TITLE: CARDIAC EFFECTS OF RITODRINE AND MAGNESIUM SULFATE

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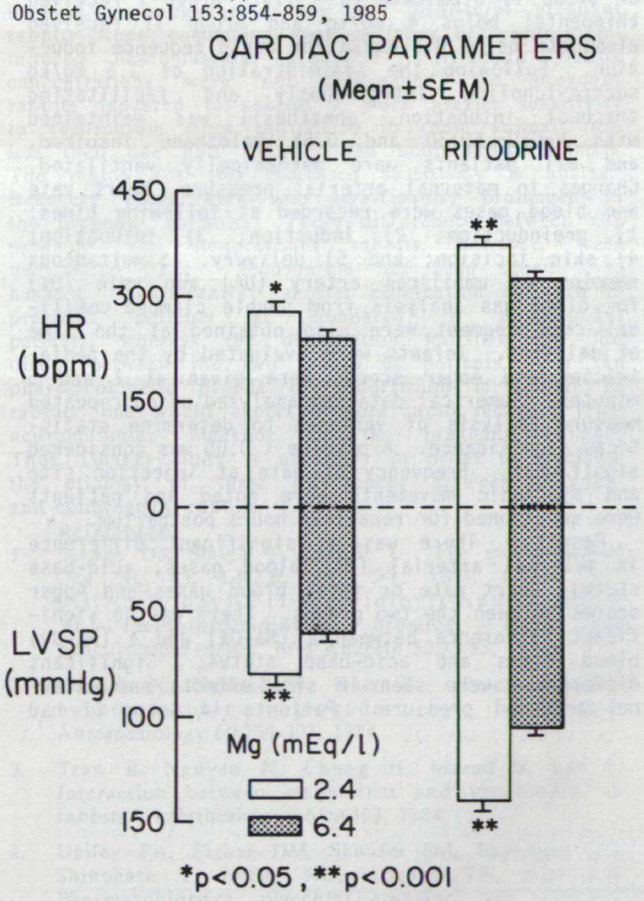
INTRODUCTION. Preterm labor complicates a significant number of pregnancies. Prematurity accounts for over 50 percent of all perinatal morbidity and mortality. In an effort to minimize the number and severity of maternal complications encountered with the use of beta-adrenergic therapy, both magnesium sulfate (Mg) and a beta-adrenergic drug (ritodrine) have been used together.[1] To our knowledge no studies have examined the precise cardiac effects of combined use of these two drugs. We, therefore, investigated the cardiac effects of Mg and ritodrine in the isolated perfused rat heart.

METHODS. Twenty Sprague-Dawley rats were heparinized and anesthetized with ether. The hearts were rapidly excised and arrested in iced saline and attached to a Langendorff apparatus. Krebs-Henseleit solution (KHS), aerated with O_2 95% and CO_2 5% constantly perfused the heart in a waterbath chamber at 37°C. A balloon catheter was inserted through the mitral valve into the left ventricle to measure systolic and diastolic pressures(LVSP,LVDP). Atrial and ventricular electrodes were placed and heart rate(HR), PR and QT intervals were measured. The hearts were randomized so that in addition to the KHS half(N=10) were perfused with ritodrine 100ng/L, and half (N=10) were perfused with the vehicle for ritodrine(acetic acid, sodium hydroxide, sodium metabisulfate and sodium chloride). After 20 minutes hemodynamic parameters were measured. Subsequently, the Mg concentration in the KHS for both groups was increased from 2.4 mEq/L to 6.4 mEq/L for 10 minutes, after which the above cardiac measurements were taken. Data is reported as $\bar{X} \pm$ SEM and was analyzed by Student's t-tests with $p < 0.05$ considered significant.

RESULTS. As compared to the hearts that were perfused with the vehicle, ritodrine produced a significant rise in the HR and LVSP and shortened the PR and QT intervals. Ritodrine's cardiac effects were attenuated by a high concentration of Mg (6.4 mEq/L). The addition of a high concentration of Mg to the perfusate with the vehicle for ritodrine caused a significant decrease in HR and LVSP.

DISCUSSION. Beta-agonists are administered to stop preterm labor because they stimulate the $beta_2$ receptors in the myometrium thereby decreasing the frequency and intensity of uterine contractions. The cardiac effects of this therapy cause significant increases in HR, SV, and cardiac output and may produce angina, ectopy, and pulmonary edema. Mg competes with calcium in the myometrical cell to inhibit the contractile reaction of actin and myosin. The addition of a high concentration of Mg to the ritodrine infusion significantly reduced the chronotropic and iontropic effect of ritodrine alone. Mg attentuates ritodrine's effects due to its unique action on cardiac function. An increase in PR and QT interval, bradycardia and decreased contractility can occur at Mg concentrations of 5-10 mEq/L.[2]

Recently, Mg has been shown to be as successful as ritodrine as the primary tocolytic agent and produced less maternal side effects.[3] Although we have shown that combining Mg and ritodrine reduces myocardial work as compared to ritodrine alone, we do not advocate the routine use of dual-agent tocolysis. Combined use of Mg and ritodrine should only be used for treatment of labor refractory to Mg.

References.

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