Magnesium Supplementation and Blood Pressure in Borderline Hypertensive Subjects: A Double Blind Study

N. M. Daly, K. G. D. Allen, M. Harris

Zusammenfassung

Im Verlaufe einer 12wöchigen Doppelblindprüfung erhielten 40 Patienten mit labilem Bluthochdruck Magnesium (zweimal täglich 250 mg MgO) oder Placebo p.o. In beiden Gruppen sank der systolische (SB) und diastolische Blutdruck (DB). Die Steigungen der Senkungskurven von SB, DB und mittlerem Blutdruck (MB) deckten in der Magnesiumgruppe höhere signifikante Schwankungen auf (p jeweils gleich 0,007, 0,02 und 0,015) als in der Placebo-Gruppe. Nach den 12 Behandlungswochen betrug die Senkung des SB (Mittelwert +/– Standardabweichung) unter Magnesium – 12,5 +/– 12,2 mmHg gegen – 0,9 +/ – 11,5 mmHg unter Placebo. Der Unterschied ist auf eine Verschiebung der Verteilung der Drücke zu niedrigen Werten hin aufzufassen (p = 0,004). Durch die Aufnahme von Magnesium mit der Nahrung konnten jeweils 75 und 88 % der von der NRC für einen männlichen und weiblichen Erwachsenen empfohlenen Normen erzielt werden. Die Aufnahme von Mg, Ca, Na, K und Lipiden mit der Nahrung blieb während des gesamten Versuchs konstant und war nicht mit der Reaktion auf die medikamentöse Magnesiumzufuhr korreliert. Die erhaltenen Resultate scheinen anzuzeigen, daß eine zusätzliche orate Magnesiumzufuhr den Blutdruck bei nicht mit Diuretika oder Antihypertensiva behandelten Patienten mit labilem Bluthochdruck wirksam senken kann.

Summary

Forty subjects with borderline hypertension were treated in a twelve-week double blind trials with oral megnesium (250 mg twice daily, as MgO) or placebo. Systolic and diastolic pressure decreased in both placebo and magnesium treated groups. The slopes of the decreases in the systolic, diastolic and mean arterial pressure (MAP) demonstrated significantly greater changes (p = .007/.02/.015) in the magnesium treated group than in controls. The decrease in systolic pressure observed at week 12 was (mean ± sem) – 12.5 ± 12.2 in the magnesium treated group and (mean ± sem) – 0.9 ± 11.5 mm Hg) in controls and was attributable to a shift in the distribution of pressures toward lower values (p = .004). Dietary Mg intake met 75 % of the NRC allowance for the adult male and 88 % for the adult female. Dietary intakes of Mg, Ca, Ma, K and fat remained constant during the study and did not correlate with response to magnesioum supplementation. The data suggests that oral magnesium supplements may be an effective agent for reduction of blood pressure in borderline hypertensives not receiving diuretics or other antihypertensive drugs.

Résumé

Au cours d'une étude en double-insu de douze semaines, 40 sujets atteints d'hypertension artérielle labile ont reçu par voie orale du magnésium (250 mg de MgO deux foix par jour) ou un placebo. Les pressions artérielles systolique (PAS) et diastolique (PAD) ont diminué dans les deux groupes. les pentes des courbes de diminution de la PAS, de la PAD et de la pression artérielle moyenne (PAM) ont révélé des variations significativement supérieures (p respectivement égal à 0,007, 0,02 et 0,015) dans le groupe magnésium que dans l'étude, la diminution de la PAS (moyenne ± ESM) était de . 12,5 ± 12,2 mmHg sous magnésium contre – 0,9 ± 11,5 mmHg sous placebo, la différence étant attribuable à un déplacement de la répartition des pressions vers les valeurs basses (p = 0,004). L'apport alimentaire en Mg a permis d'atteindre respectivement 75 % et 88 % des normes recommandées par le NRC pour un adulte de sexe masculin et de sexe féminin. Les apports alimentaires de Mg, Ca, Na, K et de lipides sont restés constants pendant la durée de l'étude et n'ont pas été corrélés à la réponse à la supplémentation magnésique. Les résultats obtenus semblent indiquer qu'une supplémentation orale en magnésium peut s'avérer efficace pour abaisser la pression artérielle chez les sujets atteints d'une hypertension labile et ne recevant ni diurétiques ni antihypertenseurs.

Introduction

The relationship between magnesium and blood pressure has been under investigation for many years. The hypotensive effect of intravenous magnesium sulfate has been observed in the treatment of pregnancy-induced hypertension [1, 2] and acute glomerulonephritis [3]. Epidemiologic studies have attempted to correlate serum magnesium and magnesium intake with blood pressure. Lower serum magnesium levels were found in hypertensive patients as compared to normotensive subjects [4]. However, the normotensive subjects were younger than the hypertensive patients. Total magnesium intake, from dietary sources and supplements inversely correlated with both systolic and diastolic blood pressure [5] and a negative correlation between

Department of Food Service and Human Nutrition, Colorado State University, Fort Collins, Colorado

erythrocyte intracellular concentration of free magnesium and diastolic blood pressure has been reported [6]. Magnesium supplementation trials in hypertensive patients have yielded inconclusive results, and tab. 1 lists the characteristics and results of several recent studies [7–17]. There is considerable variation in the design of these studies, the dose and duration of magnesium supplementation, and the presence or absence of concurrent antihypertensive and diuretic treatments. The present study was designed to re-examine the effect of oral magnesium supplementation on blood pressure in borderline hypertensive subjects who were not currently receiving diuretic or antihypertensive treatment.

Subjects and Methods

Forty subjects with borderline hypertension were treated in a twelve-week double-blind trial with either magnesium (20 subjects) or placebo (20 subjects). Approval for the study was obtained from the Committee on Human Research at Colorado State University and was conducted following the protocol of the Helsinki Doctrine regarding research with human subjects. Subjects were recruited from the metropolitan Denver area.

All subjects had systolic pressure greater than 140 mm Hg and/or diastolic pressure greater than 90 mm Hg and had not been treated with antihypertensive medication, including diuretics, for at least one year prior to the study. Subjects were excluded if they met any of the following criteria: pregnancy, mental incapacitation, alcohol or drug addiction, congestive heart failure, myocardial infarction within one year, angina pectoris, kidney stones within ten years, history of cerebrovascular accident, parathyroid dysfunction or if they were taking calcium or magnesium supplements.

Subjects were randomly assigned to treatment and control groups. The treatment group received 250 mg of elemental magnesium, as magnesium oxide, twice daily (20.6 m mol Mg/day). The control group received gelatin placebo on the same schedule. Dietary intake of magnesium, calcium, potassium and sodium were estimated by twenty-four hour dietary recalls at the beginning and at the end of the study period. At entry the subjects in treatment and control groups did not differ significantly with respect to age, employment status, percent of ideal body weight (IBW) [18], systolic or diastolic blood pressure. The treatment group consisted of eight males and twelve females (mean age 57). The control group contained ten men and ten women (mean age 61 years). Mean initial blood pressure of subjects was 144 ± 11/85 ± 9 mm Hg in the treatment group and 141 ± 12/83 ± 8 mm Hg in controls.

Blood pressure was measured at the beginning of the study and once weekly for twelve weeks. Measurements were taken in the subjects' homes at the same time of day and on the same day of the week. Blood pressures were measured with an aneroid sphygmomanometer (Prestige Medical, Northridge, CA), in the left arm with the subjects seated and arm resting on a table at heart height. Systolic pressure was measured at the first *Karotkoff* sound and diastolic pressure was measured at the disappearance of sounds. Three readings were taken with approximately two minutes between readings. The average of the two most consistent readings was recorded. The study was double blinded to insure that the measurements would be free from observer bias.

Each individual's blood pressure measurements were plotted against time (weeks of the study). The slope of the linear regression line provided an index of rate of change in blood pressure. The values of the slope of the regression lines for the treatment group were compared to the values of the slope of the regression lines for the controls using student's two-tailed t-test for independent groups. Differences between treatment and control means were tested using Wilcoxon Rank Sums analysis. Data from the

Tab. 1

Author (Reference No.)	Participants Characteristics No.	Age (yr)	Study Type % Men		BP Medications	Weeks of Mg Treatment	Mg Salt (m mol/day)	BP (mmHg) in Mg Treated Groups Pre-treated	Treatment
Resnick (7)	10 (high renin)	–	–	A	–	–	$MgSO_4$ (16)	–/96	–/88[S]
	9 (low reinin)	–	–						
Karppanen (8)	85	48	73	A	yes	12	$MgSO_4 \cdot 7H_2O$ (10 % or 20 % of table salt)[1]	141/91	135/90[S]
Motoyama (9)	21	44	100	B	no	4	MgO (25)	MAP= 111	MAP= 10[S]
Saito (10) and Hattori (11)	20	57	75	B	yes	4	MgO (25)	134/80	127/77[S]
Dyckner (12) and Dyckner (13)	39	65	33	C	yes	24	Mg aspartate HCI (15)	152/93	140/85[S]
Nowoson (14)	25	63	68	D	no[2]	8	Mg aspartate (10)	change of 2/1[NS]	
Reyes (15)	21	57	19	D	yes	3	$Mg\,Cl_2$ (16)	156/112	145/ 104[S]
Cappuccio (16)	17	52	53	E	no	4	Mg aspartate (15)	154/100	154/ 98[NS]
Henderson (17)	41	62	–	D	yes	24	MgO (13)	154/87	150/ 88[NS]

BP, blood, pressure, [1] concurrent K administration; [2] Sodium restricted diet.
A, non-randomized no placebo control; B, non-randomized cross over no wash out period; C, randomized case controlled; D, randomized double blind placebo controlled; E, randomized double blind cross over; S, significant and NS, not significant, effect of Mg supplementation.

two dietary recalls were analyzed by computer using the NUTCAL program (Department of Food Science and Human Nutrition, Colorado State University, Fort Collins, Colorado, USA) which uses the United States Department of Agriculture (Washington D. C., USA) Standard Nutrient Data base (release 3.0) as reference. Dietary magnesium intake and other selected nutrients were analyzed as co-variates (using the ANOVA procedure) with the original blood pressures and the blood pressure changes in response to magnesium to examine any confounding dietary effects.

Results

Nineteen subjects in each group completed the study. One subject, of the original twenty, in each group developed diarrhea and was withdrawn from the study. One subject in the treatment group decreased the supplemental dose of mg to 250 mg per day during the last week of the study after reportedly experiencing diarrhea. No other side effects were reported.

Sixteen of nineteen subjects in the treatment group and nine of nineteen controls showed a decrease in systolic and diastolic blood pressure; two additional subjects in the control group exhibited a slight decrease in diastolic pressure only. The magnitude of response was –11.6/–6.0 mm Hg greater in magnesium supplemented subjects (mean ± sem; –12.6 ± 12.2/–7.5 ± 9.1 mm Hg) as compared to controls (mean ± sem; –0.9 ± 11.5/–1.6 ± 4.9 mm Hg). Mean arterial pressure was calculated as: 1/3 systemic + 2/3 diastolic. MAP decrease was –9.2 ± 10.4 mm Hg (mean ± sem) in the treatment group and – 1.3 ± 7.7 (mean ± sem) in controls. This represents a 7.9 mm Hg greater decrease in MAP with magnesium supplementation. The slopes of the individual linear regression lines for the decrease in systolic and diastolic pressure were calculated in order to examine differences in the magnitude of change between groups over the entire twelve week study period (tab. 2). Decreases in systolic, diastolic and MAP were found to be significantly greater ($p = .007/.02/.015$) in the magnesium treated group.

Group mean blood pressures (systolic, diastolic and MAP), by week, are presented in fig. 1. Prior to treatment, group means of systolic, diastolic and MAP were not significantly different and individual pressures in both groups exhibited a normal distribution about the mean. The decrease in mean systolic pressure following twelve weeks of treatment with magnesium was attributable to a shift in the distribution of pressures (fig. 2) toward lower values ($p = .004$). This effect approached significance at week 11 ($p = 0.59$), but was not apparent prior to eleven weeks of treatment. The change in group means for diastolic pressure and MAP were not found to be significantly different by Wilcoxon (rank sums) analysis nor in the ANOVA for normally distributed means.

Mean dietary intake of magnesium by all subjects at the beginning of the study was 263 ± 123 mg/day and was unrelated to blood pressure. Dietary magnesium intakes did not change during the course of the study and were not correlated with response to magnesium supplementation. Dietary intake of sodium, potassium, calcium, percent total calories from fat, and polyunsaturated/saturated fatty acid (P/S) ratios were found to have no relationship with either the initial blood pressure or the change in pressure observed during the study period. Age, employment status and sex were not associated with the blood pressure changes. Prestudy weight, expressed as IBW, was slightly, but significantly, correlated with initial diastolic blood pressure (.15 mm Hg increase/each 1 % over (IBW). Subjects' body weight remained stable throughout the study period and was not correlated with changes in blood pressure.

Discussion

Previous magnesium supplement studies (tab. 1) differ in several important characteristics. The most salient diffe-

Tab. 2: Linear regression slopes of individual systolic and diastolic pressures during twelve-week study period.

	Control			Magnesium Treatment	
Subject	Systolic[1]	Diastolic[1]	Subject	Systolic[1]	Diastolic[1]
E.C.	0.3131	–0.2520	H.A.	–1.3736	–1.3626
A.D.	–0.2048	–0.5630	E.B.	–1.6211	–0.7155
B.E.	–1.6263	–0.6043	D.C.	–1.5439	–1.0714
E.G.	1.2657	0.5874	F.C.	–1.5118	–1.1128
D.H.	0.3852	0.7385	J.D.	–0.7110	–0.0056
M.H.	–0.6640	–0.2685	G.H.	–0.7779	–0.9270
B.H.	–0.2514	–0.4765	E.J.	–1.2834	–0.8091
N.H.	0.0087	0.2067	J.J.	–1.6780	–1.8880
M.M.	1.8087	0.1396	P.J.	–0.8716	–0.4527
M.N.	0.2947	–0.2118	M.K.	–0.0487	–0.4349
M.Q.	–1.6088	–0.4032	A.L.	–1.5190	–0.8059
M.R.	–1.6408	–0.0359	F.P.	–1.3476	–1.2619
E.R.	0.6715	0.3480	N.R.	0.7800	0.4680
A.S.	0.8765	0.1874	R.S.	–0.4920	–0.1731
J.T.	0.3942	–0.6236	P.S.	–1.1000	–1.0910
R.U.	–0.5000	–0.0119	A.S.	0.1710	0.7730
C.W.	–0.9440	–0.1858	L.S.	–2.9465	–1.3134
I.W.	–1.3176	–0.4580	L.S.	0.8540	1.0180
R.Y.	–1.5010	–0.5770	J.V.	–2.8778	–0.7780
Mean	–0.1031[2]	–0.1297[3]		–1.0473[2]	–0.6286[3]
sem	± .2337	± .0964		± .2395	± .1789

[1] Units of slope are mm Hg/week
[2] $p = .007$
[3] $p = .02$

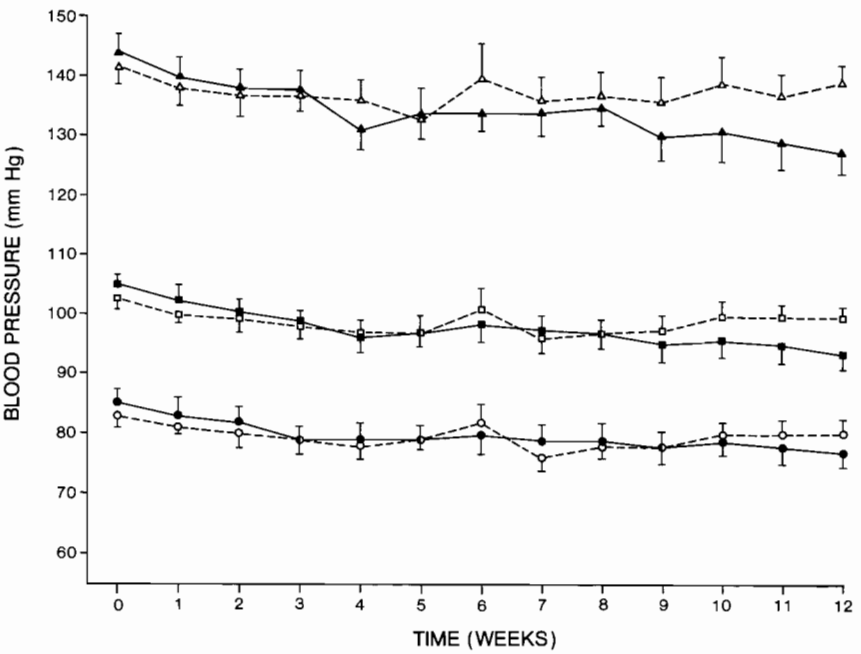

Fig. 1: Systolic, diastolic and mean arterial pressure in magnesium treated and control (placebo treated) subjects. Closed triangles = systolic pressure/magnesium; open triangles = systolic pressure/control; closed squares = MAP/magnesium; open squares = MAP/control; closed circles = diastolic pressure/magnesium; open circles = diastolic pressure/control.

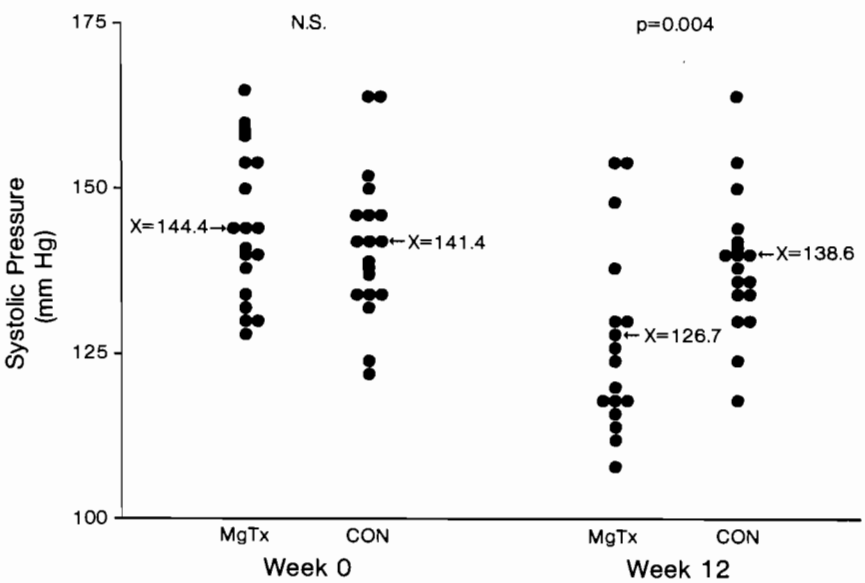

Fig. 2: Distribution of systolic and diastolic pressures in magnesium treated and control (placebo treated) groups. Group means are shown.

rences in these studies are the presence or absence of concurrent antihypertensive and diuretic treatments and the dose and duration of magnesium supplementation. Of the five studies [8, 10–13, 15, 17] where concurrent antihypertensive and diuretic treatments were given, magnesium supplements significantly reduced blood pressure in all but the study of *Henderson* et al [17]. These results may be explained by the depletion of magnesium due to long-term diuretic therapy [19]. In the studies (tab. 1) where there was no concurrent antihypertensive and diuretic treatment [9, 14, 16], only the study of *Motoyama* et al. [9] showed a significant reduction in blood pressure due to magnesium supplementation. It is perhaps important to note that the study of *Motoyama* et al. was with patients who had been removed from antihypertensive and diuretic treatment for a minimum of one month, but received a relatively high dose of magnesium (25 m mol/day) for four weeks. The studies of *Nowoson* et al. [14] and *Cappuccio* et al. [16] used considerably lower doses of magnesium, 10 and 15 m mol/day respectively, for 4 to 8 weeks. In this study, we used a higher level of magnesium (21 m mol/day) for a longer period of time, 12 weeks, in subjects not treated with antihypertensive and diuretic medication for a minimum of one year. Hence, the significant decrease in blood pressure obtained in this study may be due to the higher dosage and longer duration of magnesium supplementation.

However, these suggestions are highly conjectural since serum magnesium and urinary magnesium excretion were not measured. The longer supplementation period used in the present study (12 vs 4 weeks) may be required for the hypotensive effects and could readily account for differences in results since the nonparametric analysis did not show a significant effect until week 12 of the supplementation period. Eight of 17 patients in the trial by *Cappuccio* et al. [6], demonstrated a decrease in mean arterial pressure when compared to a placebo period. Although this drop was not significant, for the group as a whole, it may be proposed that further decrease in blood pressure may have resulted in a significant hypotensive effect with magnesium if the trial had been carried out for a longer period of time.

The mechanism through which magnesium exerts hypotensive effects is not known with any degree of certainty. Magnesium has been shown to prevent vasoconstriction, either directly [20, 21] or by attenuating response to vasoactive agents by inhibition of ionized calcium uptake by

vascular smooth muscle [22, 23]. It is possible that magnesium exerts an influence on fluid and electrolyte balance [24]; however, there is not much support for this hypothesis. Supplementation with magnesium does not routinely effect serum electrolyte concentrations nor does it alter urinary excretion of sodium, potassium nor urinary volume [12, 16, 17].

Two hypotheses may be proposed with regard to the hypotensive effectiveness of oral magnesium supplementation in responders and the lack of effectiveness in non-responders in previous studies: 1. the hypotensive effect is more pronounced in individuals with low-renin hypertension, or 2. the response to magnesium is a repletion effect and hence, dependant upon pretreatment magnesium status. Serum magnesium levels have been shown to be lower in patients with low-renin hypertension and higher in patients with high-renin hypertension, presumably because plasma renin activity alters transport of magnesium and calcium ions across cellular membranes [25]. However, *Cappuccio* et al. [16] found no difference in plasma magnesium levels in hypertensive patients with low plasma renin activity as compared to those with normal plasma renin activity and could not correlate responsiveness to oral magnesium supplementation with initial plasma renin activity. In support of the second hypothesis, intracellular and extracellular magnesium levels may be depleted by long term diuretic therapy [19]. This would explain the responsiveness of hypertensive patients in *Dyckner's* earlier study [12] to oral magnesium supplements as the patients had been maintained on long-term diuretic treatment and mean initial serum magnesium levels were low (1.68 mg/dl). In this instance, the hypotensive response was accompanied by a significant increase in serum magnesium levels to 1.87 mg/dl, which is within the normal physiological range. In contrast, hypertensive patients treated with long term diuretics in a study reported by *Henderson* [17], had initial mean serum magnesium levels of 1.87 mg/dl and did not respond to oral magnesium supplementation with either a decrease in blood pressure or an increase in serum magnesium.

It has been suggested that the American diet may be marginally deficient in magnesium [26]. However, we were unable to correlate dietary magnesium intake with either initial blood pressure or hypotensive response to magnesium. The mean magnesium intake of all subjects in this study met 75 % of the 1980 NRC Recommended Dietary Allowance [27] (RDA) for the adult male and 88 % of the RDA for the adult female. These intakes are generally judged to be adequate for the majority of individuals. However, it is not known whether these dietary levels were able to maintain serum magnesium levels within the normal range. Further investigation of the responsiveness to oral magnesium supplements in hypertensive subjects in which serum magnesium levels are low, as well as within the normal range, is needed.

Acknowledgements

The authors are thankful to Dr. *Klaus Lorenz* für translating the abstract into German.

References

[1] *Lazard, E. M.:* A preliminary report on the IV use of magnesium sulfate in puerperal eclampsia. Am. J. Obstet. Gyn. **9** (1925) 178–191.

[2] *Lazard, E. M.:* An analysis of 575 cases of eclamptic and pre-eclamptic toxemias treated by IV injections of magnesium sulfate. Am. J. Obstet. Gyn. **26** (1933) 647–659.

[3] *Rubin, M. I.:* the mode of action of magnesium sulfate in reducing the hypertension of glomerulonephritis. Am. J. Med. Sci. **201** (1941) 734–739.

[4] *Albert, D. G., Y. Morita, L. T. Iseri:* Serum magnesium and plasma sodium levels in essential vascular hypertension. Circulation **18** (1958) 761–764.

[5] *Joffres, M. R., D. M. Reed, K. Yano:* Relationship of magnesium intake and other dietary factors to blood pressure. The Honolulu heart study. Am. J. Clin. Nutr. **45** (1987) 469–475.

[6] *Resnick, L. M., R. Gupta, J. H. Laragh:* Intracellular free magnesium in erythrocytes of essential hypertension: relation to blood pressure and serum divalent cations. Proc. Natl. Acad. Sci. USA **81** (1984) 6511–6515.

[7] *Resnick, L. M., J. H. Laragh:* Calcium and magnesium therapy in subgroups of essential hypertension. Endocrine Society 65th Annual Meeting, June 8–10, 1983, San Antonio, Texas. Program and Abstract Book (1983) p. 170 (Abstract 358).

[8] *Karppanen, H., A. Tanskanen, J. Tuomilehto, P. Puska, J. Vuori, V. Jantti, M. J. Seppanen:* Safety and effects of potassium and magnesium containing low salt mixtures. J. Cardiovasc. Pharmocol. **6** (1984) S 236–S 243.

[9] *Motoyama, T., H. Sano, H. Fukuzaki:* Oral magnesium supplementation in patients with essential hypertension. Hypertension **13** (1989) 227–232.

[10] *Saito, K., K. Hattori, T. Omatsu, H. Hirouchi, H. Sano, H. Fukuzaki:* Effects of oral magnesium on blood pressure and red cell sodium transport in patients receiving long-term thiazide diuretics for hypertension. Am. J. Hypertens. **1** (1988) 71S–74S.

[11] *Hattori, K., K. Saito, H. Sano, H. Fukuzaki:* Intracellular magnesium deficiency and effect of oral magnesium on blood pressure and red cell sodium transport in diuretic-treated hypertensive patients. Japanese Circ. J. **52** (1249–1256).

[12] *Dyckner, T., P. O. Wester:* Effect of magnesium on blood pressure. Br. Med. J. **286** (1983) 1847–1949.

[13] *Dyckn*er, T., P. O. Wester, L. Widman: Effect of peroral magnesium on plasma and skeletal muscle electrolytes in patients on long-term diuretic therapy. Int. J. Cardiol. **19** (1988) 81–87.

[14] *Nowoson, C. A., T. O. Morgan:* Magnesium supplementation in mild hypertensive patients on a moderately low sodium diet. Clin, Exptl. Pharmacol. Physiol. **16** (1989) 299–302.

[15] *Reyes, A. J., W. P. Leary, T. N. Acosta-Barrios, W. H. Davis:* Magnesium supplementation in hypertension treated with hydrochlorothiazide. Current Therapeutic Res. **36** (1984) 332–340.

[16] *Cappuccio, F. P., N. D. Markandu, G. W. Beynon, A. C. Shore, B. Sampson, G. A. McGregor:* Lack of effect of oral magnesium on high blood pressure: a double blind study. Br. Med. J. **291** (1985) 235–238.

[17] *Henderson, D. G., J. Schierup, T. Schodt:* Effect of magnesium supplementation on blood pressure and electrolyte concentration in hypertensive patients receiving long term diuretic treatment. Br. Med. J. **293** (1986) 664–665.

[18] Metropolitan Life Insurance Company, 1959.

[19] *Dyckner, T., P. O. Wester:* Renal excretion of electrolytes in patients on long-term diuretic therapy for arterial hypertension and/or congestive heart failure. Acta Med. Scand. **218** (1985) 443–448.

[20] *Altura, B. M., B. T. Altura, T. Carella:* Magnesium deficiency induced spasms of umbilical vessels: relation to preeclampsia, hypertension, growth retardation. Science **221** (1983) 376–377.

[21] *Seelig, J. M., E. P. Wei, H. A. Kontos, S. C. Choi, D. P. Becker:* Effect of changes in magnesium ion concentration on cat cerebral arterioles. Am. J. Phys. **245** (1983) H22–H26.

[22] *Dunnett, J., W. Nayler:* Calcium efflux from cardiac sarcoplasmic reticulum: effects of calcium and magnesium. J. Mol & Cell. Cardiol. **10** (1978) 487–488.

[23] *Meissner, G., E. Darling, J. Eveleth:* Kinetics of rapid Ca++ release by sarcoplasmic reticulum. Effects of Ca++, Mg++, and adenine nucleotides. Biochem. **25** (1986) 236–244.

[24] *Dyckner, T., P. O. Wester:* Magnesium treatment of diuretic induced hyponatremia with a preliminary report of a new aldosterone-antagonist. J. Am. Col. Nutr. **1** (1982) 149–153.

[25] *Resnick, L. M., J. H. Laragh, J. E. Sealey, M. H. Alderman:* Divalent cations in essential hypertension. New Engl. J. Med. **309** (1983) 888–891.

[26] *Lakshmanan, F. L., R. B. Rao, W. W. Kim, J. L. Kelsay:* Magnesium intakes, balances and blood levels in adults consuming self-selected diets. Am. J. Clin. Nutr. **40** (1984) 1380–1389.

[27] Food and Nutrition Board, National Research Council: Recommended Dietary Allowances, 9th edition. National Academy of Sciences, Washington, D. C. 1980.

(Correspondence to: *M. Harris,* M.D., Department of Food Science and Human Nutrition, Colorado State University, Fort Collins, Colorado, USA)