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The Effects of Magnesium Salts on the Duration of Epinephrine-Induced Ventricular Tachyarrhythmias in Anesthetized Rats

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The effects of $MgSO_4$ or $MgCl_2$ infusion on the duration of epinephrine-induced cardiac arrhythmia were evaluated in male rats anesthetized with either halothane or pentobarbital. In addition, the duration of epinephrine-induced arrhythmia in pentobarbital (50 mg/kg) anesthetized rats was compared with the duration of arrhythmia in halothane (1.5%) anesthetized rats. During halothane anesthesia $MgSO_4$ or $MgCl_2$ infused at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ for 20 min caused a significant reduction in the duration of arrhythmia (100% and 80%, respectively) following a 4-μg/kg injection of epinephrine and a significant threefold reduction in arrhythmia duration for each salt following an 8- or 16-μg/kg injection of epinephrine. Significantly shorter periods of arrhythmia after each dose of epinephrine were seen in rats anesthetized with pentobarbital than were seen in rats anesthetized with halothane. No significant difference was seen between $MgSO_4$ or $MgCl_2$ infusions in any of these studies.

Twenty-minute infusions of $MgSO_4$ (8 $mg \cdot kg^{-1} \cdot min^{-1}$) were compared with propranolol (0.03 $mg \cdot kg^{-1} \cdot min^{-1}$) and verapamil (0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) infusions on the duration of arrhythmia after epinephrine (8 μg/kg) injections in halothane anesthetized rats. $MgSO_4$ and propranolol infusion caused a significant reduction in the duration of arrhythmia (81% and 70%, respectively). Verapamil infusion caused only a 48% reduction in arrhythmia duration. While there was no significant difference between $MgSO_4$ or propranolol, both caused a significantly greater reduction in arrhythmia than verapamil.

$CaCl_2$ (0.15 $mM \cdot kg^{-1} \cdot min^{-1}$) infusion for 5 min caused a significant fivefold increase in the duration of arrhythmia during halothane anesthesia. $MgSO_4$ (8 $mg \cdot kg^{-1} \cdot min^{-1}$ or 16 $mg \cdot kg^{-1} \cdot min^{-1}$) infusion for 20 min caused a significant dose-dependent reduction in the $CaCl_2$-caused increase in arrhythmia duration.

The results of this study show that magnesium salts effectively reduce the duration of epinephrine-induced ventricular tachyarrhythmias. In addition, under the conditions of this study, magnesium salts appear to compare favorably with propranolol and verapamil in the control of epinephrine-induced arrhythmia in rats anesthetized with halothane. (Key words: Anesthetic, volatile: halothane. Heart: dysrhythmia. Ions: magnesium; calcium. Sympathetic nervous system: epinephrine.)

MAGNESIUM SALTS have been reported to be effective for the treatment of atrial, junctional, and ventricular arrhythmias resulting from myocardial ischemia,[1] digitalis poisoning,[2] alcoholism,[3] diuretic therapy,[4] and coronary artery disease.[5] Indeed, in many instances, magnesium salts have been shown to be effective in situations where conventional antiarrhythmic agents such as lidocaine and bretylium have failed.[6] The mechanism by which magnesium converts polymorphous arrhythmias to normal sinus rhythm is thought to involve cellular membrane transport systems for potassium, sodium, and calcium. Specifically, magnesium appears to inhibit the efflux of potassium, suppress inward sodium movement, and mimic calcium channel blocking drugs by inhibiting cellular calcium uptake.[7,8] Because pharmacologic agents that reduce sodium and potassium conductance[9,10] and inhibit calcium uptake[11] tend to ameliorate arrhythmia, it was the objective of this study to evaluate the effectiveness of $MgSO_4$ or $MgCl_2$ for the treatment of ventricular arrhythmia often associated with epinephrine usage during halothane anesthesia.

Methods

Common white male rats weighing 225–275 g were used throughout the study. Following protocol approval by the Michael Reese Hospital Institutional Animal Care Committee, nonfasted male rats were surgically prepared for study after induction of anesthesia with 1.5% halothane in 100% oxygen (in some experiments, rats were anesthetized with intraperitoneal pentobarbital 50 mg/kg). After tracheostomy, the rats' lungs were mechanically ventilated with a small animal respirator set to deliver a tidal volume of 3.5 ml at 40–50 breaths per min. Respiratory rate was adjusted until an arterial blood carbon dioxide partial pressure of 40–45 mmHg was achieved. Following this, catheters were implanted into a carotid artery for the measurement of blood pressure and subclavian veins for the administration of magnesium salts or epinephrine. Needle electrodes were inserted subcutaneously in the upper aspect of each limb for the monitoring of lead II of the ECG.

The efficacy of $MgSO_4$ ($MgSO_4$ anhydrous, Sigma Chemical, St. Louis, MO) and $MgCl_2$ ($MgCl_2$ dihydride, Sigma Chemical) in the treatment of epinephrine-induced arrhythmia during halothane anesthesia was demonstrated in two ways: 1) effect on the duration of epinephrine-induced arrhythmia; and 2) changes in the epinephrine arrhythmic threshold. The purpose of these experiments was to demonstrate that the duration of epinephrine-induced arrhythmia in the rat is a quantifiable

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endpoint that compares favorably with commonly used laboratory methods that derive an epinephrine arrhythmic threshold as an endpoint. In addition, the comparative effects of $MgSO_4$, verapamil HCl (Sigma Chemical), and propranolol HCl (Sigma Chemical) on the duration of epinephrine-induced arrhythmia were determined. These experiments were conducted in order to compare the antiarrhythmic effectiveness of magnesium salts with the effectiveness of clinically accepted antiarrhythmic agents. Finally, the effect of $CaCl_2$ ($CaCl_2$ anhydrous, Sigma Chemical) infusion and $MgSO_4$ treatment on the duration of epinephrine-induced arrhythmia was evaluated. These studies explore the possibility that magnesium may produce its antiarrhythmic effects by inhibiting intracellular cellular calcium transport.

The effect of $MgSO_4$ on the epinephrine arrhythmic threshold was determined in halothane anesthetized rats as previously described by Miletich *et al.*[12] The epinephrine arrhythmic threshold is the dose of epinephrine that, upon iv injection over a 3–4-s period, causes three or more continuous or intermittent premature ventricular contractions within 15 s of injection. It is derived by mathematical interpolation from the dose of epinephrine that produces at least three premature ventricular contractions and a lower dose that does not. In our study, the dosages of epinephrine were purposely set at 0.5 μg/kg intervals. Therefore, if 10 μg/kg of epinephrine produced three or more premature ventricular contractions while 9.5 μg/kg did not, the arrhythmic threshold would be taken to be 9.75 μg/kg.

After completion of preparatory surgery under 1.5% halothane anesthesia, either $MgSO_4$ anhydrous or $MgCl_2$ dihydride was infused by constant infusion pump *via* subclavian vein at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ for 20 min. The magnesium salt concentration was adjusted so that the total volume infused was 2 ml per animal. Control animals received 2 ml of saline over a 20-min period. Immediately following the 20 min infusion, each animal was given an initial standardized dose of 0.5 μg epinephrine to establish catheter patency. Slight increases in heart rate or blood pressure were taken to mean that the subclavian catheter was functional. A second standardized dose of 12 μg/kg of epinephrine was then given to each rat. It had been determined earlier that with this dose most nontreated rats showed arrhythmias while all magnesium-treated rats did not. The 12 μg/kg dose served as an indicator of the direction in which to proceed in order to establish the arrhythmic threshold, *i.e.*, higher or lower doses of epinephrine. This practice greatly decreased the number of epinephrine injections necessary to determine the threshold. A period of 10 min was allowed between each injection. The arrhythmic threshold dose of epinephrine could usually be established in five to six injections over a period of about 60 min. In situations where numerous epinephrine injections were made, the arrhythmic threshold had a tendency to "drift." These animals were discarded and not used for tabulation of data.

In an additional group of animals, the effect of 20 min $MgSO_4$ anhydrous or $MgCl_2$ dihydride (8 $mg \cdot kg^{-1} \cdot min^{-1}$) on the duration of epinephrine-induced arrhythmic episodes was measured in either halothane or pentobarbital anesthetized rats. In the rat, epinephrine-induced arrhythmias tend to occur in a single, uninterrupted chain, the duration of which is proportionate to dose of epinephrine injected. The arrhythmic episodes are characterized by premature ventricular contractions, ventricular tachycardia, bigemini, skipped beats, and various other forms of arrhythmia. Following induction of anesthesia with either halothane (1.5% in 100% oxygen) or pentobarbital (50 mg/kg), each rat received injections of increasing dosages of epinephrine (4, 8, and 16 μg/kg) and the duration of arrhythmia was measured. A minimum of 10 min was allowed between injections so that blood pressure and heart rate could return to preinjection values. Control rats received the same epinephrine dosages. However, control rats received 20 min of saline infusion. Both experimentally treated and control rats received a total infused volume of 2 ml over the 20-min period.

In another series of experiments groups of rats anesthetized with 1.5% halothane were infused as described for 20 min with either $MgSO_4$ anhydrous (8 $mg \cdot kg^{-1} \cdot min^{-1}$), verapamil HCl (0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$), or propranolol HCl (0.03 $mg \cdot kg^{-1} \cdot min^{-1}$) followed by injection of epinephrine (8 μg/kg) and the duration of the subsequent arrhythmic episode measured. The test dose for each drug was chosen on the basis of its minimal impact on blood pressure. The selected dose for each drug was the maximal testable dose that caused approximately a 10% reduction in mean arterial blood pressure during or following 20 min of infusion.

In a final set of experiments, rats anesthetized with 1.5% halothane were infused as described with $CaCl_2$ (0.15 $mM \cdot kg^{-1} \cdot min^{-1}$) for 5 min after which an 16 μg/kg injection of epinephrine was given and the duration of arrhythmia measured. Thirty minutes after this, $MgSO_4$ was infused at a dose of either 8 $mg \cdot kg^{-1} \cdot min^{-1}$ or 16 $mg \cdot kg^{-1} \cdot min^{-1}$ for 20 min followed by a repeat 5-min infusion of $CaCl_2$ and injection of epinephrine as just described. The duration of arrhythmia following each treatment was then compared.

Blood magnesium concentrations were determined in rats anesthetized with halothane (1.5%) and infused for 20 min with either $MgSO_4$ anhydrous or $MgCl_2$ dihydride at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$. In addition, blood magnesium concentrations were determined in rats anesthetized with pentobarbital (50 mg/kg) and infused for 20 min with $MgSO_4$ anhydrous (8 $mg \cdot kg^{-1} \cdot min^{-1}$). Ar-

terial blood samples of 1 ml each were drawn before magnesium salt infusion, immediately after 20-min infusion, 30 and 60 min after stopping magnesium salt infusion, and analyzed for magnesium by atomic absorption.[13] The blood samples were then centrifuged, the plasma drawn off, and diluted 1:50 with a 0.1% lanthanum solution. The magnesium concentration of each sample was then determined with a Perkin-Elmer® Model 280 atomic absorption spectrophotometer analyzer.

Statistical significance of data was determined by paired t test, simple t test, and analysis of variance (ANOVA) in conjunction with the Bonferroni multiple comparison procedure.[14] Data are reported as means ± SD or SE, with $P < 0.05$ considered statistically significant.

Results

Rats anesthetized with 1.5% halothane in 100% oxygen demonstrated continuous, uninterrupted episodes of arrhythmia that were proportional in duration to the dose of injected epinephrine (table 1). The arrhythmic episodes were characterized by premature ventricular contractions, ventricular tachycardia, bigemini, and a variety of other unidentifiable atrial and ventricular dysrhythmias. Rats anesthetized with pentobarbital (50 mg/kg) showed significantly reduced duration of arrhythmia at each dose of epinephrine tested (table 1).

Infusion of either $MgSO_4$ anhydrous or $MgCl_2$ dihydride solutions significantly reduced the duration of epinephrine-induced arrhythmic episodes during halothane anesthesia while $MgSO_4$ anhydrous infusion significantly reduced epinephrine arrhythmia during pentobarbital anesthesia (table 1). Similarly, infusion of $MgSO_4$ or $MgCl_2$ solution also significantly increased the epinephrine arrhythmic threshold dose, *i.e.*, the amount of epinephrine necessary to cause three or more premature ventricular contractions (table 2).

$CaCl_2$ infusion caused a fivefold increase in the duration of epinephrine-induced arrhythmia during 1.5% halothane anesthesia (table 3). $MgSO_4$ (8 $mg \cdot kg^{-1} \cdot min^{-1}$ or 16 $mg \cdot kg^{-1} \cdot min^{-1}$) infusion significantly reduced the $CaCl_2$-caused increase in arrhythmia duration.

TABLE 2. The Effects of Magnesium Salt Infusion on the Epinephrine Arrhythmic Threshold Dose in Halothane-Anesthetized Rats

Treatment	Epinephrine threshold*	n
Control	9.7 ± 3.1	9
$MgSO_4$ infused†	29 ± 6‡	8
$MgCl_2$ infused†	26 ± 6‡	6

All values are mean ± SD.
* The dose of epinephrine in μg/kg that caused three or more premature ventricular contractions in rats anesthetized with 1.5% halothane in 100% oxygen.
† $MgSO_4$ or $MgCl_2$ infused at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ for 20 min prior to epinephrine injection.
‡ Significantly different from control values $P < 0.05$.

The comparative effects of $MgSO_4$ anhydrous infusion with either verapamil HCl or propranolol HCl infusion in reducing the duration of epinephrine-induced arrhythmia can be seen in table 4. All three drugs significantly reduced the duration of epinephrine-induced arrhythmia when compared to pretreatment arrhythmic durations. However, $MgSO_4$ anhydrous or propranolol HCl caused a significantly greater reduction in the duration of arrhythmia as compared with verapamil HCl treatment.

Infusion of $MgSO_4$ anhydrous solution for 20 min at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ in rats anesthetized with halothane or pentobarbital caused significant reductions in both mean arterial blood pressure and heart rate (table 5). However, in each case, blood pressure and heart rate returned to preinfusion values 30 min later.

Blood concentrations of magnesium increased significantly following infusion of $MgSO_4$ anhydrous or $MgCl_2$ dihydride solutions in rats anesthetized with halothane (table 6). However, after 60 min, blood magnesium returned to preinfusion levels. No significant difference was seen in blood magnesium levels between the two magnesium salt infusions. Similarly, blood magnesium levels

TABLE 1. Effects of Magnesium Salt Infusion on the Duration of Arrhythmia (in seconds) following Epinephrine Injection in Rats Anesthetized with Halothane or Pentobarbital

Treatment	4.0*	8.0*	16.0*	n
Pentobarbital (50 mg/kg)	0	7 ± 1.7	11 ± 2.4	6
Pentobarbital + $MgSO_4$	0	0§	0§	6
Halothane (1.5%)	11.5 ± 3†	27 ± 5†	52 ± 6†	15
Halothane + $MgSO_4$	0‡	9 ± 5‡	13 ± 5‡	8
Halothane + $MgCl_2$	2.4 ± 1.8‡	11 ± 4‡	15 ± 4‡	6

Magnesium salts were infused at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ for 20 min prior to epinephrine injection.
Duration of arrhythmic episodes is in seconds ± SD.
* Dose of epinephrine in μg/kg.
† Halothane values significantly higher than pentobarbital values, $P < 0.01$.
‡ Magnesium-halothane treated values significantly less than halothane values, $P < 0.01$.
§ Magnesium-pentobarbital values significantly less than pentobarbital values, $P < 0.01$.

TABLE 3. Effects of $CaCl_2$ Infusion on the Duration of Epinephrine-Induced Arrhythmia following $MgSO_4$ Treatment during Halothane Anesthesia.

Treatment	Control	$CaCl_2$ infused
Epinephrine (16 μg/kg)	57 ± 4	248 ± 38*
Epinephrine (16 μg/kg) $MgSO_4$ (8 mg·kg^{-1}·min^{-1})	ND	163 ± 23†
Epinephrine (16 μg/kg) $MgSO_4$ (16 mg·kg^{-1}·min^{-1})	ND	71 ± 14‡

ND Values not determined.

Duration of arrhythmia expressed as mean seconds ± SD. $MgSO_4$ was infused for 20 min. $CaCl_2$ was infused 5 min at a dose rate of 0.15 mM·kg^{-1}·min^{-1}. Control- and $CaCl_2$-infused animals were anesthetized with 1.5% halothane.

* Significantly higher than control values, $P < 0.001$; n = 26.

† Significantly lower than nonmagnesium-treated $CaCl_2$ infused value, $P < 0.01$; n = 6.

‡ Significantly lower than magnesium (8 mg·kg^{-1}·min^{-1}) treated and $CaCl_2$ infused value, $P < 0.01$; n = 6.

increased significantly following $MgSO_4$ infusion in pentobarbital anesthetized rats (table 6). However, no significant difference in blood magnesium was seen at any time period between halothane or pentobarbital anesthestized rats.

Discussion

Existing methodologies for determining the electrical or rhythmic stability of the heart under various pathologic conditions usually depend upon two elements, iv injections of large doses of epinephrine and a scheme for quantifying the resultant arrhythmia.[15] Many commonly used methods quantify the resultant arrhythmia into an endpoint known as the epinephrine arrhythmic threshold, *i.e.*, the dose of epinephrine at which arrhythmia occurs. The method employed in our study, however, used as an endpoint the duration of arrhythmia following injection of selected doses of epinephrine. In the rat, arrhythmia following epinephrine injection tends to occur in a continuous uninterrupted chain. As can be seen in table 1, the duration of arrhythmia in seconds is proportional in linear fashion to the dose of epinephrine injected. In addition, multiple injections of the same dose of epinephrine showed no sign of tolerance in that the duration of arrhythmia after eight repetitive injections remained essentially unchanged. Thus, it would appear that in the rat the duration of epinephrine-induced arrhythmia is a useful and reproducible endpoint. Also, the duration of epinephrine-induced arrhythmic episodes seem to agree well with epinephrine arrhythmic threshold dosage measurements (table 2). Of critical importance, however, is that the duration of arrhythmia can be modified in a consistent manner by agents known to ameliorate arrhythmia (tables 1 and 4). In our study, both $MgSO_4$ and $MgCl_2$ significantly reduced the duration of arrhythmia following epinephrine injection. Likewise, verapamil, a calcium channel blocker, and propranolol, a β-adrenergic receptor blocker, were also effective in reducing the duration of arrhythmia. In this respect, $MgSO_4$ was as effective as propranolol and superior to verapamil in shortening the episodes of arrhythmia. However, it should be kept in mind that the dose employed for each agent was selected because of its minimal effect on blood pressure and not necessarily on its pharmacologic arrhythmic effectiveness. In addition, it is apparent that there was little difference in effectiveness between $MgSO_4$ and $MgCl_2$ in reducing the duration of arrhythmia (table 1).

Although 20 min of magnesium salt infusion in rats anesthetized with halothane or pentobarbital approximately doubled the average blood magnesium concentration, mean arterial blood pressure and heart rate were depressed by only 10% and 20%, respectively (tables 5 and 6). Thirty minutes after the termination of magnesium salt infusion, blood pressure and heart rate returned to normal while blood magnesium concentrations remained significantly higher than control values. While a statistical correlation was not performed, it would appear that the effects of magnesium on the duration of arrhythmia is dependent on blood magnesium concentration and unrelated to magnesium caused hemodynamic changes.

Magnesium has been shown to be effective in treating a variety of forms of serious arrhythmia. The severe ventricular arrhythmias frequently associated with digitalis intoxication have been successfully treated with magnesium salts in both the clinic and laboratory.[2] In addition, arrhythmias associated with ischemic heart disease, hypokalemia, hypomagnesemia, diuretic therapy, *torsades de pointes,* alcoholism, and myocardial infarction have all proven treatable by magnesium salt infusion.[4,5,16,17] In some instances, ventricular arrhythmia resistant to treat-

TABLE 4. Comparison of $MgSO_4$, Propranolol, or Verapamil Infusions on the Duration of Epinephrine-Induced Cardiac Arrhythmia

Treatment	Pretreatment Arrhythmia	Posttreatment Arrhythmia	n
$MgSO_4$ (8 mg·kg^{-1}·min^{-1})§	31 ± 6†	6 ± 3*‡	6
Verapamil (0.5 μg·kg^{-1}·min^{-1})§	29 ± 4	18 ± 3*	6
Propranolol (0.03 mg·kg^{-1}·min^{-1})§	27 ± 6	8 ± 4*‡	6

* Significantly lower than pretreatment arrhythmia duration time; $P < 0.01$.

† Duration of arrhythmia in seconds ± SD following injection of 8 μg/kg of epinephrine.

‡ Significantly lower than verapamil values, $P < 0.05$.

§ Dose of test drug that caused less than a 10% decrease in mean arterial blood pressure following 20 min of test drug infusion.

TABLE 5. The Effects of $MgSO_4$ Infusion on Mean Arterial Blood Pressure and Heart Rate in Rats Anesthetized with Either Halothane or Pentobarbital

	Mean Arterial Pressure mmHg			Heart Rate			
	Initial	Postinfusion	30 min	Initial	Postinfusion	30 min	n
$MgSO_4$ + Halothane	96 ± 5	86 ± 3*	97 ± 6	335 ± 15	280 ± 11*	320 ± 19	16
$MgSO_4$ + Pentobarbital	105 ± 4	89 ± 7*	104 ± 4	396 ± 17†	339 ± 21*†	380 ± 14†	7

Magnesium SO_4 was infused at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$. Blood pressure and heart rate were measured initially, immediately post-20 min $MgSO_4$ infusion, and 30 min after termination of magnesium infusion.

* Values significantly lower than initial premagnesium infusion values $P < 0.05$; values are mean ± SD.

† Pentobarbital (50 mg/kg) anesthetized values significantly higher than halothane (1.5%) value $P < 0.01$.

ment with proven antiarrhythmic agents have responded dramatically to the application of magnesium sulfate.[6]

The mechanism by which magnesium attenuates arrhythmia cannot be deduced from the data presented here. Even *in vitro* cardiac electrophysiologic studies have failed to clarify the specific role of magnesium in the alleviation of cardiac arrhythmias in humans.[18] However, given the ionic nature of magnesium, it is reasonable to speculate that magnesium may interact with the transmembrane movement of ions important to the genesis of the cardiac action potential. In support of this hypothesis are the experiments in our study that show the considerable increase in the duration of epinephrine-induced arrhythmia caused by $CaCl_2$ infusion can be significantly reduced in a dose-dependent fashion by $MgSO_4$ treatment (table 3). Indeed, 16 $mg \cdot kg^{-1} \cdot min^{-1}$ of $MgSO_4$ infusion for 20 min reduces the duration of arrhythmia to control or pre-$CaCl_2$ infusion values. Although myocardial calcium concentrations were not measured in our study, it would appear that elevated blood calcium concentrations potentiate halothane-epinephrine arrhythmia possibly through elevation of the intracellular calcium concentration. It has been shown that calcium plays a key role in the genesis of ventricular arrhythmia.[19] Although calcium ions are important mediators of normal electrical activity in cardiac cells, any pharmacologic agent or pathologic event that causes intracellular calcium overload also causes serious ventricular arrhythmia. How intracellular calcium overload results in arrhythmia is not known precisely, but it is believed that excessive intracellular calcium results in prematurely released calcium from the sarcoplasmic reticulum which in turn initiates an abnormal, transient, inward current across the cell membrane causing ectopic beats and arrhythmia.[19] Halothane may contribute to the intracellular calcium overload situation. It has been shown that halothane decreases the binding of free calcium to the sarcoplasmic reticulum membrane.[20] While this effect of halothane would not necessarily increase total cell calcium, it could cause an increase in the fraction of free unbound calcium responsible for the abnormal inward currents discussed above.

It has been shown that calcium channel blocking agents such as verapamil are very effective in preventing intracellular calcium overload and ventricular fibrillation in dogs.[21] Perhaps magnesium may function in a similar manner. The demonstration that magnesium inhibits the movement of extracellular calcium into myocardial muscle cells through a competitive process at the cell membrane may be of particular importance in this respect.[7] Indeed, some believe that magnesium may function as nature's natural calcium channel antagonist.[7,22,23]

In conclusion, data from this study show that magnesium salts were effective in reducing the duration of ventricular tachyarrhythmias as caused by iv epinephrine injection in rats anesthetized with pentobarbital or halothane. Magnesium salt treatment effectively lowered the epinephrine arrhythmic threshold. It would appear, under the conditions of this study, that $MgSO_4$ is as effective as propranolol or verapamil in the treatment of epinephrine caused ventricular tachyarrhythmia.

TABLE 6. Blood Magnesium Concentrations before and after Magnesium Salt Infusion in Halothane or Pentobarbital Anesthetized Rats

Mg Salt	Anesthetic	Normal Mg	Post-Mg Infusion†	30 min Mg‡	60 min Mg‡
$MgSO_4$	Halothane	2.7 ± 0.2	6.1 ± 0.8*	3.9 ± 0.4*	3.1 ± 0.4
$MgSO_4$	Pentobarbital	2.5 ± 0.1	5.1 ± 0.5*	3.3 ± 0.4*	2.6 ± 0.3
$MgCl_2$	Halothane	2.8 ± 0.2	5.7 ± 0.6*	3.7 ± 0.3*	2.5 ± 0.6

Values are mean mEq magnesium per liter plasma ± SE.

* Significantly higher than normal blood magnesium, $P < 0.01$; n = 5.

† Blood magnesium concentrations immediately following 20-min infusion with either $MgSO_4$ or $MgCl_2$ at a dose rate of 8 $mg \cdot kg^{-1} \cdot min^{-1}$ during halothane (1.5%) or pentobarbital (50 mg/kg) anesthesia.

‡ Blood magnesium levels 30 or 60 min after terminating magnesium infusion.

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