Title: MAGNESIUM SULFATE RESEMBLES A CALCIUM CHANNEL BLOCKER IN AIRWAY SMOOTH MUSCLE

Authors: K.S. Lindeman, M.D., C.A. Hirshman, M.D.C.M., A.N. Freed, Ph.D.

Affiliation: The Johns Hopkins Medical Institutions, Baltimore, MD 21205

Introduction. There is, at present, no good way of managing anesthesia in the parturient with asthma. Magnesium sulfate ($MgSO_4$), in addition to its action as a uterine tocolytic and a vascular smooth muscle dilator, has been shown to be effective *in vivo* as a bronchodilator. It has not been possible to study in a controlled manner the efficacy of $MgSO_4$ in the parturient with asthma. However, if we understand the mechanism by which magnesium acts on airways, we may be in a better position to use this as a therapeutic modality in our patients. The mechanism of magnesium's effect on smooth muscle has not been fully elucidated; however, evidence exits for magnesium-calcium interactions, and possibly, calcium channel blockade. Calcium for airway smooth muscle contraction is thought to be mobilized through two types of calcium channels: potential-dependent (PDCC) and receptor operated (ROCC). Nifedipine, a PDCC blocker, attenuates hypocapnia-induced bronchoconstriction in canine lung periphery but has no effect on acetylcholine (Ach) or dry air-induced constriction. To define a possible effect of magnesium on calcium channels, we studied the effect of MgSO4 on hypocapnia, Ach, and dry air-induced bronchoconstriction.

Methods. A wedged bronchoscope technique was used to measure resistance to collateral flow (Rcs) in the lung periphery of six anesthetized, intubated, and mechanically ventilated dogs. Baseline Rcs was measured. Bronchoconstriction was induced by a challenge of either hypocapnia, Ach, or high flow of dry air. Rcs was measured again postchallenge and was allowed to return to baseline. IV $MgSO_4$ was infused, and the challenge was repeated. Serum magnesium levels were determined pre and post $MgSO_4$ infusion. To examine the effect of repeated challenges on Rcs, the same dogs were anesthetized and instrumented on a separate occasion. Baseline Rcs was measured. Bronchoconstriction was induced as before, and the response was measured. When Rcs returned to baseline, a second identical challenge was performed. The results of both $MgSO_4$ and control experiments were analyzed using multifactor ANOVA for repeated measures.

Results. $MgSO_4$ diminished the response to hypocapnic challenge ($p<0.01$) (Figure 1). Repeated challenges alone resulted in an enhanced response following the second challenge as compared to the first (Figure 2). $MgSO_4$ did not affect either Ach or dry air-induced constriction. Serum magnesium levels before $MgSO_4$ administration were 1.59 ± 0.04 meq/l (mean $\pm$ SE) and rose to 6.20 ± 0.13 during the $MgSO_4$ infusion.

Discussion. The actions of $MgSO_4$ in the lung periphery bear a striking resemblance to those of nifedipine. Like nifedipine, $MgSO_4$ does not appear to act as a nonspecific smooth muscle dilator, as evidenced by its lack of effect on Ach or dry air-induced constriction. Instead, $MgSO_4$ appears to act through a selective mechanism that may be similar to the mechanism of action of nifedipine. Hypocapnia is thought to induce bronchoconstriction by potentiating the influx of extracellular calcium through PDCC. In contrast, dry air-induced constriction appears to act through some mechanism other than PDCC blockade, while Ach probably acts through ROCC. Thus, our findings are consistent with the idea that $MgSO_4$ acts in the airway as a PDCC blocker. Finally, since this effect occurred at serum concentrations that are considered to be therapeutic in the treatment of preeclampsia and preterm labor, $MgSO_4$ may be useful in the prevention of bronchospasm in the obstetric patient with asthma.

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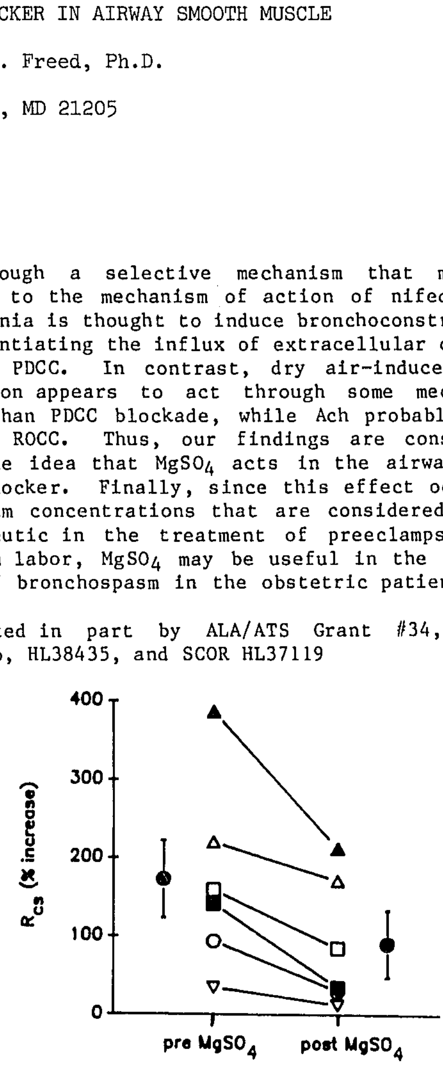

Figure 1. Effect of $MgSO_4$ on repeated challenges of hypocapnia. Individual data presented as % increase in Rcs recorded 30s postchallenge.

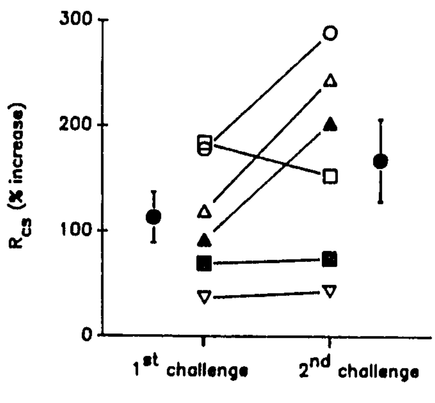

Figure 2. Effect of repeated challenges of hypocapnia. Individual data presented as % increase in Rcs recorded 30s after the first and second challenge.