Title: MAGNESIUM SULFATE-INDUCED RELAXATION OF ISOLATED HUMAN UTERINE ARTERIES

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Introduction. Magnesium sulfate ($MgSO_4$) is widely used in the management of preeclamptic patients and in premature labor. It produces mild to moderate vasodilation and is thought to improve uterine blood flow by depressing uterine hypermotility. Several mechanisms of action for the dilatory effect of $MgSO_4$ in various blood vessels have been suggested. The present study was undertaken to investigate the mechanism of action and effects of $MgSO_4$ in the isolated human uterine artery since, to our knowledge, no such studies have been done.

Methods. Use of uterine arteries from patients undergoing hysterectomy was approved by the Institutional Review Board. Ring sections (2 mm in length) of uterine arteries (ascending branch) were mounted in 5 ml-volume chambers and suffused at a constant flow rate (4 ml/min) with a polystaltic pump. The suffusate was oxygenated Krebs-bicarbonate solution (pH 7.4) maintained at 37°C. Drugs were administered in the inflowing suffusate. Changes in isometric tension were measured by a force-displacement transducer and recorded. The arterial rings with 1 g resting tension were allowed to equilibrate for about 1 hour before commencement of the experiment. All drugs were prepared daily from powder forms. In some arterial segments the endothelium was removed mechanically by gently rubbing the inside of the arterial ring.

Results. The uterine arteries were precontracted by norepinephrine (NE) (1 μM) or by potassium chloride (KCl) (35 mM) in normal Krebs solution containing 1.2 mM $MgSO_4$. Increases in the concentration of $MgSO_4$ in the normal Krebs solution to 1.7 - 6 mM produced concentration-dependent inhibition of both NE- and KCl-induced contractions. The concentrations of $MgSO_4$ that produced 50% inhibition of the contractile responses to NE and KCl were 1.8 ± 0.3 mM (n=7) and 2.9 ± 0.2 mM (n=4), respectively. The $MgSO_4$-induced relaxations of NE- and KCl-induced contractions were reversed by increased calcium chloride (4.5 mM). However, the $MgSO_4$-induced relaxation was not reversed by indomethacin (5 μM), an inhibitor of prostaglandin synthesis, by methylene blue (10 μM), an inhibitor of guanylate cyclase, or by removal of the endothelium.

Conclusion. The results show that $MgSO_4$, at 2-3 mM (4-6 mEq/l) which are therapeutic blood levels, acts as a potent dilator in human uterine arteries. The results indicate that the inhibitory effect of $MgSO_4$ may be due to an interference with the availability or activity of intracellular calcium required for activation of vascular smooth muscle contraction. The vasodilatory effect of $MgSO_4$ does not appear to be due to the release of vasodilator prostaglandins or endothelium-derived relaxing factor, or to activation of guanylate cyclase. The results are consistent with the view that, in addition to its effect on uterine motility, $MgSO_4$, by its relaxing effect on uterine arteries, may be involved in producing adequate utero-placental perfusion.

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Reference.

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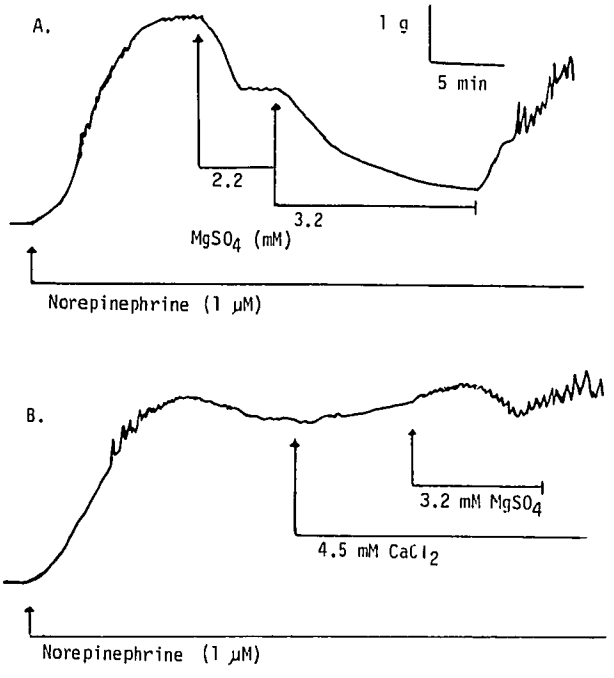

Figure 1. Experimental record showing $MgSO_4$-induced relaxation of norepinephrine-induced contraction (A) and, in same arterial ring, inhibition of relaxation by calcium chloride ($CaCl_2$) (B). Norepinephrine, at a concentration of 1 μM which produced less than a maximal contraction[1], was administered for 10 to 15 minutes until the contractile response stabilized before $MgSO_4$ or $CaCl_2$ was administered.