Title: EFFECTS OF MAGNESIUM ON THE ISOLATED RAT HEART: INTERACTION WITH INHALATIONAL ANESTHETICS

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Patients who require anesthesia may have abnormal serum magnesium levels secondary to metabolic abnormalities, drug side effects (e.g. diuretics), or therapeutic administration of magnesium for seizure prophylaxis in pre-eclamptic patients. Both high and low levels of serum magnesium are associated with alterations in cardiac conduction, automaticity and force of contraction (1). Hypomagnesemia increases sinus node automaticity and can lead to development of potentially lethal ventricular dysrhythmias. Hypermagnesemia depresses automaticity and conduction, leading ultimately to complete heart block and cardiac arrest at levels of 10-15 mEq/L. Since inhalational anesthetics also have negative chronotropic and inotropic effects, we examined the combined effects of magnesium and inhalational anesthetics on the performance of isolated perfused rat hearts.

Methods. We employed the Langendorff apparatus to perfuse ex vivo hearts with Krebs-Henseleit solution (KHS) aerated with 95 per cent O_2, and 5 per cent CO_2 warmed to 37°C. Ten to thirteen adult male Sprague-Dawley rats per treatment group were heparinized, then anesthetized with ether. Each heart was rapidly excised, arrested in iced saline, and suspended via the aortic root on the Langendorff apparatus, allowing retrograde aortic perfusion with oxygenated KHS. ECG electrodes were placed and a balloon catheter inserted in the left ventricle provided a continuous tracing from which we measured heart rate, left ventricular pressure and dP/dt. Baseline data were obtained after a 15-minute equilibration period. Each heart was then perfused sequentially with KHS containing low, normal, and high levels of magnesium (0.8, 2.4, 7.3 mEq/L) in combination with halothane (1 and 2 MAC), isoflurane (1 and 2 MAC), or no anesthetic (control). Five minutes were allowed for equilibration with each new solution before data were recorded. Following the third magnesium dose, all hearts were again perfused with standard KHS without anesthetic and values were measured 5, 10, and 15 minutes later. Heart rate and dP/dt were analyzed separately by non-parametric methods for effect of magnesium, anesthetic, and interaction between the two. Multiple comparisons were made using the Bonferroni correction with a signficance set at a p-valve less than 0.05.

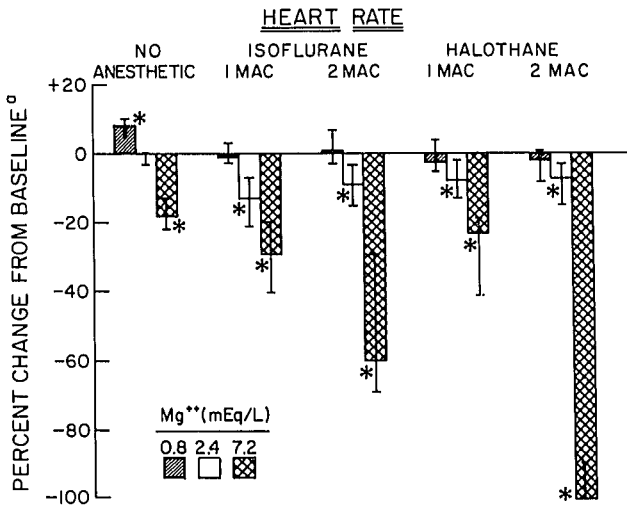
Results. Values for control groups (no anesthetic agent) showed that low magnesium levels caused increased heart rate and contractility while high magnesium caused decreased heart rate and contractility. Isoflurane and halothane caused independent depression of heart rate and contractility at either 1 MAC or 2 MAC. The two agents had similar effects on heart rate, but halothane had a significantly more depressant effect on dP/dt than isoflurane at equivalent MAC. Finally, there were significant interactions between anesthetic agents and magnesium.

The combination of high magnesium with either anesthetic at 2 MAC depressed heart rate in a synergistic fashion (Figure). The mechanism involved heart block (2:1 or 3:1) in the case of isoflurane, and cardiac arrest or near-arrest (HR < 10/minutes) in the case of halothane.

Discussion. Both magnesium and anesthetic agents independently influence heart rate and contractility in vivo. Low magnesium produces positive chronotropic and inotropic effects, and high magnesium produces negative effects. Halothane has a more depressant effect on the myocardium than isoflurane; however, this study demonstrated that both inhalational agents act to lower the threshold for heart block and cardiac arrest as well as to significantly enhance myocardial depression at high magnesium levels. These synergistic actions may result from interference with ion transport mechanisms responsible for inotropy and conduction. If similar effects occur in vivo, the risk of significant cardiovascular depression is increased in hypermagnesemic patients undergoing general anesthesia.

Reference.

1. Rude RK, Singer FR: Magnesium deficiency and excess. Ann Rev Med 32:245-259, 1981



a Bars indicate median percent deviation from baseline ± 25th percentiles.

*Differs significantly from baseline with $p < .05$

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