Hypertension

Effect of Magnesium L-Lactate on Blood Pressure in Patients with an Implantable Cardioverter Defibrillator

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BACKGROUND: Previous studies have evaluated the impact of oral magnesium on blood pressure; however, they used magnesium salts with low bioavailability, had methodological issues, and showed differing results.

OBJECTIVE: To evaluate the long-term blood pressure–lowering ability of oral magnesium L-lactate versus placebo in patients with implanted cardioverter defibrillators (ICDs).

METHODS: In this double-blind, 24-week trial, 50 patients with ICDs were randomized to receive magnesium L-lactate (6 tablets daily, supplying a total of 504 mg of elemental magnesium daily) or matching placebo for at least 12 weeks. Baseline intracellular and serum magnesium concentrations were determined. The primary efficacy endpoint was the mean sitting systolic blood pressure at 24 weeks.

RESULTS: In 50 patients who completed at least 12 weeks of follow-up, 86% of patients, regardless of randomization, had a baseline intracellular magnesium deficiency, but no patients had a serum magnesium deficiency. At 12 weeks, magnesium L-lactate significantly reduced systolic blood pressure compared with placebo (117.7 ± 11.8 vs 126.3 ± 16.7 mm Hg, respectively; $p = 0.04$). In the 45 patients who continued in the study through the 24-week time period, the systolic blood pressure reduction was maintained, but statistical significance was lost (118.1 ± 14.1 vs 125.5 ± 17.2 mm Hg, respectively; $p = 0.13$). Magnesium L-lactate did not impact diastolic blood pressure at either time period ($p \geq 0.75$ for both). Patients with a documented history of hypertension at baseline showed similar qualitative results to the primary analysis.

CONCLUSIONS: A large number of subjects with ICDs have an intracellular magnesium deficiency not captured through serum magnesium determination. The use of magnesium L-lactate in patients with an ICD results in significant improvement in systolic blood pressure at 12 weeks, which may be maintained through 24 weeks.

KEY WORDS: blood pressure, implantable cardioverter defibrillator, magnesium.

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Magnesium is the second most abundant intracellular cation, with less than 1% in the body found extracellularly. It has been demonstrated that intracellular magnesium levels are not related to serum concentrations, with intracellular repletion lagging behind serum levels in response to an intravenous infusion of magnesium.[1] Magnesium deficiency is common among patients with coronary heart disease but often goes untreated (or undertreated). Oral magnesium is available in many formulations, the majority of which are not significantly absorbed, ranging from 2% with magnesium oxide to 20% with magnesium chloride.[2] Magnesium L-lactate is a sustained-release oral formulation of magnesium with a higher bioavailability (41%) than that of other commonly used magnesium salts.[3]

Epidemiologic studies support the role that hypomagnesemia plays in the pathogenesis of hypertension.[4-7] However, clinical trials evaluating the effect of magnesium supplementation on blood pressure have shown inconsistent results, making its practical application as an antihypertensive controversial.[8-13] Motoyama et al.[8] provided 21 male patients with uncomplicated essential hypertension magnesium oxide (600 mg/day) for 4 weeks, followed by placebo for 4 weeks. They found that magnesium supplementation reduced patients' mean systolic blood pressure from 111 ± 6 mm Hg at baseline to 102 ± 6 mm Hg after 4 weeks ($p < 0.001$), which then increased to 108 ± 5 mm Hg ($p < 0.001$) after 4 weeks of subsequent placebo treatment. In an 8-week crossover study, 62 Japanese men and women with mild-to-moderate essential hypertension were randomized to re-

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ceive either magnesium oxide 480 mg/day or placebo.[9] During the follow-up period, average blood pressures (both systolic and diastolic) were significantly lower in patients receiving magnesium compared with those receiving placebo (–3.7 ± 1.3 and –1.7 ± 0.7 mm Hg, respectively; $p < 0.05$). Alternatively, a randomized, double-blind, placebo-controlled trial of 76 patients with type 2 diabetes and borderline hypertension at baseline trial found no beneficial impact of a magnesium oxide/zinc sulfate combination on either systolic or diastolic blood pressure.[10] Likewise, Doyle et al.[11] failed to identify a significant effect of a magnesium oxide–supplemented diet (21.6 mmol/day) on either systolic or diastolic blood pressure among 26 healthy normotensive individuals over a 28-day period in a placebo-controlled crossover trial.

To date, only 2 clinical trials have evaluated the impact of magnesium lactate on blood pressure.[12,13] In a prospective, double-blind trial, patients with mild-to-moderate hypertension were randomized to receive 30 mEq/day of magnesium (27.48 mEq /day magnesium lactate and 2.52 mEq/day magnesium citrate) or placebo for 6 months.[12] In patients with an average blood pressure of 159 ± 13 and 95 ± 4.8 mm Hg (systolic and diastolic, respectively), magnesium supplementation did not induce significant changes in either systolic or diastolic blood pressure compared with placebo.

There is also evidence that low body stores of magnesium increase the risk of abnormal heart rhythms, which may increase the risk of complications following a myocardial infarction.[14] In a pilot study completed in 20 patients with a history of arrhythmias requiring drug therapy, we found that 63.2% of patients had baseline intracellular magnesium concentrations below the normal reference range.[15] No deficiencies in other intracellular ions (phosphorus, chloride, calcium, potassium, or sodium) were seen. Following supplementation with magnesium L-lactate (504 mg of elemental magnesium daily) for 48 hours, the intracellular magnesium concentrations rose significantly ($p = 0.002$), with all patients achieving a concentration within the reference range. Treatment with placebo did not alter intracellular magnesium concentrations ($p = 0.32$).

Given the inconsistent efficacy data currently available with magnesium supplements in hypertensive patients, as well as the lack of trials in patients with arrhythmias, we designed the current study to evaluate the blood pressure–lowering ability of oral magnesium L-lactate versus placebo in patients with an implantable cardioverter defibrillator (ICD). The current investigation was a piggyback study of the Adjuvant Magnesium Trial (AdMag). The AdMag trial was planned to be a 12-month follow-up trial in 240 subjects with ICDs evaluating ICD shocks. That study could not be completed due to the problems with patient recruitment and patient tolerability due to the pill burden.

Methods

PARTICIPANTS

Trial participants were men and women, greater than 18 years of age, with either a newly implanted ICD or recent ICD shock (within the past 6 mo). No inclusion criteria related to baseline blood pressure or concomitant antihypertensive medications were used. Patients were excluded if they had an inability to swallow, a noncardiac disease with a survival prognosis of less than 12 months, hypermagnesemia, creatinine clearance less than 30 mL/min, lactic acidosis or systemic acidosis syndrome, or previous intolerance to magnesium L-lactate.

The study was completed in compliance with the Declaration of Helsinki and received approval from the Hartford Hospital institutional review board. All patients provided written informed consent before the study.

DESIGN

This was a 24-week, randomized, double-blind, placebo-controlled trial conducted at an urban teaching hospital in the US. Eligible patients were randomly assigned to receive magnesium L-lactate (Mag-Tab SR; Niche Pharmaceuticals, Roanoke, TX) 3 tablets twice daily (504 mg of elemental magnesium/day) or placebo for 24 weeks using an electronic random permuted block method with a block size of 10 patients per group (available at www.randomization.com). This was the same dose used in our pilot study by McBride et al.[15] Patients were stratified according to whether their ICD was newly implanted or they had an existing ICD but had received a recent ICD shock. Placebo and magnesium L-lactate tablets were matched in size, shape, and color to maintain blinding. Patients were instructed to take study medication without regard to meals. No specific dietary or drug use restrictions (including nutritional supplements) were designated.

Patients were evaluated at baseline, 12, and 24 weeks of therapy during their usual follow-up visit at our institution's ICD clinic. Demographic data including patient age, sex, ejection fraction, indication for ICD, and current medications were collected. Blood pressure readings were obtained through the use of bioelectrical impedance cardiography (ICG; Bio-Z, Cardiodynamics International Corp., San Diego, CA).[16,17] ICG sensors were placed bilaterally on the root of the neck and on the thorax at the level of the Xiphoid Process. Blood pressure was measured through the use of an oscillometric cuff placed 2.5 cm above the antecubital crease, with the bladder of the cuff placed over the brachial artery. Measurements were obtained when the ICG waveform indicator displayed signal strength of at least 75–100%. To minimize circadian variations in blood pressure, patients underwent evaluations at approximately

the same time of the day. Patients were instructed to refrain from smoking or consuming caffeinated beverages within 30 minutes of their appointment. Patients sat quietly for a minimum of 5 minutes prior to the blood pressure reading. Additionally, pill counts were performed at each follow-up appointment to ensure patient adherence throughout the study.

The primary outcome of interest was the mean sitting systolic blood pressure at 24 weeks. Additional outcomes included mean sitting systolic blood pressure at 12 weeks, and mean sitting diastolic blood pressure at both 12 and 24 weeks. Safety and tolerability assessments included the recording of all adverse events throughout the study, irrespective of suspected relation to study medication, and the monitoring of blood chemistries including serum magnesium and creatinine levels. In addition, we conducted a subgroup analysis in which blood pressure measurements were compared at each time point only in patients with a documented history of hypertension at baseline. Patients were classified as having a history of hypertension if, during their initial screening, hypertension was documented in the ICD clinic database as a prior condition in the past medical history. Patients were classified as having hypertension at baseline if their baseline blood pressure exceeded 140/90 mm Hg or 130/85 mm Hg for patients with diabetes and kidney disease, respectively. Additionally, we analyzed blood pressure at each endpoint based on whether patients had a baseline intracellular magnesium deficiency.

Intracellular magnesium concentrations were evaluated at baseline using Exatest kits (Intracellular Diagnostics, Inc., Medford, OR) by obtaining buccal scrape tissue samples prior to initiation of the study drug.[15]

STATISTICAL ANALYSIS

We calculated a sample size of 23 patients per group, which would provide 80% power to detect, at a 2-sided significance level of 0.05, an intergroup treatment difference of at least 6 mm Hg in mean systolic blood pressure between the magnesium L-lactate and placebo groups at 24 weeks, assuming a standard deviation of 7 mm Hg.[8]

Analyses were performed on all randomized patients with baseline values and at least one treatment period assessment (12 wk), without major protocol violations. Continuous variables are presented as mean ± SD (except where noted) and were compared between groups using Student's *t*-test or Mann-Whitney *U* test when appropriate (nonparametric data). Dichotomous variables are presented as percentages and were compared between groups, using a χ^2 or Fisher's exact test when appropriate. Statistical analysis was performed with SPSS version 15.0 (SPSS Inc., Chicago, IL).

This study is registered with ClinicalTrials.gov (NCT00282659).

Results

BASELINE DEMOGRAPHICS

A total of 70 patients met the study eligibility criteria and were randomized to receive double-blind treatment. Overall, 20 (28.6%) patients discontinued study treatment before the 12-week endpoint (Figure 1). Reasons for discontinuation included excessive pill burden (n = 7), withdrawal of consent (n = 6), and diarrhea (n = 3). An additional 6 (8.6%) patients discontinued before the 24-week endpoint; reasons included pill burden (n = 3), diarrhea (n = 2), and patient relocation (n = 1). Rates of premature discontinuation were similar between the 2 groups (Figure 1). Inadequate data collection prevented reporting of overall adherence rates. Baseline characteristics were similar among the magnesium L-lactate and placebo treatment groups in the 50 patients who completed at least one follow-up appointment, with the exception of age, with patients in the placebo group being significantly older than those in the magnesium L-lactate group (68.0 ± 10.4 vs 61.0 ± 13.1 y, respectively, p = 0.04; Table 1). Of note, no significant differences were seen between the treatment groups in baseline systolic or diastolic blood pressure, or in the mean number of antihypertensive medications. A total of 37 (74%) patients had a documented history of hypertension, 8 of whom (21.6%) remained hypertensive at the start of the study.

Although no significant differences were seen between the treatment groups in baseline serum or intracellular magnesium concentrations, 86% of patients, regardless of randomization, had a baseline intracellular magnesium deficiency (intracellular concentrations below the reference range of 33.9–41.9 mEq/IU), but no patients had serum magnesium deficiency (serum magnesium concentrations below the reference range of 1.6–2.7 mg/dL). In addition, no significant differences in other baseline electrolyte levels (including sodium, potassium, phosphorous, or calcium) were seen between groups (Table 1). Although follow-up intracellular magnesium level determinations could not be performed, there were no significant differences in serum magnesium levels between the magnesium and placebo groups at either 12 weeks (2.37 ± 0.2 vs 2.38 ± 0.2; p = 0.90) or 24 weeks (2.41 ± 0.2 vs 2.35 ± 0.3; p = 0.61).

EFFICACY

At the 12-week endpoint, patients treated with magnesium L-lactate had a significantly lower mean systolic blood pressure than did those receiving placebo (117.7 ± 11.8 vs 126.3 ± 16.7 mm Hg, respectively; p = 0.04; Figure 2). A similar magnitude of difference between magnesium L-lac-

tate and placebo was seen at 24 weeks, although statistical significance was lost (118.1 ± 14.1 vs 125.5 ± 17.2 mm Hg, respectively; p = 0.13). No significant differences in diastolic blood pressure were seen between magnesium L-lactate and placebo at either 12 weeks (70.8 ± 8.0 vs 70.6 ± 11.2 mm Hg, respectively; p = 0.95) or 24 weeks (71.2 ± 10.5 vs 72.0 ± 7.9 mm Hg, respectively; p = 0.78) (Figure 2).

Upon subgroup analysis, patients with a documented history of hypertension at baseline showed similar responses in the overall analysis. Significant reductions in systolic blood pressure were seen with magnesium L-lactate versus placebo at 12 weeks (118.9 ± 9.7 vs 129.2 ± 14.6 mm Hg, respectively; p = 0.02) and trends were noted at 24 weeks (118.6 ± 12.8 vs 127.4 ± 15.9 mm Hg, respectively; p = 0.10) (Figure 3). No significant differences in mean diastolic blood pressure were seen between the groups at either 12 weeks (71.0 ± 8.0 vs 70.7 ± 12.3 mm Hg; p = 0.92) or 24 weeks (71.4 ± 9.6 vs 72.4 ± 8.1 mm Hg; p = 0.75) (Figure 3). In addition, no significant differences in either systolic or diastolic blood pressure were seen between patients who had or did not have a baseline intracellular magnesium deficiency at baseline (123.4 ± 14.2/73.3 ± 10.8 vs 120.5 ± 19.6/72 ± 3.8; p = 0.67/0.77), 12 weeks (121.8 ± 15.2/70.9 ± 9.1 vs 119.3 ± 11.0/67.7 ± 7.5; p = 0.70/0.42), or 24 weeks (120.9 ± 15.0/70.7 ± 8.9 vs 125.8 ± 18.5/75.0 ± 5.6; p = 0.51/0.31).

SAFETY ANALYSIS

The overall incidence of adverse events and rate of discontinuations due to adverse events were similar in both the magnesium L-lactate and placebo groups. The most commonly reported adverse events included diarrhea, fatigue, itching, and infection (Table 2).

Discussion

This study demonstrates that magnesium L-lactate administered twice daily (504 mg/day) reduces systolic blood pressure in patients with an ICD. Patients receiving magnesium L-lactate showed a significant mean reduction of 8.6 mm Hg in systolic blood pressure after 12 weeks of therapy as compared with placebo. This effect was sustained at 24 weeks, although statistical significance was lost due to study withdrawals. Although an initially high dropout rate was seen due to the overall pill burden, and to a lesser extent, diarrhea, treatment with magnesium was well tolerated at 12 and 24 weeks as compared with placebo. There was a significant difference in age at baseline between the placebo and magnesium groups (with the placebo group being older). To investigate whether a patient's response to magnesium differed by age, we stratified the magnesium group into patients greater than and less than 64 years of age. We

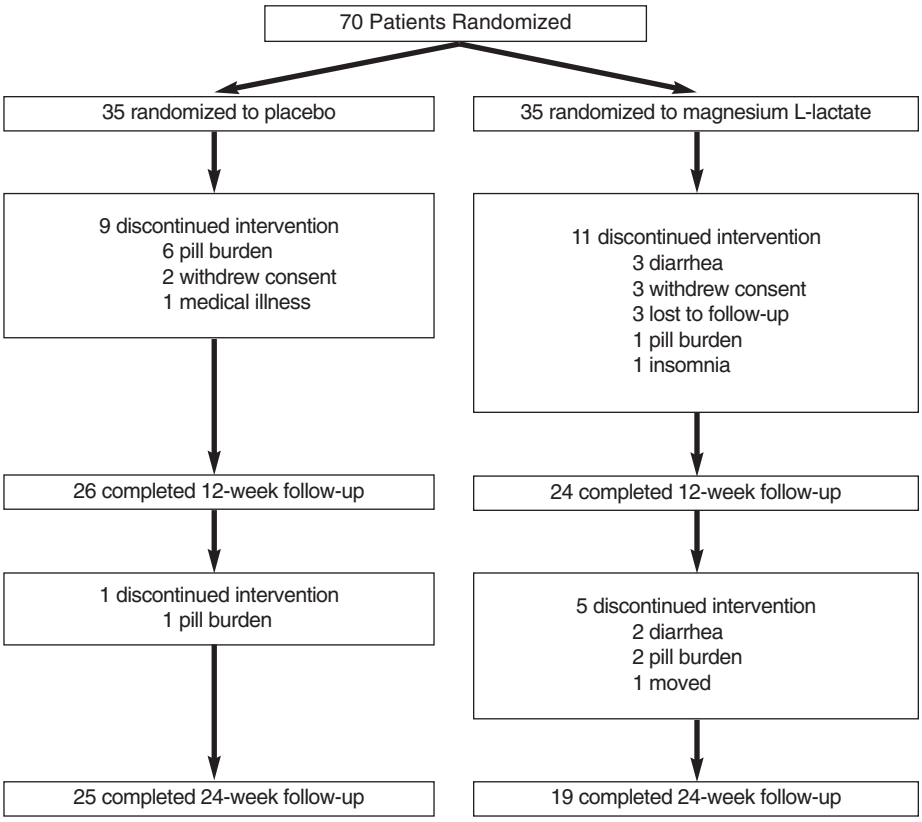


Figure 1. Trial profile.

found no significant differences at baseline, 12 weeks, or 24 weeks between older and younger patients (data not shown). Thus, we feel confident that the baseline difference in age did not impact our overall study results.

A meta-analysis of 20 randomized clinical trials evaluated the impact of magnesium supplementation on blood pressure.[18] The analysis showed that oral magnesium supplementation reduced systolic blood pressure by only 0.6 mm Hg (95% CI –2.2 to 1.0; p = 0.051) and diastolic blood pressure by only 0.8 mm Hg (95% CI –2.1 to 0.5; p = 0.142). More robust results were seen when the analysis was limited to double-blind studies and those conducted in patients with hypertension. In addition, the investigators showed that for each 10-mmol/day larger dose of magnesium used, additional decreases in systolic blood pressure of 4.3 mm Hg (95% CI 6.3 to 2.2; p < 0.001) and diastolic blood pressure of 2.3 mm Hg (95% CI 4.9 to 0.0; p = 0.09) were seen. The equivalent dose of magnesium L-lactate used in the current study was 21 mmol/day. This means that reduction in systolic and diastolic blood pressure of 8.6 and 4.6 mm Hg, respectively, would have been predicted through this calculation. In fact, we demonstrated a significant 8.6-mm Hg reduction in systolic blood pressure, as predicted by Jee et al.[18] However, significant reductions in diastolic blood pressure were not seen in our study. The majority of trials in the meta-analysis by Jee et al. used magnesium salts other than magnesium L-lactate, evaluated shorter-term antihypertensive effects, had methodologic limitations (eg, crossover design), and used a lower elemental magnesium daily dose than in our study. We do not know why oral magnesium did not impact diastolic blood pressure, but perhaps the effects were more cardioactive than vascular.

In one of the largest previous studies, Sacks et al.[13] randomized 300 normotensive women to receive either magnesium L-lactate 336 mg/day, potassium, calcium, all 3 supplements together, or placebo for 16 weeks. Baseline blood pressures were 117 ± 10 and 74 ± 7 mm Hg for systolic and diastolic, respectively, in the magnesium group and 115 ± 8 and 73 ± 6 mm Hg, respectively, in the placebo group. The mean effects for magnesium L-lactate on blood pressure as compared with placebo were –0.9 mm Hg (95% CI –2.6 to 0.8) for systolic blood pressure and –0.5 mm Hg (95% CI –2.2 to 0.8) for diastolic blood pressure, with neither difference being statistically significant. Since this study evaluated normotensive patients, it is likely that the blood pressure effects would have been blunted, an effect that has been seen in prior studies of antihypertensive medications.[19] However, the baseline blood pressures in our present study were in the normotensive range (125/75 mm Hg) and our appreciable blood pressure reductions were similar in both normotensive and hypertensive subjects. Whether we achieved more robust blood pressure reductions because we used a higher daily dose of magnesium L-lactate (as suggested by the meta-analysis by Jee et al.[18]) or because our subjects had a high prevalence of intracellular magnesium deficiency requires further study.

Table 1. Baseline Characteristics of Randomized Patients Who Completed at Least One Follow-Up Appointment[a]

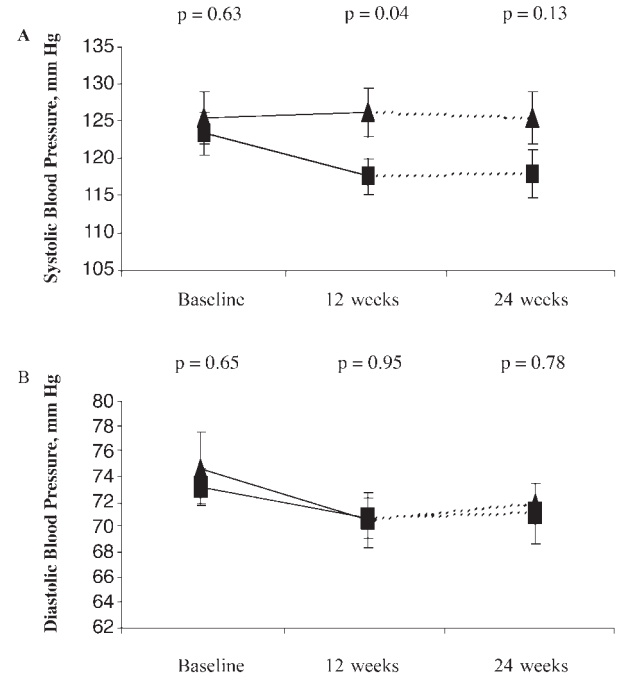
Variable	Placebo (n = 26)	Magnesium L-lactate (n = 24)	p Value
Age (y)	68.0 ± 10.4	61.0 ± 13.1	0.04
Sex (male)	17 (65.4)	21 (87.5)	0.07
Ethnicity			
white	22 (84.5)	18 (75.0)	0.40
black	2 (7.7)	5 (20.8)	0.24
Hispanic	2 (7.7)	1 (4.2)	>0.99
Primary prevention	19 (73.1)	19 (79.2)	0.61
Secondary prevention	7 (26.9)	5 (20.8)	0.61
History			
alcohol use	13 (50.0)	9 (37.5)	0.37
cigarette smoking	4 (16.7)	9 (37.5)	0.08
diabetes	6 (23.1)	6 (25.0)	0.87
myocardial infarction	19 (73.0)	14 (58.3)	0.19
heart failure	15 (57.7)	18 (75.0)	0.26
Baseline serum creatinine (mg/dL)	1.08 ± 0.28	1.09 ± 0.24	0.93
Baseline serum magnesium (mEq/L)	2.23 ± 0.19	2.18 ± 0.19	0.46
Baseline intracellular electrolytes (mEq/L)			
magnesium	32.5 ± 2.0	32.4 ± 1.7	0.84
calcium	4.14 ± 0.9	4.34 ± 1.7	0.61
sodium	4.53 ± 0.9	4.04 ± 0.9	0.08
potassium	124.28 ± 33.4	127.0 ± 46.9	0.83
phosphorus	16.14 ± 2.0	16.79 ± 2.8	0.38
Baseline drugs			
ACE inhibitor	18 (69.2)	13 (54.2)	0.27
antiarrhythmic	5 (19.2)	2 (8.3)	0.42
ARB	3 (11.5)	7 (29.2)	0.12
β-blocker	23 (88.5)	22 (91.7)	>0.99
CCB	2 (7.7)	1 (4.2)	>0.99
diuretic	13 (50.0)	13 (54.2)	0.77
Antihypertensives	2.3 ± 1.0	2.3 ± 0.6	0.79
History of hypertension	20 (76.9)	17 (70.8)	0.62
Hypertension at baseline	7 (26.9)	5 (20.8)	0.61
Mean systolic BP (mm Hg)	126.5 ± 19.3	123.8 ± 13.5	0.57
Mean diastolic BP (mm Hg)	75.1 ± 14.9	73.2 ± 7.4	0.58

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker.
[a]Data are presented as mean ± SD or n (%), except where otherwise noted.

The pathophysiologic role of magnesium deficiency in blood pressure homeostasis has been acknowledged since the early 1980s. Resnick et al.[20] observed that patients with essential hypertension had consistently lower levels of intracellular magnesium than did their normotensive controls. They also observed a strong inverse relationship between intracellular magnesium and blood pressure, with lower magnesium levels associated with higher blood pressure. Studies inducing experimental magnesium deficiencies have also demonstrated significant vasoconstriction and frank hypertension.[21-23]

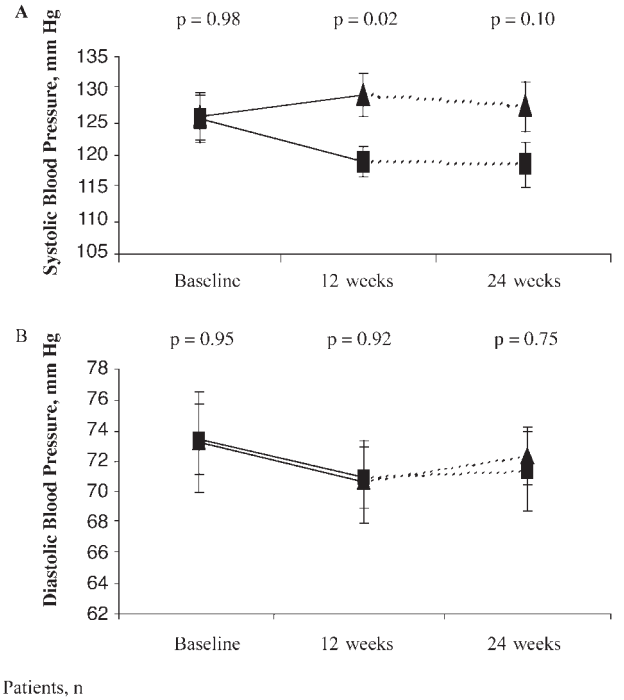
Our trial suffers from a few limitations. We wanted to evaluate a population that likely had baseline intracellular magnesium deficiency. In our previous studies, patients with arrhythmias were found to exhibit baseline intracellular magnesium deficiency 63–89% of the time.[15,24] This was similar to the present study in which 86% of patients had magnesium deficiency. Unfortunately, this population of patients with ICDs also consumed numerous daily medications and it was difficult to recruit patients who would take an additional 6 tablets daily and continue to take their assigned treatments once randomized. While we are confident that the systolic blood pressure effects seen in the 50 patients completing 12 weeks of therapy would be similar in the overall population of 70 patients who were randomized into the trial, this is only conjecture. While the systolic blood pressure effects of magnesium L-lactate were maintained at 24 weeks, with additional attrition, we were unable to achieve statistical significance at this point. In addition, no dietary or nutritional restrictions were placed on study subjects. Although thorough medication screenings were performed during each follow-up visit, we cannot rule out the possibility that study subjects were receiving magnesium from other food sources or nutritional supplements. The potential effects of this supplemental magnesium intake are therefore unknown.

Patients with ICDs have a high prevalence of intracellular magnesium deficiency that is not fully reflected by their serum magnesium concentrations. Magnesium L-lactate supplementation reduced systolic blood pressure but not diastolic blood pressure in this population at 12 weeks, an effect that was sustained at 24 weeks. A unique formulation of magnesium L-lactate is being developed that should allow the delivery of about the same amount of elemental magnesium but with fewer tablets. This new formulation might allow patients to achieve the same benefits that we found in our trial without the same pill burden, and therefore may enhance long-term adherence.



Patients, n			
Magnesium L-lactate	24	24	19
Placebo	26	26	25

Figure 2. Impact of magnesium L-lactate on mean (A) systolic and (B) diastolic blood pressure. Data presented as mean ± SEM.



Patients, n			
Magnesium L-lactate	17	17	14
Placebo	20	20	19

Figure 3. Impact of magnesium L-lactate on mean (A) systolic and (B) diastolic blood pressure in patients with a history of hypertension. Data presented as mean ± SEM.

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Table 2. Safety and Tolerability[a]

ADEs	Placebo (n = 26)	Magnesium L-Lactate (n = 24)	p Value
Any ADE	9 (34.6)	7 (29.2)	0.68
Any serious ADE[b]	1 (3.8)	1 (4.2)	>0.99
Most frequent ADEs			
diarrhea	1 (3.8)	4 (16.7)[c]	0.18
fatigue	3 (11.5)	0 (0)	0.24
itching	2 (7.7)	2 (8.3)	>0.99
infection	2 (7.7)	2 (8.3)	>0.99
dizziness	2 (7.7)	1 (4.2)	>0.99
dyspnea	2 (7.7)	1 (4.2)	>0.99
minor bleeding	2 (7.7)	1 (4.2)	>0.99
vision changes	2 (7.7)	1 (4.2)	>0.99
dry mouth	2 (7.7)	0 (0)	0.49
weight gain	1 (3.8)	1 (4.2)	>0.99
anorexia	1 (3.8)	1 (4.2)	>0.99

[a]Data are presented as n (%) of patients reporting adverse drug events (ADEs). Individual ADEs reported in >2% of all patients in any treatment group who completed at least 12 weeks of follow-up are presented.
[b]Patient in the placebo group experienced rectal bleeding, patient in the magnesium group experienced severe kidney stones.
[c]Two of 4 subjects discontinued therapy due to diarrhea (Figure 1).

Efecto del L-Lactato de Magnesio sobre la Presión Sanguínea de Pacientes con un Desfibrilador de Cardioversión Implantable: Un Estudio de Doble Ciego, Controlado con Placebo, Randomizado, de 24 Semanas de Duración

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EXTRACTO

ANTECEDENTES: Existen estudios previos que han evaluado el impacto del magnesio oral sobre la presión sanguínea; sin embargo, dichos estudios utilizaron sales de magnesio con biodisponibilidad baja, carecían de metodología óptima, y mostraban resultados distintos.

OBJETIVO: Evaluar la habilidad del L-lactato de magenesio oral de bajar la presión sanguínea a largo plazo en comparación con el placebo en pacientes con desfibriladores de cardioversión implantados (DCIs).

METODOS: En este estudio de doble-ciego, de 24 semanas de duración, 50 pacientes con DCIs recibieron L-lactato de magnesio (6 tabletas diarias supliendo 504 mg de magnesio elemental diarios) o placebo por al menos 12 semanas. Se determinaron las concentraciones basales intracelulares y séricas de magnesio. El parámetro de eficacia final fue la presión sanguínea sistólica media a las 24 semanas.

RESULTADOS: De los 50 pacientes que completaron al menos 12 semanas de seguimiento, 86% de ellos, independientemente del tratamiento asignado, mostraron deficiencia basal de magnesio intracelular pero no sérica. A las 12 semanas, el L-lactato de magnesio redujo significativamente la presión sanguínea comparado con el placebo (117.7 ± 11.8 vs 126.3 ± 16.7 mm Hg, respectivamente; p = 0.04). En los 45 pacientes que continuaron el estudio hasta las 24 semanas, la reducción en la presión sistólica se mantuvo pero su significancia estadística se perdió (118.1 ± 14.1 vs 125.5±17.2 mm Hg, respectivamente; p = 0.13). El L-lactato de magnesio no produjo ningún impacto sobre la presión sanguínea diastólica a los dos tiempos de tratamiento evaluados (p ≥ 0.75). Los pacientes con una historia documentada de hipertensión durante la evaluación basal mostraron resultados similares cuantitativos a los del análisis primario.

CONCLUSIONES: Un gran número de sujetos con DCIs poseen deficiencia de magnesio intracelular que no es captada por la determinación de magnesio sérica. El uso del L-lactato de magnesio en pacientes con DCIs da como resultado un mejoramiento significativo en la presión sanguínea sistólica a las 12 semanas que puede mantenerse hasta las 24 semanas de tratamiento.

Traducio por Encarnación C. Suárez

Une Étude de 24 Semaines Menée à Double-Insu avec une Répartition Aléatoire et Contrôlée avec Placebo pour Évaluer l'Effet du Lactate de Magnésium sur la Pression Artérielle des Patients avec un Défibrillateur Implantable

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RÉSUMÉ

OBJECTIF: Plusieurs essais cliniques ont évalué l'effet du magnésium administré par voie orale sur la pression artérielle; toutefois, plusieurs lacunes méthodologiques dont l'étude de formulations de sels de magnésium possédant une faible biodisponibilité et menant à des résultats contradictoires, étaient présentes dans ces essais. Le but du présent essai était d'évaluer la capacité du L-lactate de magnésium à réduire, sur une période prolongée de 24 semaines, la pression artérielle des patients ayant un défibrillateur implantable.

MÉTHODOLOGIE: Cet essai mené à double-insu sur une période de 24 semaines a évalué près de 50 patients qui ont été randomisés à recevoir soit un placebo, soit du L-lactate de magnésium à raison de 6 comprimés par jour pour un apport total quotidien de 504 mg de magnésium élémentaire. Les concentrations intracellulaire et sérique de magnésium ont été déterminées lors de l'entrée dans l'étude. Le paramètre principal d'efficacité était la pression systolique moyenne en position assise à la semaine 24.

RÉSULTATS: Des 50 patients ayant complété un suivi initial de 12 semaines, près de 86%, indépendamment de leur randomisation, avaient une déficience intracellulaire en magnésium. Aucun patient n'avait toutefois une hypomagnésémie sérique. Après 12 semaines de traitement, le L-lactate de magnésium a permis une réduction significative de la pression systolique comparativement au placebo (117.7 ± 11.8 vs 126.3 ± 16.7 mm Hg, respectivement; p = 0.04). Quarante-cinq patients ont poursuivi l'étude pour un total de 24 semaines. Le bénéfice observé à douze semaines s'est maintenu chez ces patients bien que les résultats ne soient pas demeurés statistiquement significatifs (118.1 ± 14.1 vs 125.5 ± 17.2 mm Hg, respectivement; p = 0.13). Le L-lactate de magnésium n'a eu aucun effet bénéfique sur la pression diastolique aux semaines 12 et 24 (p ≥ 0.75 pour chacune des périodes). Les patients ayant une histoire documentée d'hypertension lors de leur l'entrée dans l'étude ont démontré des résultats qualitatifs similaires à ceux de l'ensemble de la population étudiée.

CONCLUSIONS: Les résultats de cette étude démontrent qu'une large proportion de patients ayant un défibrillateur implantable semble avoir une déficience intracellulaire en magnésium qui n'est pas reflété par les taux sériques de magnésium. L'utilisation du L-lactate de magnésium chez cette population permet une réduction significative de la pression artérielle systolique à 12 semaines et à 24 semaines.

Traduit par Sylvie Robert