Published in final edited form as:

Am J Cardiol. 2016 September 15; 118(6): 849–853. doi:10.1016/j.amjcard.2016.06.041.

Effects of Potassium Magnesium Citrate Supplementation on 24-hour Ambulatory Blood Pressure and Oxidative Stress Marker in Prehypertensive and Hypertensive Subjects

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Abstract

Diet rich in fruits, vegetables, and dairy products, known as the Dietary Approaches to Stop Hypertension (DASH) diet, is known to reduce BP in hypertensive patients. More recently, the DASH diet was shown to reduce oxidative stress in hypertensive and nonhypertensive humans. However, the main nutritional components responsible for these beneficial effects of the DASH diet remain unknown. Because the DASH diet is rich in potassium (K), magnesium (Mg), and alkali, we performed a randomized, double-blinded, placebo-controlled study to compare effects of KMg Citrate (KMgCit), K Chloride (KCl), and K Citrate (KCit) to allow dissociation of the three components of K, Mg, and Citrate on 24-hour ambulatory BP and urinary 8-isoprostane in hypertensive and prehypertensive subjects, using a randomized crossover design. We found that KCl supplementation for 4 weeks induced a significant reduction in nighttime SBP compared to placebo (116±12 vs. 121±15 mmHg, respectively, $p < 0.01$ vs. placebo) while KMgCit and KCit had no significant effect in the same subjects (118±11 and 119±13 mmHg respectively, $p > 0.1$ vs. placebo). In contrast, urinary 8-isoprostane was significantly reduced with KMgCit powder compared to placebo (13.5±5.7 vs. 21.1±10.5 ng/mgCr, respectively, $p < 0.001$) while KCl and KCit had no effect (21.4±9.1 and 18.3±8.4, respectively, $p > 0.1$ vs. placebo). In conclusion, our

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Statement of Financial Disclosure:

The authors report no conflicts of interest to disclose.

study demonstrated differential effects of KCl and KMgCit supplementation on BP and the oxidative stress marker in prehypertensive and hypertensive subjects. Clinical significance of the anti-oxidative effect of KMgCit remains to be determined in future studies.

Keywords

Magnesium; citrate; cardiovascular risk factors; hypertension; prehypertension

We performed a randomized, double-blinded, placebo-controlled crossover study to compare effects of KMg Citrate, KCl, and K Citrate on 24-hour ambulatory BP in hypertensive and prehypertensive subjects. To avoid the confounding influence of K or Mg depletion, which may further contribute to BP elevation, we excluded patients treated with diuretics. Since recent studies have demonstrated benefit of the DASH diet in reducing oxidative stress in patients with heart failure with preserved ejection fraction ¹, gestational diabetes ², and polycystic ovarian disease ³, we also compare effects of KMgCitrate, KCl, and K Citrate vs. placebo on a urinary marker of oxidative stress.

Methods

Thirty subjects with prehypertension (n = 6) or stage I hypertension (n = 24) participated in the study after providing written informed consent. The study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. All subjects had systolic blood pressure between 120-159 mmHg and diastolic between 80-99 mmHg on 3 determinations by oscillometric technique in the seated position. The subjects had no history of diabetes mellitus, renal impairment (serum creatinine > 1.4 mg/dL), active cardiac or liver disease, esophageal-gastric ulcer, gastroesophageal reflux disease, chronic diarrhea, chronic non-steroidal anti-inflammatory drug use, treatment with diuretics, renal tubular acidosis, hypercalcemia, or hypocalcemia. Each subject underwent a 4-phase study, using a randomized crossover design. During each phase, subjects received one of the study drugs each for 4 weeks; 1) Placebo Phase (microcrystalline cellulose diluted in water twice daily), 2) KCl Phase (40 meq KCl powder/day), 3) K Citrate Phase (40 meq K₃Cit powder/day diluted in water), and 4) K Mg Citrate Phase (KMgCit, 40 meq K, 20 meq Mg and 74 meq citrate powder/day, IND 116,208). Subjects were instructed to take study drugs in two divided doses twice daily after dissolution in 250 ml of water. Each phase was followed by at least 1 week of washout. All study drugs were prepared in a similar powder sachets form to ensure double-blinding. All subjects were maintained on their customary diet throughout the study. During the study, participants were seen every 2 weeks in the research clinic. During each clinic visit, BP was measured by nursing staff, using the same validated oscillometric device (Welch Allyn, Vital Signs, N.C.), after the patient had been resting quietly for 5 minutes as recommended by guidelines ⁴. BP measurement during a single visit was repeated 3 times separated by 1 minute and these BP values were averaged.

24-hour ambulatory BP monitoring (ABPM) was performed at baseline and after 4 weeks of each study drug, using a SpaceLabs model 90207 (SpaceLabs Inc., Issaquah, Washington, USA) as previously described ⁵. Measurement of arterial stiffness was performed during the fourth week of treatment in each phase after an overnight fast, using arterial tonometry

technique. Arterial tonometry and simultaneous ECG were obtained from the brachial, radial, femoral, and carotid arteries using a pulse transducer device (Cardiovascular Engineering, Inc. Waltham, MA) as previously described ^{6,7}. 24-hour urine sample were collected during the last week of treatment for K, pH, citrate, Mg, sodium (Na), calcium (Ca), phosphorus (Pi), sulfate (S), creatinine (Cr) and total volume. Similarly, blood samples were collected after 4 weeks of treatment after an overnight fast for K, Na, Cl, and carbon dioxide (CO₂), Mg, Cr, Ca, Pi, parathyroid (PTH), 1,25-dihydroxyvitamin D (1,25-(OH)₂ D).

Urinary 8-isoprostane (8-isoP) was measured using an enzyme immunoassay kit (Cayman Chemical, Ann Arbor, MI) based on competitive binding between 8-isoprostane and 8-isoprostane-acetylcholinesterase (AChE) conjugate (8-Isoprostane Tracer) for limited specific binding sites compared against a standard curve at 412 nm as previously described ⁸.

Plasma and urinary electrolytes including Pi, Ca, Mg, and Na were determined with methods presented as previously described ^{9,10}.

Mixed effects linear models were used to conduct the repeated measures analysis to assess differences between KCl, KCit, KMgCit, and placebo phases. Contrasts from these models were used for pair-wise comparisons. Treatment order was also assessed in our mixed-effects models and was included as a fixed effect to test for interactions between study drug and treatment order; no effect of treatment order on any outcome variables was found. The 0.05 level of significance was used for model main effects and the 0.01 level of significance was used for pair-wise tests to adjust for multiple testing. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). All tests were two-sided and a p-value < 0.05 was considered statistically significant. Augmented pressure was presented as median and interquartile range. Other variables are presented as means ± standard deviation.

Results

Baseline characteristics of all subjects are shown in Table 1. There were 6 prehypertensive subjects and 24 subjects with stage I hypertension. Among hypertensive subjects, 17 of 24 received antihypertensive treatment prior to study participation. All treated subjects received single drug regimen prior to participation in the study (6 were on beta blockers, 11 on angiotensin receptor blockers or angiotensin converting enzyme inhibitors, or calcium channel blockers), which was continued at the same dose throughout the study.

Serum K and 24-hour urinary K excretion were increased during KCl, KCit, and KMgCit phases compared to placebo phase (p < 0.01 vs. placebo, Table 2). Serum Mg was increased during KMgCit phased compared to placebo and KCl phases (both p < 0.01). 24-hour urinary Mg excretion was increased during KMgCit phase compared to placebo and KCit (both p < 0.01). There was a tendency for 24-hour urinary Mg excretion to be higher during KMgCit when compared to KCl but the difference did not reach statistical significance (p = 0.017)

KCl significantly reduced nighttime SBP compared to placebo ($p < 0.01$ vs. placebo, Table 2). The lowest 24-hour ambulatory SBP was observed on KCl but the omnibus effect was not statistically significant. (mixed model p value = 0.07, $p = 0.01$ vs. placebo). In contrast, KMgCit had no significant effect on 24-hour ambulatory BP or nighttime BP in the same subjects. Central aortic BP as well as indices of vascular stiffness, including PWV, augmentation index, and augmented pressures were not altered by KCl, KMgCit, or KCit supplementation when compared to placebo (Table 3). Serum level of $1,25(\text{OH})_2\text{D}$ was increased by KCit compared to placebo while KMgCit and KCit resulted in similar $1,25(\text{OH})_2\text{D}$ levels compared to placebo (Table 2). Serum PTH was not altered by KCl, KMgCit, or KCit supplementation when compared to placebo (Table 2).

Urinary 8-isoprostane following 4 weeks of treatment was significantly reduced with KMgCit powder compared to KCl and placebo (13.5 ± 5.7 vs 21.4 ± 9.1 vs. 21.1 ± 10.5 ng/mgCr, respectively, $p < 0.001$ vs. KCl and placebo, Figure 1). There was no significant difference in urinary 8-isoP between KMgCit vs KCit ($p = 0.037$) and between KCit powder and placebo ($p = 0.14$).

Discussion

The major findings of our study are two fold. First, supplementation of KCl induced a small but significant reduction in nocturnal BP in prehypertensive and hypertensive subjects but had no effect on urinary 8-isoprostane. Second, KMgCit, induced a robust decrease in a marker of oxidative stress without altering BP in the same population, suggesting its novel anti-oxidative action.

Mechanism underlying differential effects of KCl vs. KMgCit on lowering BP is unknown. One possibility is that magnesium or citrate may negate antihypertensive action of K, during KMgCit phase. However, this is unlikely since average nighttime SBP was also lower during KCit and KMgCit phases when compared to placebo phase though the difference did not achieve significance. Thus, it is plausible that our study is underpowered to detect a small BP lowering effect of KMgCit. Another possibility is nonadherence to study drugs. However, this is unlikely as urinary K excretion increased during KCl, KMgCit, and KCit, when compared to placebo phase by an average of 40 meq/day, which is identical to amount of K supplementation in each phase. Since KMgCit and KCit were not more effective than KCl in lowering BP, potassium is likely to be the unifying component responsible for nighttime BP reduction observed in our study.

Our study also provided the first direct evidence for the anti-oxidative action of KMgCit. Although previous studies have demonstrated reduction in markers of oxidative stress after treatment with the DASH diet in other populations, dietary sodium restriction was thought to be the main cause of reduced oxidative stress as subjects randomized to the DASH diet also received low sodium diet of < 100 meq per day¹⁻³. In contrast, participants in our studies were allowed to maintain their typical diet; their 24-hour urinary Na excretion averaged 180 meq. Despite the high level of Na intake in our study above the recommended allowance for hypertensive patients, KMgCit induced a robust reduction urinary 8-isoP by 36%. Because KMgCit was also superior to both KCl and KCit in lowering urinary 8-isoP despite similar

K and citrate content, our study suggested that magnesium was the major component responsible for this anti-oxidative property. Mechanism underlying the anti-oxidative effect of KMgCit is unknown. Magnesium deficiency has been shown to augment aldosterone-induced increase in renal oxidative stress via increasing NADPH oxidase activity and increased p47phox expression in mice ¹¹. High Mg diet has been shown to attenuate aldosterone-induced increase in NADPH oxidase activity in the kidneys of mice with genetically low intracellular Mg ¹¹. Furthermore, previous studies in healthy humans have suggested an inhibitory influence of dietary Mg supplementation on the circulating aldosterone levels, which could further reduce activity of NADPH oxidase ¹². However, none of our subjects have known conditions that predispose to Mg depletion or activation of reninangiotensin-aldosterone system such as diuretic treatment or chronic diarrhea.

Since urinary 8-isoP tended to be lower during KCit when compared to placebo, we cannot exclude the possibility of synergistic action of Mg and alkali on the anti-oxidative action of KMgCit. Previous studies have suggested an inhibitory influence of alkali supplementation in the generation of oxidative stress. Supplementation of citrate precursor with calcium/potassium salt of hydroxycitric acid was shown to reduce inflammation and oxidative stress in obese Zucker rats ¹³. In contrast, induction of metabolic acidosis with oral ammonium chloride was shown to increase amino acid oxidation in healthy humans ¹⁴.

Clinical relevance of decreased oxidative stress associated with KMgCit is unknown at the moment. Increased oxidative stress has been shown to contribute to impaired skeletal muscle vasodilation during exercise in healthy humans and animals without hypertension ^{15,16}. Studies in humans without heart failure have implicated the role of oxidative stress in endothelial dysfunction and exercise intolerance ¹⁷⁻¹⁹, which was independent of blood pressure. Increased oxidative stress has also been implicated in the pathogenesis of insulin resistance and diabetes mellitus ^{20,21}. Increased plasma 8-isoP associated with increased risk of atherosclerosis as evidenced by coronary artery calcification in a population-based study of healthy young adults ²². More recently, serum and urinary 8-isoP have been shown to predict cardiovascular events in patients with atrial fibrillation ²³ and acute coronary syndrome ²⁴, which was independent of traditional cardiovascular risk factors. More studies are needed to determine long term effects of KMgCit on exercise capacity, insulin sensitivity, and cardiovascular outcomes in hypertensive patients.

The strength of our study included the use of randomized double-blinded study design to test effects of KMgCit supplementation on cardiovascular risk factors in hypertensive and prehypertensive patients. Our study is limited to small sample size and inclusion of patients mostly with mild uncomplicated hypertension, which was well controlled on a single drug regimen. Furthermore, none of the subjects had low serum Mg under 1.8 mg/dL or serum K below 3.5 meq/L or on diuretic therapy. Nevertheless, our study demonstrated a robust action of KMgCit supplementation in reducing oxidative stress marker during treatment, independent of BP reduction. Future studies are needed to determine effects of KMgCit on BP and oxidative stress in patients with conditions associated with Mg or K depletion.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

None

Sources of funding: Supported by grants to Dr. Vongpatanasin from the UT Southwestern O'Brien Kidney Research Center (P30 DK-079328) and Clinical Metabolism Fund of the Center of Mineral Metabolism and Clinical Research.

References

1. Hummel SL, Seymour EM, Brook RD, Sheth SS, Ghosh E, Zhu S, Weder AB, Kovacs SJ, Kolias TJ. Low-sodium DASH diet improves diastolic function and ventricular-arterial coupling in hypertensive heart failure with preserved ejection fraction. *Circ Heart Fail*. 2013; 6:1165–1171. [PubMed: 23985432]
2. Asemi Z, Samimi M, Tabassi Z, Sabihi SS, Esmailzadeh A. A randomized controlled clinical trial investigating the effect of DASH diet on insulin resistance, inflammation, and oxidative stress in gestational diabetes. *Nutrition*. 2013; 29:619–624. [PubMed: 23466048]
3. Asemi Z, Samimi M, Tabassi Z, Shakeri H, Sabihi SS, Esmailzadeh A. Effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: a randomized clinical trial. *Nutrition*. 2014; 30:1287–1293. [PubMed: 25194966]
4. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Hypertension*. 2005; 45:142–161. [PubMed: 15611362]
5. Raheja P, Price A, Wang Z, Arbique D, Adams-Huet B, Auchus RJ, Vongpatanasin W. Spironolactone prevents chlorthalidone-induced sympathetic activation and insulin resistance in hypertensive patients. *Hypertension*. 2012; 60:319–325. [PubMed: 22733474]
6. Inrig JK, Van Buren P, Kim C, Vongpatanasin W, Povsic TJ, Toto RD. Intradialytic hypertension and its association with endothelial cell dysfunction. *Clinical Journal of the American Society of Nephrology : CJASN*. 2011; 6:2016–2024. [PubMed: 21757643]
7. Inrig JK, Van Buren P, Kim C, Vongpatanasin W, Povsic TJ, Toto R. Probing the mechanisms of intradialytic hypertension: a pilot study targeting endothelial cell dysfunction. *Clinical Journal of the American Society of Nephrology : CJASN*. 2012; 7:1300–1309. [PubMed: 22700888]
8. Ravikumar P, Ye J, Zhang J, Pinch SN, Hu MC, Kuro-o M, Hsia CC, Moe OW. alpha-Klotho protects against oxidative damage in pulmonary epithelia. *Am J Physiol Lung Cell Mol Physiol*. 2014; 307:L566–575. [PubMed: 25063799]
9. Hu MC, Shi M, Cho HJ, Adams-Huet B, Paek J, Hill K, Shelton J, Amaral AP, Faul C, Taniguchi M, Wolf M, Brand M, Takahashi M, Kuro OM, Hill JA, Moe OW. Klotho and phosphate are modulators of pathologic uremic cardiac remodeling. *Journal of the American Society of Nephrology : JASN*. 2015; 26:1290–1302. [PubMed: 25326585]
10. Panesso MC, Shi M, Cho HJ, Paek J, Ye J, Moe OW, Hu MC. Klotho has dual protective effects on cisplatin-induced acute kidney injury. *Kidney International*. 2014; 85:855–870. [PubMed: 24304882]
11. Yogi A, Callera GE, O'Connor SE, He Y, Correa JW, Tostes RC, Mazur A, Touyz RM. Dysregulation of renal transient receptor potential melastatin 6/7 but not paracellin-1 in aldosterone-induced hypertension and kidney damage in a model of hereditary hypomagnesemia. *Journal of Hypertension*. 2011; 29:1400–1410. [PubMed: 21602712]
12. Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude R. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension*. 1993; 21:1024–1029. [PubMed: 8505087]

13. Asghar M, Monjok E, Kouamou G, Ohia SE, Bagchi D, Lokhandwala MF. Super CitriMax (HCA-SX) attenuates increases in oxidative stress, inflammation, insulin resistance, and body weight in developing obese Zucker rats. *Mol Cell Biochem.* 2007; 304:93–99. [PubMed: 17503004]
14. Reaich D, Channon SM, Scrimgeour CM, Goodship THJ. Ammonium Chloride-Induced Acidosis Increases Protein Breakdown and Amino-Acid Oxidation in Humans. *American Journal of Physiology.* 1992; 263:E735–E739. [PubMed: 1415693]
15. Fadel PJ, Farias Iii M, Gallagher KM, Wang Z, Thomas GD. Oxidative stress and enhanced sympathetic vasoconstriction in contracting muscles of nitrate-tolerant rats and humans. *The Journal of Physiology.* 2012; 590:395–407. [PubMed: 22106180]
16. Thomas GD, Zhang W, Victor RG. Impaired modulation of sympathetic vasoconstriction in contracting skeletal muscle of rats with chronic myocardial infarctions: role of oxidative stress. *Circulation Research.* 2001; 88:816–823. [PubMed: 11325874]
17. Dekleva M, Celic V, Kostic N, Pencic B, Ivanovic AM, Caparevic Z. Left ventricular diastolic dysfunction is related to oxidative stress and exercise capacity in hypertensive patients with preserved systolic function. *Cardiology.* 2007; 108:62–70. [PubMed: 17003543]
18. Pierce GL, Lesniewski LA, Lawson BR, Beske SD, Seals DR. Nuclear factor- $\{\kappa\}$ B activation contributes to vascular endothelial dysfunction via oxidative stress in overweight/obese middle-aged and older humans. *Circulation.* 2009; 119:1284–1292. [PubMed: 19237660]
19. Pingitore A, Lima GP, Mastorci F, Quinones A, Iervasi G, Vassalle C. Exercise and oxidative stress: potential effects of antioxidant dietary strategies in sports. *Nutrition.* 2015; 31:916–922. [PubMed: 26059364]
20. Evans JL, Goldfine ID, Maddux BA, Grodsky GM. Are oxidative stress-activated signaling pathways mediators of insulin resistance and beta-cell dysfunction? *Diabetes.* 2003; 52:1–8. [PubMed: 12502486]
21. Sinaiko AR, Steinberger J, Moran A, Prineas RJ, Vessby B, Basu S, Tracy R, Jacobs DR Jr. Relation of body mass index and insulin resistance to cardiovascular risk factors, inflammatory factors, and oxidative stress during adolescence. *Circulation.* 2005; 111:1985–1991. [PubMed: 15837953]
22. Gross M, Steffes M, Jacobs DR Jr. Yu X, Lewis L, Lewis CE, Loria CM. Plasma F2-isoprostanes and coronary artery calcification: the CARDIA Study. *Clinical Chemistry.* 2005; 51:125–131. [PubMed: 15514100]
23. Pignatelli P, Pastori D, Carnevale R, Farcomeni A, Cangemi R, Nocella C, Bartimoccia S, Vicario T, Saliola M, Lip GY, Violi F. Serum NOX2 and urinary isoprostanes predict vascular events in patients with atrial fibrillation. *Thromb Haemost.* 2015; 113:617–624. [PubMed: 25392853]
24. LeLeiko RM, Vaccari CS, Sola S, Merchant N, Nagamia SH, Thoenes M, Khan BV. Usefulness of elevations in serum choline and free F2)-isoprostane to predict 30-day cardiovascular outcomes in patients with acute coronary syndrome. *The American Journal of Cardiology.* 2009; 104:638–643. [PubMed: 19699337]

Figure 1. Urinary 8-isoprostane levels following 4 weeks of treatment with Potassium Magnesium Citrate (KMgCit), Potassium Citrate (KCit), Potassium Chloride (KCl) and Placebo.
†p < 0.001 comparing KMgCit vs both KCl and placebo

Table 1

Baseline characteristics

Variables	
Age (years)	54±12
Black	12 (40%)
Female	16 (53%)
Weight (kg)	90±18
Body Mass Index (kg/m ²)	31± 5
Office Systolic Blood Pressure (mmHg)	125±11
Office Diastolic Blood Pressure (mmHg)	81±8
Office Heart Rate (bpm)	72±11
24-hr Systolic Blood Pressure Average (mmHg)	126±10
24-hr Diastolic Blood Pressure Average (mmHg))	79±10
24-hr Heart Rate Average (bpm)	76±11
24-hr Daytime Systolic blood pressure (mmHg)	129±10
24-hr Daytime diastolic blood pressure (mmHg)	81±11
24-hr Daytime Heart Rate (bpm)	77±11
24-hr Nighttime Systolic Blood Pressure (mmHg)	117±12
24-hr Nighttime Diastolic Blood Pressure (mmHg)	71±10
24-hr Nighttime Heart Rate (bpm)	70±11
Calcium (mg/dl)	9.5±0.5
Phosphorus (mg/dl)	3.6±0.1
Magnesium (mg/dl)	2.2±0.3
Sodium (meq/L)	139±2
Potassium (meq/L)	4.2±0.3
Chloride (meq/L)	105±2
Bicarbonate (meq/L)	23±2
Urea nitrogen (mg/dl)	13.7±3.5
Creatinine (mg/dl)	0.9±0.2
Albumin (g/dl)	4.2±0.6
Parathyroid hormone (g/ml)	59±31
1,25-dihydroxyvitamin D (pg/ml)	73±34

Values presented as mean ± standard deviation or n (%).

Table 2

Hemodynamic and biochemical data after 4 weeks of treatment.

Variable	Placebo n = 30	Potassium Chloride n = 30	Potassium Citrate n = 30	Potassium Magnesium Citrate n = 30	Mixed Model p value
Weight (kg)	89±18	89±18	90±18	89±17	0.40
Body Mass Index (kg/m ²)	30±12	31±5	31±5	31±5	0.37
Office Systolic Blood Pressure (mmHg)	129±12	127±11	125±13	124±11	0.16
Office Diastolic Blood Pressure (mmHg)	81±9	80±9	81±8	81±9	0.70
Office Heart Rate (bpm)	70±12	68±9	70±10	70±11	0.17
24-hr Average Systolic Blood Pressure (mmHg)	129±13	126±9 [*]	127±10	127±11	0.07
24-hr Average Diastolic Blood Pressure (mmHg)	80±11	78±9	78±9	79±10	0.20
24-hr Average Heart Rate (bpm)	76±15	74±10	76±11	75±10	0.43
24-hr Daytime Systolic Blood Pressure (mmHg)	132±13	129±10	130±12	130±12	0.21
24-hr Daytime Diastolic Blood Pressure (mmHg)	82±12	81±10	81±10	81±11	0.37
24-hr Daytime Heart rate (bpm)	76±11	76±10	78±11	76±10	0.48
24-hr Nighttime Systolic Blood Pressure (mmHg)	121±15	116±12 [*]	118±11	119±13	0.03
24-hr Nighttime Diastolic Blood Pressure (mmHg)	73±10	70±9	71±9	73±10	0.05
24-hr Nighttime Heart Rate (bpm)	70±11	68±10	71±10	71±10 [†]	0.04
Calcium (mg/dl)	9.5±0.4	9.5±0.4	9.4±0.7	9.6±0.4	0.23
Phosphorus (mg/dl)	3.5±0.6	3.5±0.5	3.6±0.5	3.4±0.5	0.30
Magnesium (mg/dl)	2.1±0.2	2.1±0.2	2.2±0.2	2.3±0.3 ^{*†}	0.001
Sodium (meq/L)	138±1	138±2	137±2	138±2	0.22
Potassium (meq/L)	4.2±0.3	4.4±0.3 [*]	4.3±0.3 [*]	4.4±0.3 [*]	0.0001
Chloride (meq/L)	105±2	105±2	104±2 [†]	104±2 [†]	0.01
Bicarbonate (meq/L)	23±2	22±2	23±2	23±2	0.55
Urea nitrogen (mg/dl)	12.9±3.4	13.6±3.4	13.9±3.5	14.1±3.5	0.13
Creatinine (mg/dl)	0.9±1.1	0.9±0.2	0.9±0.2	0.9±0.2	0.96
Albumin (g/dl)	4.4±0.3	4.3±0.6	4.4±0.2	4.4±0.2	0.31
Parathyroid hormone (g/ml)	58±30	65±43	66±37	61±28	0.46
1,25- dihydroxyvitamin D (pg/ml)	71±29	76±31	82±37 [*]	77±32	0.09
Klotho (%)	19±9	19±11	19 ±12	21±12	0.71
24 hour Urine Data					
Total Volume (L/day)	2.0±0.6	1.9±0.7	2.0±0.5	2.0±0.7	0.95
pH	6.0±0.4	6.0±0.6	6.4±0.6 ^{*†}	6.7±0.4 ^{*†‡}	<0.0001

Variable	Placebo n = 30	Potassium Chloride n = 30	Potassium Citrate n = 30	Potassium Magnesium Citrate n = 30	Mixed Model p value
Calcium (mg/day)	181±101	160±92	148±78	158±94	0.10
Magnesium (mg/day)	97±40	104±52	100±43	121±44 ^{*†}	0.01
Phosphorus (mg/day)	842±301	868±364	858±306	764±278	0.32
Creatinine (mg/day)	1451±389	1477±492	1501±474	1393±436	0.59
Sodium (meq/day)	173±61	184±65	190±100	187±78	0.64
Potassium (meq/day)	58±30	95±34 [*]	84±31 [*]	91±37 [*]	<0.0001
Citrate (mg/day)	668±262	753±308	908±385 ^{*†}	995±407 ^{*†}	<0.0001
Sulphate (mmol/day)	16.8 ±5.6	17.6±7.6	17.4±5.0	16.5±5.1	0.77

Data are shown as mean ± standard deviation.

^{*}
p 0.01 vs placebo

[†]
p 0.01 vs KCl

[‡]
p 0.01 vs KCit.

Table 3

Central aortic blood pressure and indices of vascular stiffness after 4 weeks of treatment

Arterial Vascular Studies	Placebo n = 30	Potassium Chloride n = 30	Potassium Citrate n = 30	Potassium Magnesium Citrate n = 30	Mixed model p value
Carotid-Radial Pulse Wave Velocity (m/s)	9.6±2.0	9.2±1.8	9.3±1.8	9.1±1.7	0.35
Carotid-Femoral Pulse Wave Velocity (m/s)	8.9±1.8	8.7±1.5	8.8±1.6	8.7±1.7	0.64
Radial Systolic Blood Pressure (mmHg)	135±17	132±14	134±16	132±17	0.81
Radial Diastolic Blood Pressure (mmHg)	79±9	77±9	76±7	77±7	0.17
Central Systolic Blood Pressure (mmHg)	126±14	123±13	125±16	121±11	0.18
Central Diastolic Blood Pressure (mmHg)	79±8	77±9	76±7	77±7	0.12
Augmentation Index (%)	11±14	10±11	12±14	9±13	0.41
Augmented Pressure (mmHg)	4(2, 9)	4(1, 8)	5(1, 11)	3(0, 7)	0.07

Data are shown as mean ± standard deviation or median (interquartile range).