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Effects of oral magnesium supplementation on insulin sensitivity and blood pressure in normo-magnesemic nondiabetic overweight Korean adults

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KEYWORDS
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Overweight

Abstract *Background and aim:* Little is known about the effect of magnesium on insulin sensitivity and BP in healthy individuals. Therefore, we investigated whether magnesium could improve insulin sensitivity and blood pressure (BP) in normo-magnesemic nondiabetic overweight adults.
Methods and results: In a double-blinded, placebo-controlled, randomized trial, a total of 155 participants (BMI $\geq$ 23 kg/m^2) received either 12.3 mmol (300 mg) of elemental magnesium in the form of magnesium oxide (n = 75) or placebo (n = 80) each day for 12 weeks, constituting the intent-to-treat population. A repeated-measures ANOVA was used to evaluate the between-group changes in variables during the study. The baseline characteristics between the intervention and control groups were similar. There were no significant differences between the groups in the pattern of change of the homeostasis model assessment insulin resistance index, BP over time during the 12-week study. In subgroup analysis, magnesium supplementation (n = 8, 27, and 24, respectively) lowered BP much more than placebo (n = 16, 29, and 25, respectively) in those subjects whose systolic BP $\geq$ 140 mmHg, diastolic BP 80–90 mmHg, and diastolic BP $\geq$ 90 mmHg at the start of the study (P = 0.016, 0.043,

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and 0.023, respectively); in comparison, those subjects whose initial BP reading was low at baseline did not show a change in BP. No significant adverse events related to magnesium supplementation were recorded.
Conclusions: These results suggested that magnesium supplementation does not reduce BP and enhance insulin sensitivity in normo-magnesemic nondiabetic overweight people. However, it appears that magnesium supplementation may lower BP in healthy adults with higher BP.

Introduction

Magnesium depletion is associated with several lifestyle-related diseases, including diabetes mellitus (DM) and hypertension [1]. Magnesium plays a major role in regulating insulin action and insulin-mediated glucose uptake [2]. Magnesium supplementation has been shown to be associated with improved glucose metabolism and insulin action in most, but not all, studies [3,4]. In addition, prospective cohort studies have reported a statistically significant reduction in the risk of type 2 DM among individuals with higher magnesium intake [5,6].

Many studies have also suggested that reduced magnesium concentrations are associated with endothelial dysfunction, increased vascular reactivity, increased vascular tone, elevated blood pressure (BP) and the development of chronic complications [7]. Epidemiological and experimental studies support a role for low levels of magnesium in the pathophysiology of hypertension [8,9]. Significant, dose-dependent reductions in BP due to magnesium supplementation have been demonstrated by meta-analysis [10], although clinical trials involving magnesium supplementation in hypertensive patients have produced inconsistent results [11].

Although there is evidence to suggest that magnesium supplementation may help improve insulin sensitivity in type 2 DM with or without magnesium deficiency and that it may be useful as an adjuvant therapy in a subgroup of patients with hypertension [3–9], the benefits of magnesium supplementation in healthy individuals, especially Asian people, to our knowledge, has not yet been established. In addition, little is known about the effect of magnesium on metabolism in people without hypomagnesemia, although magnesium supplements are commonly available without prescription at drug and health food stores everywhere. Overweight or obese adults are at risk for its metabolic consequences such as diabetes and hypertension [12]. Therefore, we investigated whether magnesium supplementation also affected insulin sensitivity and BP in healthy overweight or obese Korean subjects without overt diabetes and hypertension.

Methods

Participants

This study was approved by the institutional review board of the Food Medical Research Institute, Pusan National University, and was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all subjects recruited through advertisements in local media before enrollment in the study. Being overweight was defined as having a body mass index (BMI) $\geq 23\ kg/m^2$ and obesity was defined as a BMI $\geq 25\ kg/m^2$ the based on the Asia-Pacific criteria [13]. Then, a total of 196 adults between the ages of 30 and 60 years and with a BMI $\geq 23\ kg/m^2$ were initially enrolled through a tertiary hospital and three secondary hospitals in Busan. The subjects had not taken any supplements or medications, including anti-diabetic drugs, anti-hypertensive drugs, steroids, or hormonal products, during the previous 4 weeks. The subjects were not pregnant women and those suffering from chronic illnesses, including chronic liver and renal diseases, severe bradycardia, myasthenia gravis, and hypermagnesemia. For safety reasons, the subject was also excluded if a participant's systolic BP was above 160 mmHg or diastolic BP above 110 mmHg before enrollment in the study. A total of 192 participants were screened before randomization. Thirty seven participants met exclusion criteria. Finally 155 (80.7%) participants were enrolled. Before the baseline period, the participants were randomly assigned to one of the two groups: the intervention group ($n = 75$), whose members received 12.3 mmol (300 mg) of elemental magnesium per day in the form of magnesium oxide, and the control group ($n = 80$), whose members received a placebo. This dose of magnesium was chosen from magnesium difference between control diet and fruits-and-vegetables diet or combination diet rich in fruits, vegetables, and low-fat dairy foods and with reduced saturated and total fat from chemical analyses of the menus prepared in the Dietary Approaches to Stop Hypertension study [14]. The study medications, which were supplied by TEI Korea Co., Ltd. (Seoul, Korea), were indistinguishable from each other. Six participants in the intervention group and 8 in the control group dropped out during the study without completing the study procedure. The characteristic of those who withdrew were similar to those who participated. The subjects were assessed for safety and compliance at every visit with 1-month interval. Compliance was assessed by a pill count.

At the start of the study, the subjects were asked to maintain their usual diet (1600–1700 kcal/d; 60% carbohydrate, 15% protein, and 25% fat based on food frequency questionnaire, FFQ) and level of physical activity throughout the study period. Each subject's diet including magnesium was monitored by a semi-quantitative FFQ at baseline and after 12 weeks. Participants were asked to report the frequency of consumption of 53 food items contained in the semi-quantitative FFQ over the 2 weeks prior to administration by an experienced dietitian. Then magnesium intake was categorized into quintile categories for comparison of magnesium intake between baseline and

12 weeks. Physical activity was assessed using the International Physical Activity Questionnaire at baseline and after 12 weeks [15]. We expressed physical activity levels as MET-minute. METs are multiples of the resting metabolic rates. A MET-minute is computed by multiplying the MET score of an activity by the minutes performed. MET-minute scores are equivalent to kilocalories for a 60 kg person.

Randomization

Simple randomization based on random numbers tables was used to assign each participant to the intervention or control group. The participants were assigned randomization numbers sequentially on recruitment to the study and the randomization codes were held by the company who had manufactured the magnesium and the dummy placebo. The person deciding whether participants would be included in the study did not know the randomization assignments. The measurements were conducted by persons who were not aware of the randomization of the participants.

Baseline and follow-up measurements

Height and weight were measured using standard protocols with subjects in light gown and without shoes. BMI was calculated as weight (kg) divided by height squared (m^2). A mercury sphygmomanometer was used to measure the BP of each subject, in the sitting position after a 10-min resting period. Two readings each for the systolic and diastolic BPs were recorded at 3-min intervals, and the average of each measurement was included in our analysis.

Blood samples after a 12-h fast were taken at baseline (pre-randomization) and 12 weeks after randomization. Plasma glucose was measured by the glucose oxidase method within 4 h of collection. Lipids were determined enzymatically using an ADVIA 1650 chemistry system (Bayer Vital, Fernwald, Germany). Insulin level was measured by radioimmunoassay (COAT-A-Count, Diagnostic Products, Los Angeles, CA, USA) with intra- and inter-assay variation coefficients of 4.2 and 6.3%, respectively. The homeostasis model assessment insulin resistance index (HOMA-IR) (fasting insulin (μIU/mL) $\times$ fasting glucose (mmol/L)/22.5) was used for estimating insulin sensitivity [16]. Serum magnesium was measured using colorimetric methods by an automatic analytical instrument (Hitachi 7600-100 Automatic Analyser, Hitachi, Japan). We also assessed the magnesium concentration in hair to find the chronological nutritional status. The subjects were asked not to chemically process their hair for at least 2 weeks, and all hair analyses were conducted using inductively coupled plasma-mass spectrometry (Elan 9000, PerkinElmer, Inc., CT, USA) [17].

Statistical analysis

The primary outcome variables were HOMA-IR, systolic BP, and diastolic BP. The calculated sample size is 63 patients in each group in order to have 80% power to detect a difference in the mean HOMA-IR of 0.5, assuming that standard deviation is 1.0 in primary outcome variables with an alpha error of 5% [3]. This sample size was also enough based on a previous study to evaluate effect of oral magnesium on high BP [18]. When the test data was unavailable, the last recorded data was used in the analysis (called the last observation carried forward). Efficacy analyses were based on the intent-to-treat (ITT) population of subjects who received at least one dose of prescribed magnesium or placebo and had at least one assessment post-baseline. The D'Agostino–Pearson test was used to test the normality of variables. Results are shown as mean and s.d. or median and inter-quartile ranges as appropriate, because variables were not all normally distributed. The between-group comparisons for baseline characteristics and its changes after 12 weeks were done with the two-sample *t*-test or Mann–Whitney *U*-test for continuous variables as appropriate or chi-square test in case of categorical variables. The within-group comparisons were done with a paired *t*-test or Wilcoxon signed-rank test when appropriate. A repeated-measures ANOVA was used to evaluate the between-group changes in variables during the study. Furthermore, subgroup analysis will be performed for the following predefined subgroups according to baseline BP: systolic BP ($<$120, 120–139, and $\geq$140 mmHg) and diastolic BP ($<$80, 80–90, and $\geq$90 mmHg). A *P*-value less than 0.05 was considered statistically significant. The SPSS version 11.0 statistical package was used for all statistical analyses.

Results

Subjects characteristics

Randomization was successful, as the two groups generated were comparable for most variables, with no significant differences in the baseline demographic, anthropometric, and nutritional data between the intervention and control groups (Table 1). Physical activity as MET-minute and magnesium intake score remained unchanged throughout the 12 weeks either within the group or between the groups. There were also no statistically significant differences in fasting glucose, insulin, HOMA-IR, lipids, BP, serum magnesium, or hair magnesium at baseline between the groups (Table 2). None of the subjects had lower total serum magnesium concentrations at baseline.

Safety

Most of the study subjects completed the protocol without adverse symptoms. One patient reported loose stools, but the situation was resolved after a few days without medication, and the subject asked to continue the study medication.

Within-group analyses

After the intervention, HOMA-IR remained unchanged during the experimental period. After 12 weeks, systolic BP was significantly decreased in both groups ($P < 0.001$ by paired *t*-test), but diastolic BP was significantly decreased only in the intervention group ($P = 0.006$ by paired *t*-test).

Table 1 Sociodemographic and anthropometric characteristics of the study subjects at the start of treatment.

	Magnesium ($n = 75$)	Placebo ($n = 80$)	*P*-value
Age (years)[a]	39.6 ± 7.9	40.5 ± 7.3	0.470
Males (%)[b]	50.6	49.4	0.546
Height (cm)[a]	166.4 ± 7.9	166.3 ± 8.5	0.959
Weight (kg)[a]	74.2 ± 12.0	72.6 ± 10.6	0.379
Body mass index (kg/m^2)[a]	26.7 ± 2.8	26.1 ± 2.3	0.204
Smoker (%)[b]	50.8	49.2	0.609
Alcohol drinker (%)[b]	53.5	46.5	0.151
Activity (MET-minute)[c,d]	2229 (960—3060)	2220 (1035—3600)	0.968
Magnesium intake (quintile)[c]	2.02 (1.54—2.79)	2.02 (1.55—2.78)	0.674

Data are expressed as means ± s.d. or frequency (percent). Activity and magnesium intake are as medians and interquartile ranges.

[a] Two-sample *t*-test.

[b] Chi-square test.

[c] Mann—Whitney *U*-test.

[d] One MET-minute is roughly equivalent to 1 kcal/min for a 60 kg person.

High-density lipoprotein cholesterol and serum magnesium levels decreased significantly in both groups ($P < 0.001$ by paired *t*-test). Hair magnesium levels decreased significantly in only control group. No significant difference was detected in any other metabolic characteristic in both groups during experimental period (Table 2).

Between-group analyses

Table 2 shows the differences in the change of metabolic characteristics between the intervention and control groups during the experimental period. Two-way ANOVA for repeated measures revealed no significant main effects of intervention and time. There was no significant effect of magnesium supplementation on HOMA-IR, systolic or diastolic BP over time. No significant effect of magnesium supplementation over time also was detected in any other metabolic characteristic between the groups at week 12.

We then examined whether the difference in BP change from baseline to 12 weeks between groups differed in particular subgroups of subjects. When dividing subjects according to baseline BP into subgroups, there were also no differences in the baseline demographic, anthropometric, and nutritional data between the intervention and control groups (data not shown). Repeated-measures ANOVA revealed a significant decrease in BP over time in particular subgroups of subjects, which tended to be greater for the intervention group, although the difference in BP between the subgroups at baseline was not statistically significant. The decrease in systolic BP was greater in the subgroup of subjects in the intervention group ($n = 8$, -17.1 ± 4.2 mmHg) with systolic BP ≥140 mmHg at the start of the study than those subjects in the control group ($n = 16$, -6.7 ± 10.7 mmHg) ($P = 0.016$); in comparison, those

Table 2 Metabolic characteristics at the start of the study and after 12 weeks of treatment.

Variables	Magnesium ($n = 75$)			Placebo ($n = 80$)			*P*-value[a]	*P*-value[b]
	Week 0[c]	Week 12	Δ12−0 weeks	Week 0[c]	Week 12	Δ12−0 weeks		
Fasting glucose (mmol/l)	5.07 ± 0.50	5.14 ± 0.52	0.08 ± 0.50	5.10 ± 0.51	5.14 ± 0.52	0.05 ± 0.50	0.194, 0.424	0.706
Fasting insulin (IU/ml)	11.2 ± 4.69	11.9 ± 7.81	0.69 ± 5.78	11.2 ± 4.41	10.6 ± 5.47	−0.60 ± 5.21	0.306, 0.308	0.147
HOMA-IR	2.54 ± 1.08	2.74 ± 1.76	0.02 ± 1.38	2.55 ± 1.08	2.48 ± 1.70	−0.07 ± 1.55	0.205, 0.698	0.253
Total cholesterol (mmol/l)	4.91 ± 0.82	5.06 ± 0.80	0.15 ± 0.57	5.00 ± 0.98	5.11 ± 0.87	0.17 ± 0.58	0.023, 0.160	0.698
LDL cholesterol (mmol/l)	3.01 ± 0.72	2.91 ± 0.68	−0.11 ± 0.52	3.08 ± 0.87	2.99 ± 0.75	−0.10 ± 0.52	0.083, 0.233	0.812
HDL cholesterol (mmol/l)	1.13 ± 0.24	1.05 ± 0.21	−0.09 ± 0.16	1.12 ± 0.25	1.04 ± 0.20	−0.09 ± 0.16	0.000, 0.000	0.952
Triacylglycerol (mmol/l)	1.61 ± 0.85	1.70 ± 1.20	0.08 ± 1.10	1.61 ± 1.12	1.60 ± 1.07	0.09 ± 1.09	0.519, 0.948	0.588
Systolic BP (mmHg)	124.7 ± 12.3	119.2 ± 11.7	−5.57 ± 10.21	126.7 ± 13.5	122.8 ± 13.9	−3.93 ± 9.55	0.000, 0.000	0.302
Diastolic BP (mmHg)	83.5 ± 9.68	80.6 ± 9.33	−2.91 ± 8.84	83.3 ± 9.55	82.7 ± 10.3	−0.59 ± 9.29	0.006, 0.406	0.061
Serum-Mg (mmol/l)	0.94 ± 0.06	0.88 ± 0.07	−0.06 ± 0.07	0.94 ± 0.06	0.87 ± 0.06	−0.06 ± 0.07	0.000, 0.000	0.718
Hair-Mg (μg/g)	8.51 ± 6.76	7.23 ± 5.76	−1.29 ± 5.87	10.28 ± 9.32	8.19 ± 7.02	−1.26 ± 5.83	0.061, 0.014	0.332

HOMA-IR, homeostasis model assessment insulin resistance index; LDL, low density lipoprotein; HDL, high density lipoprotein; BP, blood pressure; and Mg, magnesium. Data are means ± s.d. Δ12−0 weeks, difference compared with baseline.

[a] Paired *t*-test for within-group (*P*-value in magnesium, *P*-value in placebo group).

[b] Two-way repeated-measures ANOVA over time for between groups.

[c] $P > 0.05$ by two-sample *t*-test.

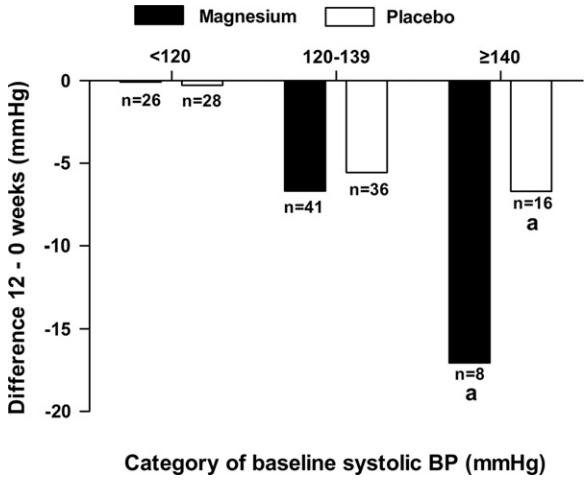

Figure 1 Mean changes of systolic blood pressure (BP) from baseline to 12 weeks in magnesium and placebo groups according to category of systolic BP at the start of the study. [a]$P < 0.05$ by two-way repeated-measures ANOVA over time.

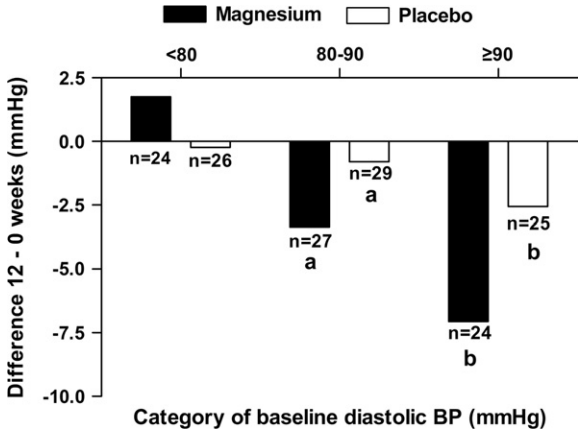

Figure 2 Mean changes of diastolic blood pressure (BP) from baseline to 12 weeks in magnesium and placebo groups according to category of diastolic BP at the start of the study. [a,b]$P < 0.05$ by two-way repeated-measures ANOVA over time.

subjects whose initial systolic BP reading was low at baseline did not show a change in systolic BP (Fig. 1). Moreover, the decrease in diastolic BP with magnesium supplementation was significantly more than with placebo in both the baseline diastolic BP 80–90 mmHg and ≥90 mmHg subgroups (-3.4 ± 8.3 vs. -0.8 ± 6.6 mmHg, $P = 0.043$ and -3.4 ± 8.3 vs. -0.8 ± 6.6 mmHg, $P = 0.023$), respectively. For subgroup with diastolic BP < 80 mmHg magnesium supplementation did not have any significant effect on lowering diastolic BP (Fig. 2).

Discussion

Although inverse associations between an individual's magnesium intake and the risk of type 2 diabetes have been reported, most of those studies were carried out in Western countries [3,6,11], and thus their results may not be directly applied to Korean and other Asian people. The present study was designed specifically to determine the effect of magnesium supplementation on insulin sensitivity and BP in overweight or obese Korean people with no diabetes or hypertension.

Accumulating evidence suggests that magnesium may be involved in the pathogenesis of diabetes and hypertension [2]. Magnesium depletion affects 25–40% of patients with diabetes, including well-controlled type 2 diabetics [19]. Most of epidemiologic studies have shown an inverse association between magnesium intake and fasting insulin concentration or the incidence of type 2 diabetes [2,5,20] although associations for magnesium-rich diets in these studies may reflect other beneficial dietary components such as fibers in foods that are high in magnesium. Thus, magnesium supplements could be an alternative tool for the prevention of type 2 DM and metabolic syndrome. However, the existing data regarding the effects of magnesium supplementation on the metabolic profile in humans are inconsistent, with several reports showing a beneficial effect on glucose metabolism and insulin action [3], and others showing the opposite [4]. Moreover, a recent clinical trial showed a beneficial effect of magnesium supplementation on fasting and postprandial glucose levels and insulin sensitivity in type 2 diabetics with a low total serum magnesium level [21]. There is also evidence that magnesium supplementation has a relatively small beneficial effect on insulin sensitivity in non-diabetics with insulin resistance and hypomagnesemia [22]. However, we observed no significant effect of magnesium supplementation on insulin sensitivity in the present study. Some of these discrepancies may result from differences in the duration or design of the study, type and dose of magnesium, or ethnic background of the subjects [3,5,20,21]. The elemental magnesium doses varied from 10 to 40 mmol/day (median, 15.4 mmol/day) in studies that evaluated the effects of magnesium supplementation on BP [10] and were also similar to that used in the studies that tested the effects of magnesium supplementation on glycaemic control in type 2 diabetes [23]. In our study, participants in the intervention group received rather modest 12.3 mmol (300 mg) of elemental magnesium per day in the form of magnesium oxide.

A recent cross-sectional study suggested that exceeding the recommended dietary intake of magnesium might not provide additional benefit with respect to insulin sensitivity [24]. A strong inverse correlation has been shown between magnesium intake and the risk of type 2 diabetes in subjects with low magnesium intake [6]. Hence, magnesium supplementation may be most beneficial for individuals with magnesium deficiency. However, the benefits of supplementation on insulin sensitivity may vary among different ethnic groups. The dietary magnesium intake of Taiwanese adults was found to be comparatively lower than that of adults in Western countries; however, no association between diabetes and low dietary magnesium was found [25]. In addition, magnesium supplementation has not been proven to change the serum magnesium level in all previous studies of magnesium, with some reports showing an increase [3,22] and others showing no effect [26–28]. In the present study, there was a significant decrease in serum and hair magnesium after 12 weeks of treatment with

respect to baseline value not only in the placebo group but also in the intervention group, although the decrement for hair magnesium had a borderline statistical significance ($P = 0.061$) in individuals with magnesium supplementation. Song et al. [23] have reported that the level of magnesium showed fluctuation over the course of magnesium treatment in their meta-analysis, suggesting the time course of response in serum magnesium levels on magnesium supplementation. Vormann [29] suggested that the total intake and excretion of magnesium is in balance due to an adaptation of the homeostatic mechanism, despite of a broad range of magnesium supplementation. To our knowledge, no change was seen in serum magnesium levels after magnesium supplementation when the subjects had no evidence of magnesium deficiency at the beginning of the study [26,27], although oral magnesium supplementation can normalize hypomagnesemia mainly in patients with low serum magnesium concentrations ($<$0.74 mmol/L) at baseline [3,22]. Erythrocyte magnesium levels did not change after oral magnesium supplementation due to increased urinary magnesium excretion in normo-magnesemic subjects. In our study, the total serum magnesium levels of the subjects were also within a normal range (0.75—0.96 mmol/L) at baseline and oral magnesium supplements did not influence serum magnesium. Alcohol intake is known to be associated with low serum magnesium levels. Acutely, alcohol intake decreases serum magnesium by increasing its excretion in the urine. With chronic alcohol intake, body stores of magnesium become depleted [30]. In this study, alcohol use was common among subjects (53.5 and 46.5 percent for intervention and control group, respectively). It is also known that cigarette smoking had a statistically significant association with low HDL cholesterol [31]. The proportion of smoker in our study was strikingly high at 50 percent in both groups, which was 2 times more likely than western people [8]. These explanations partially accounts for decrease in serum magnesium as wells as plasma HDL cholesterol levels even after 12 weeks of magnesium supplementation in both groups. Otherwise, the lack of effects of magnesium supplementation on markers of magnesium status may either reflect lack of treatment compliance of the participants or lack of validity of the magnesium markers. Nevertheless, we cannot completely explain the reason for changes in serum magnesium and HDL cholesterol in either intervention or placebo groups in the present study, because relevant information about the effect of magnesium is yet unavailable in normo-magnesemic nondiabetic overweight or obese adults.

Hypertension is another pathological condition resulting from altered cellular magnesium metabolism. Recent studies of extracellular ion levels have shown that the intracellular free magnesium level is strongly related to hypertension, suggesting a pathophysiological link between magnesium depletion and hypertension [1]. However, the therapeutic role of magnesium in hypertension remains unclear, although it is currently used in such critical situations as malignant hypertension and preeclampsia [32]. Thus, considering the currently available data, a role for decreased magnesium levels in the pathophysiology of hypertension appears likely, despite no confirmation of a consistent, reproducible effect of magnesium supplementation on BP [33]. Furthermore, there are few studies showing that magnesium supplementation decreases BP in normal subjects [34].

Although there were some high BP readings (Figs. 1 and 2), an abnormal reading during a single visit does not establish the presence of hypertension and we did not include subjects with anti-hypertensive medication. In this randomized study of nondiabetic overweight adults, unlike insulin sensitivity, the BP showed significant reductions following magnesium supplementation in overweight healthy adults with higher BP. The effect of magnesium on BP seems to be independent from action of magnesium on insulin sensitivity. Magnesium supplementation lowered BP much more than placebo in those subjects with systolic BP $\geq$140 mmHg or diastolic BP $\geq$80 at the start of the study; in comparison, those subjects whose initial BP reading was low at baseline did not show a change in BP (Figs. 1 and 2). Our results are consistent with those of a previous study, although the subjects in that study were hypertensive; they reported that magnesium supplementation lowered BP in hypertensive subjects and that the effect was greater in subjects with higher initial BP [9]. However, some negative studies included Western adults with high normal BP readings as subjects [18,35]. Of a meta-analysis of 20 randomized clinical trials, only one trial used double-blinded parallel arm design to test the effects of magnesium supplementation on BP in normotensive men and women for at least 12 weeks. As a result, there was no reduction in BP from magnesium supplementation [35].

The present study was different as a 12-week, randomized, double blind, placebo-controlled, multicenter study in overweight adults without hypertension or diabetes compared to previous studies. Kawano et al. [9] and Cappuccio et al. [18] used paired *t*-test for comparison of data between the control and Mg supplementation periods, because their study was done in a randomized crossover manner. However, we considered time as a within-subjects factor and treatment group as a between-subjects factor using repeated-measures ANOVA in order to study the effect of magnesium on BP over time.

In the present study, reductions of 5.6 mmHg in the systolic BP and 2.9 mmHg in the diastolic BP were observed following 12 weeks of magnesium supplementation at 12.3 mmol/day, although this change was not significantly different as compared with the change in the control group. Especially, reduced diastolic BP in this study is consistent with those of a previous meta-analysis, which showed a dose—response relationship between magnesium and diastolic BP [10]. In that study, reduction of 2.3 mmHg in the diastolic BP was observed following magnesium supplementation at 10 mmol/day.

Magnesium supplementation is considered a food supplement, not a drug, and it is available in many countries including Korea. Our study has some limitations, including the relatively short duration of the study and the fact that no attempt was made to measure ionized and urinary magnesium. Applied dose of elemental magnesium in the present study was rather modest, but rather, may not be high enough to achieve the desired outcomes of our research. Furthermore, since our results were obtained in subjects with normal serum magnesium levels, the present findings cannot be generalized conditions associated to magnesium depletion. The other limitations are the lack of

direct physiological measure of glucose and insulin homeostasis and potassium measurements. However, HOMA-IR is an inexpensive and simple method in determining insulin sensitivity and previous studies have shown that HOMA-IR highly correlates with gold standard euglycemic—hyperinsulinemic clamp in Asian peoples with or without type 2 diabetes [36,37]. WHO also recommended this method for epidemiological study [38]. Potassium may play a role in hypertension or be an indicator for mineralocorticoid excess state. Generalizabilty of our study to non-Korean populations is also uncertain, because all of the participants were Korean. In addition, the power for group analysis may not adequate, because the sample size of our study was calculated based on Western studies. Significant effect of magnesium on BP in those with a higher BP at baseline may be due to chance in limitation section, thus further research is needed to reconfirm these findings.

In conclusion, this study showed that magnesium supplementation does not reduce BP and enhance insulin sensitivity in normo-magnesemic nondiabetic overweight people. However, it appears that magnesium supplementation may lower BP in healthy adults with higher initial BP. These findings suggest that magnesium supplementation may help prevent the progression of hypertension in normomagnesemic nondiabetic overweight people with higher BP, although mechanisms of counter-regulation preventing further BP increase remain to be elucidated.

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