Original Article

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고령 고혈압 환자에서 천일염의 혈압 감소 효과: 예비 무작위 대조시험

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Anti-Hypertensive Effect of a Solar Salt Diet in Elderly Hypertensive Patients: A Preliminary Randomized, Double-Blind Clinical Trial

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Background: High sodium and/or low mineral intake are known to be associated with elevated blood pressure. It has been reported that substituting low-sodium, mineral-rich salt for refined salt lowers blood pressure (BP). And solar salt is emerging as a low sodium high mineral salt for a healthy diet in Korea. Therefore, this double-blind, randomized, and placebo-controlled trial was conducted to explore changes in BP from substituting refined salt with solar salt among hypertensive elderly subjects.
Methods: Forty-three hypertensive and institutionalized elderly individuals aged 65 years or older were enrolled. Thirty-eight subjects (88.4%) completed the study. Subjects were provided with either a solar salt- or refined salt-based diet for eight weeks.
Results: Systolic BP decreased significantly in the solar salt-based diet group after 2, 4, and 8 weeks when compared to the refined salt-based diet group. And, diastolic BP was lowered significantly in the solar salt-based diet group compared to that in the refined salt-based diet group after 8 weeks. In addition, urinary sodium/potassium, and angiotension converting enzyme activity decreased significantly in the solar salt-based diet group compared to the refined salt-based group. Urinary potassium excretion was significantly increased in the solar salt-based diet group.
Conclusions: These results may provide clinical evidence that solar salt has beneficial effects on BP in elderly patients. And, people such as Koreans, who do not consume enough minerals, may experience a greater anti-hypotensive effect by using solar salt. However, further large-scale studies are necessary.
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INTRODUCTION

Hypertension is more prevalent, less controlled, and more severe in the elderly, affecting more than two out of every three individuals over the age of 75.[1] Although many elderly hypertensive patients use anti-hypertensive medications, it is necessary to consider all medical conditions and history before prescribing anti-hypertensive medications as adverse effects can occur frequently. In addition, there has been an increasing tendency not to treat high blood pressure with anti-hypertensive medications in the elderly.[2] Instead, modifications in lifestyle, such as reduced sodium intake, are more importantly suggested as a first approach.

High sodium intake is associated with elevated blood pressure (BP) and increased risk of cardiovascular disease (CVD).[3] And, it has been shown that a high salt intake is an independent factor in predicting the risk of type 2 diabetes.[4] There have been many animal experiments, epidemiological studies, and clinical trials concluding that hypertension and CVD can be prevented by decreasing dietary sodium.[5,6] It has also been reported that dietary minerals have a beneficial effect on blood pressure, especially in hypertensive patients.[7] However, the hypotensive effect of each mineral supplementation is not consistent.[7] Increasing the intake of a variety of minerals is more effective in lowering BP than a single mineral.[7] Furthermore, the anti-hypertensive effect of the Dietary Approaches to Stop Hypertension diet, which includes numerous minerals such as potassium, calcium, and magnesium, was much greater than reduced sodium intake.[8] Therefore, the replacement of refined salt with low-sodium, mineral-rich salt has been suggested as an effective alternative to reducing salt and increasing minerals in the diet. Studies have shown that substituting mineral-rich salt for refined salt lowered BP in subjects with hypertension.[9-12]

Solar salt is produced from the evaporation and concentration of seawater. It contains a smaller percentage of NaCl (85.03%) than regular refined table salt (99.05%). And, solar salt contains abundant minerals, including calcium (1,495 ppm), potassium (2,494 ppm), and magnesium (8,190 ppm).[13] Solar salt, as a low sodium-high mineral salt, in the diet may be useful in controlling high BP in elderly hypertensive patients. To date, no clinical study has been conducted comparing the effects of consuming solar salt and refined salt.

The purpose of this study was to explore the blood pressure lowering effect of a solar salt diet in hypertensive elderly subjects compared to those on a refined salt diet.

METHODS

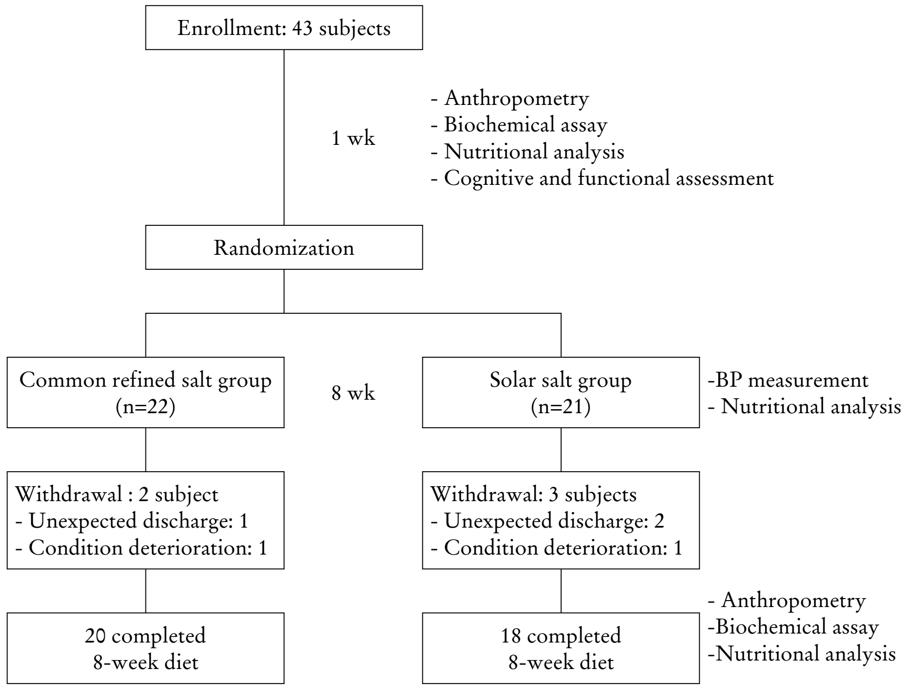
1. Study subjects

Subjects were inpatients recruited from the department of family medicine and physical medicine & rehabilitation at a nursing hospital for the elderly from October 2009 to February 2010. Study procedures were explained to participants and their guardians. Eligible subjects were aged 65 years or older and had been diagnosed with hypertension. Hypertension was defined as systolic BP ≥140 mmHg/diastolic BP ≥90 mmHg.[14] or the use of anti-hypertensive medication. Subjects were excluded if they had one or more of the following: 1) malignant cancer; 2) life expectancy less than six months; 3) Global Deterioration Scale (GDS) stage 7/bed-ridden status; 4) acute exacerbation of chronic disorders; 5) renal dysfunction (high than normal range of serum creatinine); 6) unable to ingest solid food; or 7) change of anti-hypertensive medication within 4 weeks prior to screening. A total of 43 elderly patients with hypertension hospitalized with chronic diseases volunteered for the study. Among 140 hospitalized patients, 12 patients without hypertension patients, 8 cancer patients, 10 patients with late dementia (GDS 7) or a bed-ridden status, 26 patients with unstable conditions due to acute exacerbation of chronic disease or an acute illness (such as urinary tract infection), 5 patients with abnormal renal function, 4 patients with change to their anti-hypertensive medications within 4 weeks prior to screening, and 32 patients in for short-term admission, scheduled for discharge within 2 weeks, or not admitted at least 4 weeks prior to screening were excluded. This study was conducted according to the Declaration of Helsinki and the study protocol was approved by the Institutional Review Board of the Chung-ang University Hospital. Written informed consent was obtained from every participant and guardian.

2. Study design

A randomized, double-blind clinical trial was carried out for eight weeks to compare the effects of solar and refined

Figure 1. Flowchart of the study design and study subjects. BP, blood pressure.



salts on blood pressure in patients with hypertension (Fig. 1). Assuming a significant level (α)=0.05 and a one-sided test, the intended sample of 36 recruited subjects provided a power of 80%. In our study, the primary outcome measure was systolic BP at week 8. In a previous study,[13] systolic BPs at 8 weeks in the control group and mineral salt group were 161.0±2.1 and 151.8±2.1 mmHg, respectively. We wanted the capability to show a difference of 2 mmHg in systolic BP between the groups. The drop-out rate was expected to be less than 15% and we asked 43 patients to participate in this study.

Among the subjects, two subjects in the solar salt group and one from the refined salt group were excluded from the study due to unexpected discharge from the hospital; and two other subjects, one from each group, were excluded because of deteriorating conditions. Thirty-eight subjects completed the study, for a completion rate of 88.4%.

Study subjects were randomized in a double-blind fashion to receive either a solar salt- or a refined salt-based diet. Randomization was performed by creating a table of random numbers, which assigned each subject into either group. The investigator and subjects were unaware of the type of salt contained in the meals. Subjects were provided with a meal composed of 2,000 kcal/day for males and 1,600 kcal/day for females according to the Dietary Reference Intakes for Koreans (KDRIs).[15] For both groups, 5,000 mg/day of sodium was provided based on the average Korean consumption,[16] as a sudden application of the KDRI (goal: 2,000 mg/day) resulted in a decrease in dietary intake due to significant changes in palatability to the subjects. Each meal was prepared by adding 2.4 g refined salt (sodium 1,000 mg) or 2.8 g solar salt (sodium 1,000 mg) to a low-salt diet (sodium 2,000 mg/day). Subjects and care workers were educated on the restrictions of extra snacks. The solar salt-based diet group was provided meals using seasoning, soybean paste, and kimchi (Korean-style fermented vegetables) made from solar salt (Shinan, Jeollanam-do, Korea). Subjects were evaluated after eight weeks, while continuing their anti-hypertensive therapy.

3. Measurements

Anthropometric evaluation, nutritional analysis, and biochemical assays were performed for each patient. Medical history, current medical conditions, and medication data were collected from medical records. For cognitive and functional assessment at baseline, valid and reliable instruments including Korean Mini-Mental State Examination (K-MMSE),[17] Korean Activities of Daily Living (K-ADL),[18] Seoul-Instrumental Activities of Daily Living (S-IADL),[19] and GDS[20] were performed. MMSE is a brief 30-point questionnaire test that is used for screening cognitive impairment. Scores of 24 and higher indicate normal cognition. Scores of less than 19 suggest dementia.[17] ADL and IADL are functional assessment tools, particularly in regards to people with disabilities and the elderly. ADL and IADL consist of 7 items (points range: 0-14) and 15 items (points range: 0-45), repectively.[18,19] Higher scores imply low functional status. GDS is a useful tool for staging dementia (1-7).[20] Stages 5, 6, and 7 suggest early dementia (moderately severe cognitive decline), middle phase of dementia (severe cognitive decline), and late dementia (very severe cognitive decline), respectively.[20]

Body weight was measured to the nearest 0.1 kg using an electronic scale, and height was measured to the nearest 0.1 cm using a stadiometer. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Blood pressure was measured to the nearest 1 mmHg using a mercurial sphygmomanometer via the auscultatory method twice a day (8 a.m. and 8 p.m.) and was calculated as an average value. Dietary intake of subjects was evaluated twice a week (Tuesdays and Saturdays) by directly weighing the foods consumed by individuals by a trained dietitian. Dietary data were collected from a week before randomization to the end of the trial. With this information, energy and nutrient intake were analyzed using the CAN-Pro 3.0 program (The Korean Nutrition Society, Seoul, Korea) developed by the Korean Nutrition Society.

Biochemical tests were performed on blood samples collected after overnight fasting (>8 hours). Serum levels of fasting glucose, total cholesterol, high density lipoprotein (HDL)-cholesterol, and triglyceride were measured using an ADVIA 1650 Chemistry system (Siemens, Tarrytown, NY, USA). Blood urea nitrogen, creatinine, and serum and urine electrolytes including sodium, potassium and chloride, were measured by an ADVIA 1650 Chemistry system (Siemens). Fasting insulin levels were measured via an electrochemiluminescence immunoassay (Roche, Indianapolis, IN, USA), and insulin resistance was estimated according to the homeostasis model assessment of insulin resistance (HOMA-IR) index [(insulin (μIU/mL) ×fasting blood glucose (mg/dL)/18)/22.5]. Angiotensin converting enzyme (ACE) levels were measured using an enzyme- linked immunosorbent assay (R&D Systems, Minneapolis, MN, USA), and the inter- and intra-assay variabilities were 5.9±1.6 and 3.7±0.3%, respectively.

4. Statistical analyses

Data are presented as median (25-75%). Baseline characteristics in subjects were compared using Wilcoxon rank sum test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables in cells with an expected count less than 5. Changes in systolic and diastolic BPs, and other clinical parameters were calculated using the Wilcoxon rank sum test or the Wilcoxon signed rank test between groups or within each group according to the randomization. And, the Kolmogorov-Smirnov normality test on the ACE values was performed. To examine the change of ACE levels between groups, ANCOVA (Analysis of Covariance) was used. Significance was defined at the 0.05 level of confidence. All calculations were performed using the SAS 9.1 statistics package (SAS Institute Inc., Cary, NC, USA).

RESULTS

1. Clinical characteristics of the subjects at baseline

The clinical characteristics of subjects according to solar or refined salt-based diets are shown in Table 1. No statistical differences were seen in age, BMI, gender, BP and pulse rate, cognitive and functional assessment, or medical history between the groups. Twenty-seven patients (71.05%) were currently using one or more anti-hypertensive medications. Four patients in each group have taken an anti-hypertensive medication (solar-salt group: 1 diuretic, 2 calcium channel blocker (CCB), and 1 ACE inhibitor or angiotensin receptor blocker (ARB); refined salt group:1 diuretic, 3 CCB). Users (P=0.980) and types (P=0.450) in blood pressure-lowering agents were not different between the groups. There were no significant differences in the levels of fasting glucose (P=0.130) and insulin (P=0.600); HOMA-IR (P=0.860); total cholesterol (P=0.750); triglyceride (P=0.480); HDL-cholesterol (P=0.360); low density lioprotein-cholesterol (P=0.540); blood urea nitrogen (P=0.970) and creatinine (P=0.120); serum sodium (P=0.200), potassium (P=0.160), and chloride (P=0.450); or urinary sodium (P=0.770), potassium (P=0.970), and chloride (P=0.690) between the two groups. Also, angiotensin converting enzyme activity (solar salt group:

107.3±33.98 ng/mL, refined salt group: 100.19±45.44 ng/mL; *P*=0.300) was not different (Table 1).

2. Nutrient status before and after trial

Total calorie and nutrient intake before and after the trial are described in Table 2. There were no significant differences in baseline nutrient intake between the groups. Intake of total calorie, protein, fat, and carbohydrate did not differ with change to the type of salt (Table 2).

3. Clinical outcomes of solar- or refined salt-based diet before and after 8 weeks

Pre- and post-study data are presented in Table 3. There were significant decreases in systolic BP (*P*=0.007) and urinary sodium/potassium (*P*=0.040) within the solar salt group after trial. And, serum (*P*=0.030) and urinary (*P*=0.008) potassium levels were increased within the solar salt group after the trial. In the refined salt group, no significant differences were found after the trial.

Table 1. Clinical characteristics of the subjects at baseline

	Solar salt (n=18)	Refined salt (n=20)	P^a
Age, y	79.5 (75-88)[b]	80.0 (77-84)[b]	0.520
Body mass index, kg/m^2	24.4 (19.9-25.8)[b]	23.8 (19.2-25.3)[b]	0.270
Sex			0.170
Male	9 (64.29)[c]	5 (25.00)[c]	
Female	9 (36.00)[c]	15 (75.00)[c]	
Blood pressure, mmHg			
Systolic	127.5 (121-140)[b]	129.0 (122-136)[b]	0.300
Diastolic	74.0 (70-94)[b]	76.0 (70-88)[b]	0.610
Pulse rate, beat/min	75 (70-82)[b]	72 (69-78)[b]	0.250
Geriatric functional assessment, score			
MMSE-K	21 (13-23)[b]	20 (12-23)[b]	0.380
K-ADL	4.0 (2-7)[b]	4.0 (1-8)[b]	0.610
S-IADL	29.5 (20.0-38)[b]	32 (30-38)[b]	0.470
GDS	4.0 (3-5)[b]	5.0 (4-5)[b]	0.440
Antihypertensive medication	13 (72.2)[c]	14 (66.6)[c]	0.980
Diuretics	2 (15.38)[c]	1 (7.14)[c]	
Calcium channel blockers	12 (92.31)[c]	13 (92.86)[c]	
ACE inhibitors or ARBs	8 (61.54)[c]	6 (42.86)[c]	
Beta-blockers	2 (15.38)[c]	3 (21.43)[c]	
Medical history			
Cardiovascular disease[d]	8 (44.44)[c]	9 (42.86)[c]	0.990
Diabetes mellitus	8 (44.44)[c]	6 (28.57)[c]	0.760
Dyslipidemia	2 (11.11)[c]	1 (4.76)[c]	0.590
Dementia	6 (33.33)[c]	7 (33.33)[c]	1.000
Osteoporosis	3 (16.67)[c]	7 (33.33)[c]	0.290

Abbreviations: MMSE-K, mini-mental state examination-Korean version; K-ADL, Korean activities of daily living; S-IADL, Seoul- instrumental activities of daily living; GDS, global deterioration scale; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker.
[a]Calculated using a Wilcoxon rank sum test, Fisher's exact test or χ^2 -test.
[b]Median (25-75%).
[c]Number (%).
[d]Cerebral infarction, cerebral hemorrhage, myocardial infarction, angina or atherosclerosis.

Table 2. Changes in nutrient intake by the weighing method after 8 weeks

	Solar salt (n=18)		P^a	Refined salt (n=20)		P^a
	Pre (baseline)	Post (8 wk)		Pre (baseline)	Post (8 wk)	
Calorie intake, kcal	1,299.06 (1,142.71-1,729.12)[b]	1,324.52 (1,011.63-1,732.43)[b]	0.770	1,271.91 (1,044.55-1,503.03)[b]	1,355.25 (1,178.77-1,475.32)[b]	0.120
Protein, % energy	16.61 (15.27-18.87)[b]	16.48 (14.53-17.78)[b]	0.770	17.94 (16.24-19.70)[b]	17.01 (16.15-17.62)[b]	0.160
Fat, % energy	19.92 (15.20-22.37)[b]	20.87 (14.97-23.08)[b]	0.090	20.60 (19.41-23.85)[b]	22.00 (18.87-23.03)[b]	0.930
Carbohydrate, % energy	63.14 (58.72-69.44)[b]	62.65 (58.81-70.36)[b]	0.640	62.30 (55.77-63.82)[b]	60.97 (58.90-64.98)[b]	0.650

[a]Calculated using a Wilcoxon signed rank test.
[b]Median (25-75%).

Table 3. Changes in study outcomes of solar- or refined salt-based diet after 8 weeks[a]

	Solar salt (n=18)			Refined salt (n=20)		
	Pre (baseline)	Post (8 wk)	P^b	Pre (baseline)	Post (8 wk)	P^b
Body mass index	24.4 (19.9-25.8)	24.8 (19.8-26.0)	0.820	23.8 (19.2-25.3)	23.9 (19.5-25.8)	0.750
Blood pressure, mmHg						
Systolic[c]	127.5 (121-140)	110 (102-120)	0.007	129.0 (122-136)	128.5 (120-136)	0.930
Diastolic	74.0 (70-94)	69.0 (66-74)	0.090	76.0 (70-88)	78 (72-88)	0.930
Pulse rate, beat/min	75 (70-82)	77 (70-82)	0.720	72 (69-78)	72 (69-76)	0.830
Antihypertensive medication	13 (72.2)	10 (55.6)	0.300	14 (70.0)	15 (75.0)	0.730
Glucose tolerance index						
Fasting glucose, mg/dL	95.0 (90-110)	93.5 (86.0-131.0)	0.770	90.5 (83.0-97.5)	90.0 (82.0-100.0)	0.410
Fasting insulin, μIU/mL	9.24 (6.22-12.79)	8.18 (6.54-11.72)	0.310	9.20 (6.77-12.24)	9.40 (6.74-11.74)	0.900
HOMA-IR	2.30 (1.35-3.32)	2.33 (1.43-3.93)	0.280	2.25 (1.79-3.04)	2.27 (1.82-3.42)	0.900
Lipid profile						
Total cholesterol, mg/dL	184 (156-221)	166 (132-201)	0.080	169 (158.5-201.5)	164 (143-194)	0.620
Triglyceride, mg/dL	142.5 (11.20-220.0)	141 (105-270)	0.920	135.5 (101.5-157.5)	116 (101-156)	0.230
HDL-cholesterol, mg/dL	34.6 (32.0-43.1)	36.55 (32.60-43.75)	0.670	33.45 (30.60-45.70)	34.0 (32.0-46.3)	0.170
Renal function test						
Blood urea nitrogen, mg/dL	14.5 (10.3-16.2)	12.85 (11.00-15.25)	0.920	13.45 (10.10-18.40)	12.47 (10.90-15.80)	0.860
Creatinine, mg/dL	0.9 (0.8-1.3)	0.8 (0.7-1.25)	0.530	0.9 (0.8-1.0)	0.9 (0.8-1.0)	0.780
Electrolyte						
Serum sodium, mEq/L	138 (138-140)	138.5 (136.0-142)	0.530	137.5 (136.0-140)	140 (136-142)	0.110
Serum potassium, mEq/L	4.2 (4.0-4.5)	4.45 (3.80-4.60)	0.030	4.00 (3.80-4.35)	4.05 (3.80-4.20)	0.320
Urinary sodium, mEq/L	80 (57-109)	94 (46-121)	0.890	88 (54-118)	86.5 (49.0-120)	0.460
Urinary potassium[c], mEq/L	30 (24-32.5)	36.5 (30.5-49)	0.008	25.5 (17-38)	23.5 (14.5-36.5)	0.340
Urinary sodium/potassium[c]	2.34 (1.97-3.64)	2.07 (1.25-3.21)	0.040	2.67 (2.20-4.59)	3.44 (2.47-4.39)	0.520

Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high density lipoprotein.
[a]Values are presented as median (25-75%) or N (%).
[b]Calculated using a Wilcoxon signed rank test or χ^2-test within each group.
[c]Statistical significance at $P<0.05$ according to a Wilcoxon rank sum test for comparing % change between two groups.

There were significant differences in the to systolic BP (solar salt: -15.38% [-16.67~-8.33], refined salt: 0% [-7.69~15.38], *P*=0.040), urinary potassium excretion (solar salt: 5.27% [2.74-16.63], refined salt: -1.15% [-11.25~2.56], *P*=0.010), and urinary sodium/potassium (solar salt: -18.03% [-31.38~-2.00], refined salt: 2.92% [-1.23~5.23], *P*=0.003). The systolic BP decreased significantly after 2, 4, and 8 weeks within the solar salt-based diet group (all *P*<0.050), and was also significantly different after 2, 4, and 8 weeks between the two groups (all *P*<0.050, Fig. 2A). Changes in the diastolic BP were not observed after 2, 4, and 8 weeks within either group, but significant differences were observed between the two groups after 8 weeks (*P*=0.045, Fig. 2A). ACE activity decreased significantly in the solar salt-based diet (*P*=0.030, Fig. 2B) compared to the refined salt-based diet group after adjusting for age and sex.

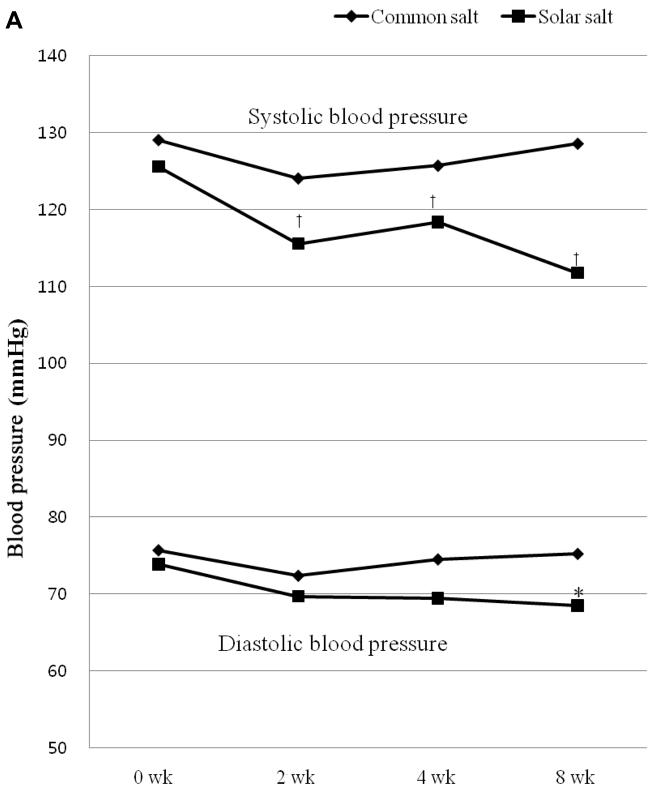
After adjusting for total calories and urinary sodium using ANCOVA for differences by calorie intake, we assessed the changes to the BP in the two groups. There were significant differences in systolic BP (*P*=0.020) and the rate of change of the systolic BP (*P*=0.040) in the solar salt group compared to the refined salt group. Systolic BP (least square mean [standard error]) decreased by 14.12 (4.92) mmHg in the solar salt group and 1.48 (5.34) mmHg in the refined salt group, and the rate of change to systolic BP was -10.85 (3.77)% in the solar salt group and 0.14 (4.10)% in the refined salt group (data is not shown).

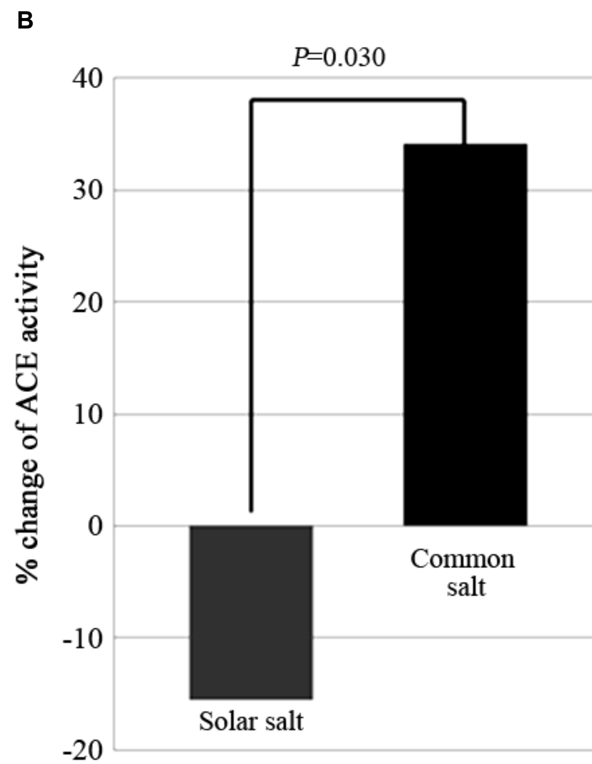
Also, in the case of including drop-out patients for the analysis of intention to treat, systolic BP for the solar salt group (n=21) was 130 (121-140) mmHg in the pre-study and 114 (110-132) mmHg in the post-study (*P*=0.010), and that of the refined salt group (n=22) was 129 (122-138) mmHg in pre- study and 129 (120-138) mmHg in post-study (*P*=0.910). Also, the rate of change of the systolic BP was significantly different between the two groups (*P*=0.009) (data is not shown) (Table 3).

DISCUSSION

The results of this study indicate that a solar salt-based diet had beneficial effects on blood pressure in institutionalized, elderly patients with hypertension. In addition, urinary

Figure 2. (A) Changes in systolic and diastolic blood pressures with intake of solar or refined salt over eight weeks. *P*-values were calculated using Wilcoxon rank sum test and Wilcoxon signed rank test. (B) The rate of change in ACE activity with intake of solar (least square mean [SE]: -15.45 [16.13]) or refined salt (least square mean [SE]: 34.09 [14.82]) before and after the study. *P*-values were calculated using ANCOVA. ACE, angiotensin converting enzyme; SE, standard error.





sodium/potassium and ACE activity decreased significantly in the solar salt-based diet group compared to the refined salt-based group; and the urinary potassium excretion increased significantly in the solar salt-based diet.

In some previous studies,[9-12] a fall in systolic BP of 5-10 mmHg was reported by replacing refined salt with low sodium, high potassium, high magnesium mineral salt in subjects with treated or untreated mild to moderate hypertension (above the mean systolic BP of 150 mmHg at baseline). Our solar salt study result is consistent with these previous studies, although each study had different mineral content of salt substitutes, characteristics of subjects, and intervention period. And, the hypotensive effect of solar salt in this trial was not inferior to the previous studies. Subjects in this study were hospitalized patients. Therefore, their BP was relatively well-controlled with medication (baseline systolic blood pressure/diastolic blood pressure 128.5/76 mmHg). Nevertheless, we could still identify the hypotensive effect of mineral salt. In addition, our results suggest the possibility of a preventive effect by replacing refined salt with solar salt for pre-hypertension individuals (systolic BP at 120-139 mmHg or a diastolic BP at 80-89 mmHg).

In particular, the elevation of the systolic BP is a result of the loss of arterial elasticity, or compliance, and is a characteristic of the elderly.[21,22] Systolic BP is a better indicator of increased cardiovascular risk in the elderly and is more reliable than diastolic BP alone.[23] Thus, the remarkable decrease in the systolic BP in the solar salt-based diet group is strong evidence for switching to a solar salt-based diet to prevent or manage cardiovascular diseases in the elderly.

Although there was no statistical significance, three subjects (1 diuretic user [hydrochlorothiazide 12.5 mg] and 2 CCB users [amlodipine maleate 5 mg]) did not need anti-hypertensive medication while on the solar salt-based diet. Anti-hypertensive medications were also reduced from the combination therapy of CCB (amlodipine maleate 5 mg) and ARB (losartan 50 mg) to CCB mono-therapy in one patient on the solar salt diet. These effects of consuming solar salt may be more important in elderly hypertensive patients.

Urinary potassium excretion and sodium/potassium changed in the solar salt group. Minerals such as potassium, calcium, magnesium, and sodium in the body have a reciprocal relation. Possible explanations for the association of these minerals, contrary to sodium, with hypotensive effects have been suggested by experimental studies. First, potassium supplement increased sodium excretion in high sodium intake Dahl salt-sensitive rats.[24] Second, these minerals can directly influence vascular relaxation and dilatation by changing the cell membrane potential in the vascular smooth muscle and endothelial cells[25-27] and by increasing nitric oxide production in the endothelium.[24] Third, modulation of the renin-angiotensin-aldosterone system (RAAS), a hormone system regulating blood pressure and fluid balance, can be involved in the hypotensive effect via these minerals directly or indirectly. Changes in calcium and magnesium fluxes across cell membranes are reflected in plasma rennin activity in hypertension.[28,29] Extracellular ionized calcium inhibits rennin secretion through the calcium- sensing receptors localized in the juxtaglomerular apparatus.[30] Blood pressure in the solar salt-based diet group did not increase as much as that in the refined salt-based diet group of Dahl salt-sensitive rats.[31] Plasma ACE activity in the solar salt-based diet group was also lower than that in the refined salt-based diet group.[32] Finally, possible mechanism offered by some previous researches is the anti-oxidative effect of the mineral abundant solar salt. It is also known that sodium enhances oxidative stress.[32] However, production of peroxides was lower with solar salt than with regular refined salt.[33] The antioxidative effects of *Cheonggukjang*, soybeans naturally fermented by Bacillus *subtilis*, made using solar salt were higher than that made using regular refined salt.[34] Furthermore, solar salt fed mice showed higher suppression of tumor growth, increases in natural killer cell activity, and inhibition of lipid peroxidation than regular refined salt fed mice in the Sarcoma-180 cell transplanted mice.[35] Although the mechanism by which solar salt-based diet modulates vascular tone is not fully understood, decrease in sodium retention, vasodilation and improvement of endothelial function, modulation of RAAS, and the anti-oxidative effect may be important factors.

According to the Korea National Health and Nutrition Examination Survey, there is an inadequate intake of calcium and potassium. Calcium intake was 66% of the Recommended Nutrient Intake (RNI) and potassium was 78% of the RNI in females older than 1 year old.[36] Therefore, substituting low-sodium and abundant mineral solar salt for refined salt may have a greater anti-hypotensive effect in Koreans.

ACE activity was reduced in the solar salt group. However, unexpectedly, increased ACE activity in the refined salt group was much greater than the decreased ACE activity in the solar salt group. Increased ACE expression is well-known to be related to a higher risk of cardiovascular disease development and progression.[37] ACE inhibitors are widely used to reduce blood pressure and prevent renal complication.[38] But the mechanisms that regulate ACE expression are still unclear.[39] The reason for the increased ACE activity in the refined salt group is difficult to explain properly. We cannot exclude the possibility of the influence of other factors than salt.

This study has some limitations including its small sample size. The design was non-community-based and, along with this, there is a potential for selection bias. Due to the small number of subjects, it was difficult to assess other beneficial effects or mechanisms besides the anti-hypertensive effects of solar salt intake. However, because salt-based foods, including such dishes as Kimchi and other salt-fermented fish products, are very diverse among the foods consumed regularly by Koreans, we had to conduct a trial with a small number of subjects for dietary control. In order to not alter individual salt taste preferences, we had to provide equivalent sodium content to both groups. This study supports the beneficial effects of solar salt intake, including sodium reduction. And, in a nutrient database used for this study, solar salt is not included. We could not evaluate properly the mineral intake of the solar salt-based diet group. Thus, measuring urinary sodium and potassium excretion was the only option. Also, we cannot clarify the effect of refined salt in type and dose of antihypertensive medication. In conclusion, our results may provide clinical evidence that solar salt is beneficial for lowering or maintaining a healthy blood pressure. However, further large-scale studies and trials considering variable antihypertensive medication are necessary to investigate the other potential benefits of solar salt intake in elderly patients with hypertension.

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요 약

연구배경: 나트륨 과다 섭취와 적은 미네랄 섭취는 혈압 상승과 연관된 것으로 알려져 있으며, 정제 소금을 저염도, 고미네랄 천일염으로 대체하는 것은 혈압을 낮춘다고 보고되고 있다. 천일염은 한국에서 건강한 식습관을 위한 저염도, 고미네랄 소금으로 부상되고 있다. 따라서 정제 소금을 천일염으로 대체한 고령 고혈압 환자의 혈압 변화에 대하여 연구하기 위하여 무작위 이중 맹검 위약 대조시험을 시행하였다.

방법: 43명의 65세 이상 노령 고혈압 환자가 이 실험에 최초 등록되었고, 이 중 38명(88.4%)이 시험을 완료했다. 연구 대상은 실험군으로 천일염 그리고 대조군으로 정제염을 섭취하는 식생활을 8주 동안 진행하였다.

결과: 천일염을 섭취하는 집단은 정제염을 섭취하는 대조집단과 비교하였을 때 수축기 혈압이 2, 4, 8주 후에 크게 감소하였고, 확장기 혈압 또한 8주 후에 크게 떨어졌다. 또한 천일염을 섭취하는 집단에서는 소변 중 나트륨/칼륨과 ACE 활동이 정제염을 섭취하는 집단보다 크게 감소하였다. 소변 중 칼륨 배설 또한 크게 증가하였다.

결론: 이러한 결과는 고령 환자에서 천일염이 혈압에 유익한 효과가 있다는 임상 증거를 제공하고 있으며, 한국인과 같이 충분한 미네랄 섭취가 부족한 경우에 천일염을 사용하여 더 큰 항고혈압 효과를 가질 수도 있을 것으로 보인다. 따라서 추가적인 대규모 연구가 요구된다.

중심 단어: 고혈압, 혈압, 고령, 천일염, 무작위 대조 시험

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