expressed as mean (\pm SEM) percent of the baseline for that dose of vasopressor. Standard error bars, if not shown, are included within the height of the squares or circles for each data point. *P* values are reported for the overall difference between the MgSO₄ and control groups.

MgSO₄ reduced the hypertensive response to cocaine in term pregnant sheep.¹⁸ In addition, magnesium inhibits catecholamine release following sympathetic stimulation *in vivo*.¹⁹

Results of the present study can be better understood through a discussion of α_1 - and α_2 -adrenoceptor actions in the systemic and uterine vasculature. Phenylephrine, a postjunctional α_1 -adrenergic agonist, is a substrate for the same neuronal reuptake mechanism as NE.²⁰ Phenylephrine's effects at postjunctional α_1 -adrenoceptors are not susceptible to antagonism by calcium-channel blockers.²¹

ST-91 activates α_2 -adrenoceptors located both pre- and postjunctionally in the blood vessel wall. Prejunctional α_2 adrenoceptors inhibit NE release from the neuron into the neuromuscular junction. Activation of postjunctional α_2 adrenoceptors causes vasoconstriction.²² ST-91 acts predominantly as a vasopressor through activation of these postjunctional α_2 adrenoceptors.^{22,23}

Postjunctional α_2 -adrenoceptor stimulation is accompanied by calcium influx across the cell membrane, activating intracellular contractile proteins.²⁴ Calcium-channel blockers reduce muscle contraction by inhibiting this transmembranous calcium influx.^{24,25} In addition, α_2 -adrenoceptors stimulate the release of endothelium-derived

relaxing factor *via* a calcium independent mechanism.^{26,27} Thus, calcium-channel blockade by MgSO₄ may block the effects of postjunctional α_2 -adrenoceptors and allow the vasodilating actions of α_2 -agonists to prevail.²⁸

In the present study, MgSO₄ significantly attenuated the systemic vascular effects of *only* the α_2 -adrenergic agonist ST-91, and it attenuated the uterine vascular effects of *both* the α_1 - and α_2 -adrenergic agonists. Thus, the effect of magnesium on systemic postjunctional α_2 -adrenoceptors appeared to have greater importance than its effects on NE release and reuptake at systemic nerve terminals. In contrast, Lee *et al.*¹⁰ showed that MgSO₄ blunted the increase in maternal mean arterial blood pressure in response to fixed angiotensin II and NE boluses in a dose-dependent fashion in pregnant rabbits. One potential flaw in the design of that study was the lack of control animals; thus, other confounding factors, such as the fluid volume infused, order of dose administration, and time in the laboratory, could not be separated from the effects of MgSO₄. Furthermore, α_1 - and α_2 -adrenoceptor distribution differs according to the vascular bed, vessel size, and/or species that is studied.²² For example, relative proportions of α_1 - and α_2 -adrenoceptors appear to differ between the uterine and systemic vasculature. Magness and Rosenfeld²⁹ observed that the uterine vasculature of

gravid ewes was more responsive than was the systemic vasculature to α_1 -adrenergic agonists. Furthermore, during *in vitro* investigations of near-term gravid ewes, uterine artery smooth muscle contraction was primarily mediated by α_1 -adrenoceptors.³⁰ α_2 -adrenoceptors, though potentially present, were much less important in mediation of uterine artery contraction.³⁰ In contrast, the present study showed a marked increase in UVR in response to ST-91, suggesting that α_2 -agonists can play a significant role in uterine artery smooth muscle contraction.

The study by Chestnut *et al.*² showed that $MgSO_4$ worsened the hypotensive response to hemorrhage in gravid ewes. Although we speculated that $MgSO_4$ attenuated systemic vascular smooth muscle response to endogenous vasopressors, in the present study this hypothesis was confirmed only with the α_2 -adrenergic agonist ST-91. Of course, the intravenous infusion of individual vasopressor agents does not necessarily mimic the global compensatory response to a cardiovascular stress such as hemorrhage. Not only is there regional variation in the density of adrenergic receptors, but undoubtedly there is variation in the local concentration of endogenous vasopressors at their various sites of action. Further, magnesium may not affect vascular tone solely by direct action. For example, $MgSO_4$ may attenuate the endogenous release of catecholamines, angiotensin II, and/or AVP in response to hemorrhage. Cohen and Kitzes¹⁹ observed that $MgSO_4$ inhibited catecholamine release in humans. In addition, during epidural anesthesia-induced sympathetic blockade, Peters *et al.*³¹ demonstrated that blood pressure is partially maintained by vasopressin release in nonpregnant dogs. Thus, blockade of vasopressin release could be one mechanism by which $MgSO_4$ decreases maternal blood pressure during epidural anesthesia and/or hemorrhage.^{4,7-9}

Another possible explanation for our findings is that $MgSO_4$ attenuates the systemic vascular responses to endogenous vasopressors other than α_2 -adrenergic agonists *only* in the presence of hypotension or hypovolemia, neither of which were present in this study. The vasopressor agents used in this study have complex neural, hormonal, and direct cardiac effects.^{32,33} As a result, their net effect on the global responses examined in this study is a result of many actions. Thus, the present study does not elucidate all potential mechanisms or sites at which magnesium may have an effect.

In conclusion, $MgSO_4$ attenuated the hypertensive response to the α_2 -adrenergic agonist ST-91 but not the response to phenylephrine, angiotensin II, or AVP. Furthermore, $MgSO_4$ significantly attenuated the increase in UVR during phenylephrine, ST-91, and angiotensin II infusions and the decrease in UBF during phenylephrine and angiotensin II but not AVP infusions. $MgSO_4$ nearly significantly attenuated the decrease in UBF during ST-

91 infusion. Although caution must be used in extrapolating these data to humans, the present study suggests that $MgSO_4$ antagonizes the effects of endogenous α_2 -adrenergic agonists on the systemic vasculature. In addition, $MgSO_4$ seems to antagonize the effects of α_1 -adrenergic agonists, α_2 -adrenergic agonists, and angiotensin II on the uterine vasculature, resulting in some protection of UBF. This effect of $MgSO_4$ on the uterine vasculature may help protect the fetus in situations of maternal stress.

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