TITLE: CIRCULATORY RESPONSE TO CEREBRAL COMPRESSION AFTER α-ADRENERGIC AND VASOPRESSIN BLOCKADE IN FETAL SHEEP

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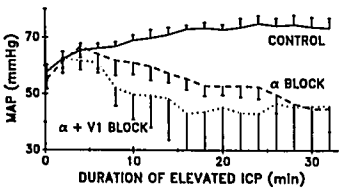
Difficult labor is associated with elevated fetal plasma levels of catecholamines and arginine vasopressin (AVP). In fetal sheep, cerebral compression without decreased $Pa0_2$ increases mean arterial pressure (MAP) and progressively increases plasma catecholamines and AVP. We evaluated the role of the α-adrenergic system and AVP in producing peripheral vasoconstriction and preserving cerebral 0_2 consumption ($CMR0_2$) during cerebral compression.

Near-term fetal sheep were catheterized for blood flow measurements (ml/min/100g) with radiolabelled microspheres 2 days prior to the experiment. Cerebral compression was produced by ventricular infusion of mock cerebrospinal fluid. Intracranial pressure (ICP) was elevated to baseline MAP of each animal over a 2 min period and then kept fixed for 30 min. Data were analyzed by ANOVA with repeated measures and Dunnett's test ($p<.05$). Three groups were studied: control (n=5); α-adrenergic blockade (phentolamine; 2 mg/kg + 1.5 mg/kg/hr, iv; n=6); combined α-adrenergic + AVP V1 receptor blockade (phentolamine+Manning compound 10 μg/kg iv;n=3).

MAP increased during the first 6 min in all groups (Figure). In the control group, MAP increased further and stabilized by 16 min, whereas in both blocker groups MAP returned to baseline levels. At 30 min in the control group, decreases in blood flow occurred in small intestine (295 ± 48 to 112 ± 41), skin (19 ± 3 to 6 ± 1) and kidney (184 ± 12 to 80 ± 34), but not in placenta (270 ± 29 to 278 ± 31) (±SE). One animal in each of the blocker groups experienced cardiovascular collapse prior to 30 min. In the remaining animals, intestinal and skin blood flow were not significantly changed. In the control group the increase in MAP maintained cerebral blood flow (CBF) at a level sufficient to preserve $CMR0_2$ (4.0 ± .4 to 3.3 ± .4 ml 0_2/min/100g), but with α-adrenergic blockade, CBF fell to near-zero levels.

We conclude that the α-adrenergic and AVP pressor systems are critical for preserving $CMR0_2$ during persistent elevation of ICP in the fetal sheep. Other systems (e.g ß-adrenergic system) may be recruited during brief, transient ICP elevations, but in the absence of α-adrenergic tone, the response is shortlived. (Supported by HL-38285)



A945

TITLE: MYOCARDIAL DEPRESSION INDUCED BY MAGNESIUM AND NIFEDIPINE IN THE ISOLATED PERFUSED RAT HEART

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Introduction: Magnesium (Mg) is commonly used in the treatment of preterm labor and preeclampsia. Recently nifedipine (Ni), a calcium channel blocker, has also been used as an oral tocolytic and an antihypertensive agent in the management of pregnancy-associated hypertension.[1] There have been case reports of marked hypotension occuring when nifedipine was employed for control of hypertension in patients receiving magnesium.[2] This study was designed to determine the effects of magnesium and nifedipine on the isolated rat heart.

Methods: Thirty Sprague-Dawley rats were heparinized and lightly anesthetized with ether. Each heart was excised, attached to a Langendorff system, and perfused with an oxygenated Krebs-Henseleit solution containing MgSO4 2.4 mEq/L at 37.5 C. After a 15 minute equilibration period, heart rate (HR), left ventricular pressure (LVP), and dP/dt were recorded, and the hearts were randomly divided into 3 groups. In group 1 (Mg) ,the Mg concentration of the perfusate was increased to 6.4 mEq/L. In group 2 (Ni), nifedipine, 2 ug/min, was infused via a side port. In group 3 (Mg+ Ni), the Mg concentration was increased to 6.4 mEq/L and Ni was infused (2ug/min). After a ten minute equilibration period, measurements were repeated. A one-way analysis of variance and student's t-test were used for statistical analysis. $P < 0.05$ was considered significant.

Results: There were no significant differences between the groups in baseline HR, LVP, and dP/dt. There was a significant reduction in LVP and dP/dt in all groups. In addition, there was a significant reduction in HR in the Mg and Mg + Ni groups. Ni + Mg resulted in a significantly greater % decrease in LVP (-56%) than either Mg (-35%) or Ni (-37%) ($p<.001$). Ni + Mg also produced a greater % decrease in dP/dt (-73%) than either Mg (-46%) or nifedipine (-51%) ($p<.001$).

Discussion: This study demonstrates that independently Mg and Ni produce myocardial depression in the isolated rat heart model. Furthermore, the combined effect of these two drugs produces a greater degree of myocardial depression than either drug alone. This effect is likely the result of calcium channel antagonism by both drugs. The results of this study suggest caution when Mg and Ni are combined in clinical practice because of the profound myocardial depression that may occur.

[1]Br J Obstet Gynecol 93:933-937,1986.
[2]Am J Obstet Gynecol 159:308-309,1988.