Journal of Cardiovascular Pharmacology
6:S236–S243 © 1984 Raven Press, New York

Safety and Effects of Potassium- and Magnesium-Containing Low Sodium Salt Mixtures

*Heikki Karppanen, †Antti Tanskanen, ‡Jaakko Tuomilehto, §Pekka Puska, ‖Juhani Vuori, ‖Veikko Jäntti, and ‖Maija-Liisa Seppänen

**Department of Pharmacology, University of Helsinki, and §Department of Epidemiology, National Public Health Institute, Helsinki, †Department of Community Health and ‡Research Institute of Public Health, University of Kuopio, Kuopio, and ‖Deaconess Institute, Oulu, Finland*

Summary: The main purpose of the present studies was to examine the safety of salt mixtures in which 35 or 55% of the NaCl in common table salt was replaced by potassium and magnesium salts. For 41 elderly hospitalized patients common salt from the hospital kitchen was replaced by Na^+-K^+-Mg^{2+} salt for 3–5 weeks; for in 85 drug-treated outpatients home use of NaCl was replaced by the use of Na^+-K^+-Mg^{2+} salt for 6 months. The patients' acceptance of the Na^+-K^+-Mg^{2+} salt was good. No metabolic or other side effects could be detected while the salt was being used. Na^+-K^+-Mg^{2+} salt was associated with a fall in blood pressure in drug-treated hypertensive patients, a rise in serum magnesium and in previously low serum potassium concentrations, a fall in raised fasting blood glucose levels, and an improvement in oral glucose tolerance. The results demonstrate that a considerable part of the NaCl in common table salt could be replaced by potassium and magnesium salts without causing potassium or magnesium toxicity. The results also lend support to the concept that an increase in potassium and magnesium intake and a decrease in sodium intake may have beneficial effects in a substantial number of people. **Key Words:** Hypertension—Salt—Sodium—Potassium—Magnesium—Blood glucose.

A reduction in sodium intake has been recommended for the prevention and treatment of arterial hypertension (1–3). A decrease in the intake of sodium also improves the therapeutic effect and diminishes the side effects of diuretics (4).

There is increasing evidence suggesting that the intake of potassium in relation to that of sodium may markedly influence the metabolism and effects of sodium (5). Some studies suggest that the sodium/potassium ratio in the diet is a more important determinant of blood pressure than the quantity of sodium alone (5–8). An antihypertensive effect of an increased intake of potassium has been demonstrated in several studies (9–12).

Magnesium has an important role in the regulation of both sodium and potassium metabolism (13,14). The intake of magnesium in industrialized countries appears to be generally lower than the recommended daily allowance (15,16). A magnesium deficiency due to dietary inadequacies, prolonged use of diuretics (17–19), or other factors increases the risk of potassium deficiency and cardiac arrhythmias (18–20). There is also evidence suggesting that a magnesium deficiency may induce resistance to the effects of antihypertensive agents (21). In addition, Dyckner and Wester (22) reported a remarkable antihypertensive effect of magnesium supplementation.

The available evidence therefore suggests that increased intakes of both potassium and magnesium, alone or combined with a reduction in the intake of sodium, might be beneficial for a substantial number of people.

It was considered that a simultaneous increase in the intakes of potassium and magnesium and a decrease in the intake of sodium could be conveniently brought about by changing the composition of table salt (23). However, excessive doses of po-

Address correspondence and reprint requests to Dr. Karppanen at Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland.

tassium and magnesium may induce side effects (24). Therefore the main aim of the present studies was to examine the safety of salt mixtures in which part of the NaCl was replaced by potassium and magnesium salts. The effects of such salt mixtures on elderly hospitalized patients and on younger hypertensive outpatients are reported here.

METHODS

Studies on elderly hospitalized patients

Study 1. Twenty-three long-stay hospitalized patients (17 women and six men) were included in the study. The mean age was 77 years (range, 52–95 years). Nineteen of the patients were receiving digoxin therapy. Ten patients were under treatment with diuretics; one received furosemide alone, one received hydrochlorothiazide alone, five received a combination of hydrochlorothiazide and amiloride, and one received a combination of furosemide and triamterene. Three patients were taking oral antidiabetic drugs.

During the control period two blood samples for laboratory determinations were taken at a 2-day interval. On the day after the second blood sampling the hospital kitchen replaced the use of common salt (NaCl) with the use of a salt mixture with the following composition: NaCl, 65%; KCl, 25%; and $MgCl_2 \cdot 6H_2O$, 10% ($Na\text{-}K^+\text{-}Mg^{2+}$ salt). This mixture was the only salt used in the hospital kitchen for 5 weeks. The patients were not told that the composition of salt in their diet had been changed. While $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt was being used, blood samples for laboratory determinations were taken at 1, 2, 3, and 5 weeks.

Study 2. Eighteen long-stay hospitalized patients (15 women and three men) were included in this study. The mean age was 76 years (range, 57–95 years). Thirteen of the patients were receiving digoxin therapy. Ten patients were receiving diuretics: three of them furosemide alone, one hydrochlorothiazide alone, five a combination of hydrochlorothiazide and amiloride, and one a combination of furosemide and triamterene. One of the patients was taking an oral antidiabetic drug.

The patients were allocated at random into two groups of nine. During the run-in period four blood samples were taken at 1-week intervals. After the run-in period of 4 weeks Group I received a diet in which the hospital kitchen used $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt (see above) instead of NaCl. The diet of Group II was otherwise the same as that of Group I, but NaCl was used in its preparation. Three weeks later Group I was switched back to a diet with NaCl, while the diet of Group II was prepared for 3 weeks using $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt. During this experiment blood samples for laboratory determinations were taken at 1-week intervals.

Studies on drug-treated hypertensive outpatients

Eighty-five patients (62 men and 23 women) with treated hypertension but otherwise healthy were included in this study. They had been under regular blood pressure control for at least 1 year before the study. All patients belonged in World Health Organization Stage I or II.

The mean age of the patients was 48 years (range, 29–63 years), and the mean duration of the preceding antihypertensive drug treatment 6 years (range, 1–22 years). Fifty-nine patients were taking diuretics. In 45 of them a potassium-sparing drug, either amiloride or triamterene, was combined with the saluretic agent. The diuretic or other antihypertensive medication was not changed for any of the patients during the study.

During the control period blood pressure was measured on three visits, and body weight was recorded. The average of these measurements was calculated and used in comparisons with the values obtained during $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt periods. During the control period a 24-h urine sample was also collected, and a blood sample was taken for laboratory determinations.

After the control measurements the patients were randomized into two groups which were given one of the following two different $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt mixtures in a double-blind manner. The patients were asked to use $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt at home as a substitute for common table salt (NaCl). The $Na^+\text{-}K^+\text{-}Mg^{2+}$ test salt mixtures had the following compositions: test salt 1 (TS 1)—NaCl, 65%; KCl, 25%; and $MgSO_4 \cdot 7H_2O$, 10%; test salt 2 (TS 2)—NaCl, 45%; KCl, 35%; and $MgSO_4 \cdot 7H_2O$, 20%. TS 1 was commercially available $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt (Mineral Salt®/Seltin®, Salco Companies, Helsinki, Finland, and Cederroths AB, Stockholm, Sweden), but it was packed in numbered white boxes similar to those used for TS 2, which was specially prepared for the study.

Group I used TS 1 for the first 3 months and TS 2 for another 3 months thereafter, while Group II used TS 2 during the first and TS 1 during the second 3-month period.

While TS 1 or TS 2 was being used, the patients visited the clinic at 2-week intervals. Blood pressure, heart rate, and body weight were recorded on each visit. For each test salt period six measurements of these three variables were thus available, and their arithmetic mean was used in the analysis of the results. Blood samples were taken and 24-h urine samples collected at the end of each test salt period.

TABLE 1. *Acid-base balance before and during the use of a $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt mixture in elderly hospitalized patients*[a]

Variable	Control		$Na^+\text{-}K^+\text{-}Mg^{2+}$ salt			
	Day −3	Day −1	Day 7	Day 14	Day 21	Day 35
Blood pH	7.39 ± 0.007	7.39 ± 0.008	7.38 ± 0.006	7.39 ± 0.007	7.40 ± 0.006	7.38 ± 0.008
Blood P_{CO_2} (mm Hg)	6.0 ± 0.16	5.9 ± 0.22	5.5 ± 0.20	5.8 ± 0.19	5.6 ± 0.15	6.5 ± 0.22
Blood HCO_3 (mmol/L)	25.3 ± 0.37	25.3 ± 0.42	23.3 ± 0.56	24.8 ± 0.28	24.8 ± 0.35	26.2 ± 0.34

[a] Means ± SE are given. n = 23. Time before (−) and after commencement of the use of $Na^+\text{-}K^+\text{-}Mg^{2+}$ salt is indicated.

TABLE 2. *Serum cholesterol, triglyceride, creatinine, and urate levels before and during use of a Na^+-K^+-Mg^{2+} salt mixture in elderly hospitalized patients*[a]

Variable	Control		Na^+-K^+-Mg^{2+} salt			
	Day −3	Day −1	Day 7	Day 14	Day 21	Day 35
Cholesterol (mmol/L)	5.7 ± 0.19	5.2 ± 0.18	5.5 ± 0.22	5.6 ± 0.20	5.7 ± 0.23	5.8 ± 0.20
Triglycerides (mmol/L)	1.7 ± 0.25	1.5 ± 0.20	1.8 ± 0.27	1.8 ± 0.31	1.8 ± 0.25	1.6 ± 0.20
Creatinine (μmol/L)	82 ± 5.3	82 ± 4.5	75 ± 5.2	75 ± 5.2	97 ± 5.5	87 ± 4.8
Urate (μmol/L)	321 ± 23.9	307 ± 25.1	316 ± 23.1	306 ± 23.0	316 ± 19.2	313 ± 18.3

[a] Means ± SE are given. n = 23. Time before (−) and after commencement of the use of Na^+-K^+-Mg^{2+} salt is indicated.

Systolic and diastolic (Phase V) blood pressures were measured in the right arm by two trained nurses after 5 min of rest in a sitting position. Standard mercury sphygmomanometers with a cuff size of 12.5 × 40 cm were used. The blood pressure values were recorded to the nearest 2 mm Hg. The arithmetic mean of two measurements was taken as the blood pressure of the patient in subsequent calculations.

The patients received both written and verbal advice on the collection of 24-h urine samples, and the urinary excretion of creatinine was also determined to detect incomplete samples.

Laboratory determinations. Radioimmunoassay was used to determine the levels of serum insulin (Phadebas Insulin Test, Pharmacia Diagnostics AB, Uppsala, Sweden), serum C-peptide (RIA-mat C-Peptid, Byk-Mallinckrodt, Dietzenbach, Germany), and plasma glucagon (Cambridge Nuclear Radiopharmaceutical Co., Billerica, MA). Serum high-density lipoprotein (HDL) cholesterol was measured by the electrophoretic method (Helena Laboratories, Beaumont, TX). For determination of the acid-base balance a Radiometer (Copenhagen, Denmark) device, BMS 3 Mk 2, was used. Other laboratory determinations were performed in the laboratory of the Deaconess Institute at Oulu and the Department of Biochemistry of the National Public Health Institute, Helsinki.

An oral glucose tolerance test was performed after a fast of 12 h. A blood sample for determination of the fasting glucose level was taken; thereafter a glucose solution (1 g glucose/kg body weight) was given, and blood samples for the determination of blood glucose levels were taken at 30, 60, 90, and 120 min.

RESULTS

Studies on elderly hospitalized patients

Study 1. While Na^+-K^+-Mg^{2+} salt was being used, no significant changes in the acid-base balance occurred as compared with the values obtained during the preceding control period (Table 1). The average serum cholesterol, triglyceride, creatinine, and urate levels (Table 2), as well as serum sodium, potassium, calcium, and chloride levels (Table 3), also remained unchanged. In one patient with serum potassium levels of 5.2 and 5.3 mmol/L and serum creatinine levels of 110 and 120 μmol/L during the control period, the serum potassium value increased to 5.8 mmol/L at 3 weeks. However, on continuation of use of Na^+-K^+-Mg^{2+} salt no further rise in serum potassium was seen, and the 5-week level was 5.7 mmol/L. Only one patient in the study had hypokalemia (serum potassium level, <3.5 mmol/L). Her serum potassium values were 3.3 and 3.1 mmol/L during the control period. While Na^+-K^+-Mg^{2+} salt was being used, the serum potassium level was 3.6 at 1 week, 3.3 at 2 weeks, 3.7 at 3 weeks, and 3.6 at 5 weeks.

Serum magnesium levels were significantly increased while Na^+-K^+-Mg^{2+} salt was being used (Fig. 1). Hypermagnesaemia (serum magnesium level, >1.2 mmol/L) did not develop in any of the patients.

A significant fall in blood glucose levels took place while Na^+-K^+-Mg^{2+} salt was being used (Fig. 2).

Study 2. No significant hematological changes occurred in either patient group during the time Na^+-K^+-Mg^{2+} salt was being used (Fig. 3). Serum cholesterol, HDL cholesterol, urate, and creatinine values (Fig. 4), as well as the average serum sodium and potassium levels (data not shown), also remained unchanged during this period. No statistically significant changes in the average blood glucose, serum insulin, serum C-peptide, or plasma

TABLE 3. *Serum electrolyte levels before and during use of a Na^+-K^+-Mg^{2+} salt mixture in elderly hospitalized patients*[a]

Variable	Control		Na^+-K^+-Mg^{2+} salt			
	Day −3	Day −1	Day 7	Day 14	Day 21	Day 35
Sodium (mmol/L)	138 ± 0.8	137 ± 0.8	136 ± 0.8	138 ± 0.9	138 ± 0.8	138 ± 0.7
Potassium (mmol/L)	4.3 ± 0.10	4.2 ± 0.12	4.2 ± 0.11	4.2 ± 0.11	4.3 ± 0.11	4.2 ± 0.11
Calcium (mmol/L)	2.26 ± 0.023	2.26 ± 0.023	2.30 ± 0.023	2.25 ± 0.017	2.30 ± 0.024	2.23 ± 0.016
Chloride (mmol/L)	99 ± 0.9	98 ± 1.1	95 ± 1.2	99 ± 1.0	97 ± 1.0	96 ± 0.8

[a] Means ± SE are given. n = 23. Time before (−) and after commencement of the use of Na^+-K^+-Mg^{2+} salt is indicated.

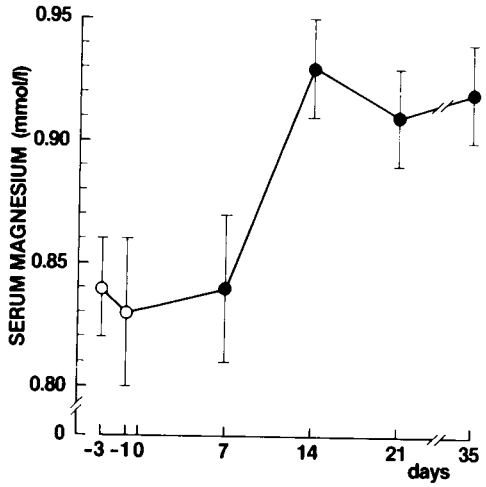

FIG. 1. Serum magnesium levels before and during use of a Na^+-K^+-Mg^{2+} salt mixture in elderly hospitalized patients. The mean ± SE for 23 patients is shown. Open circles indicate control values 3 days and 1 day before commencement of use of the salt mixture; solid circles indicate serum magnesium values during use of the salt. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods. The values are significantly higher at 14–35 days as compared with the average control values ($p < 0.01$–0.001, paired *t* test).

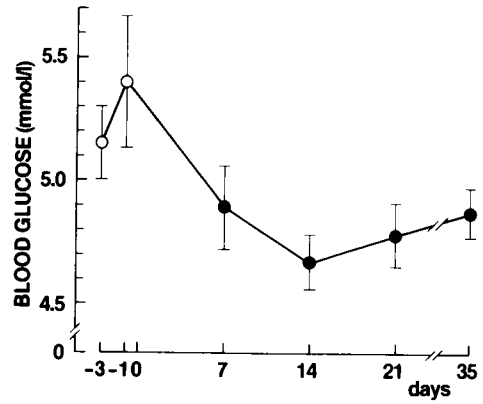

FIG. 2. Blood glucose levels before and during use of a Na^+-K^+-Mg^{2+} salt mixture in elderly hospitalized patients. The mean ± SE for 23 patients is shown. Open circles indicate control values 3 days and 1 day before commencement of use of the salt mixture; solid circles indicate blood glucose values during use of the salt. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods. The values are significantly lower at 7 days ($p < 0.05$), 14 and 21 days ($p < 0.001$), and 35 days ($p < 0.01$) as compared with the average control values (paired *t* test).

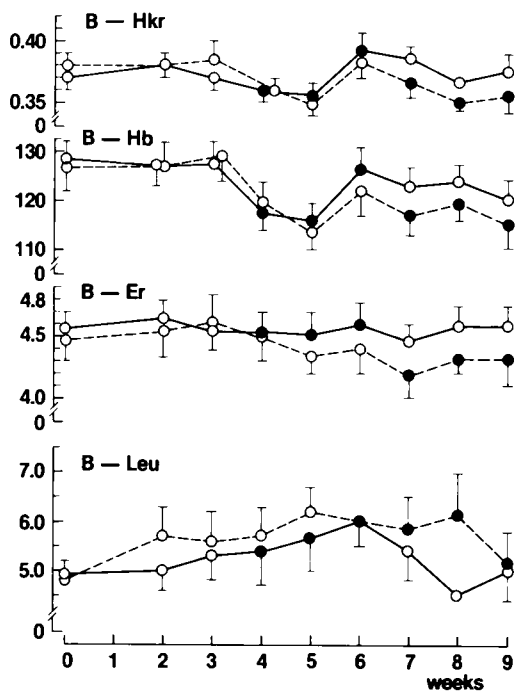

FIG. 3. Blood hematocrit (B-Hkr), hemoglobin level (B-Hb, g/L), erythrocyte count (B-Er, $\times 10^6/mm^3$), and leukocyte count (B-Leu, $\times 10^3/mm^3$) in two groups of elderly hospitalized patients. Open circles indicate values during use of common table salt (NaCl), and solid circles during use of the Na^+-K^+-Mg^{2+} salt mixture. Vertical bars indicate SEM. The number of patients was nine in both groups. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods.

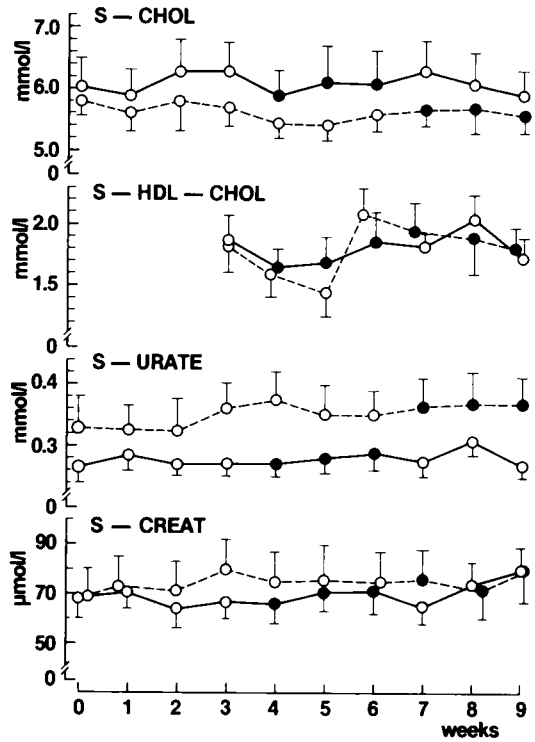

FIG. 4. Serum cholesterol (S-CHOL), high-density lipoprotein cholesterol (HDL-CHOL), urate (S-URATE), and creatinine (S-CREAT) levels in two groups of elderly hospitalized patients. Open circles indicate values during use of common table salt (NaCl), and solid circles during use of the Na^+-K^+-Mg^{2+} salt mixture. Vertical bars indicate SEM. The number of patients was nine in both groups. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods.

glucagon levels took place in either patient group while Na^+-K^+-Mg^{2+} salt was being used (Fig. 5). Although large differences in serum insulin and C-peptide, as well as plasma glucagon, levels existed between different patients and, therefore, also between the two patient groups, the level of each of these variables remained remarkably constant in the same patient throughout the study.

Oral glucose tolerance improved markedly while Na^+-K^+-Mg^{2+} salt was being used as compared with the glucose tolerance test performed during the control period (Fig. 6).

Studies on drug-treated hypertensive outpatients

With the use of TS 1 the results were similar in Groups I and II. Further, there were no statistically significant differences between Groups I and II with the use of TS 2. Therefore the results from Groups I and II were combined in the final analysis.

Urinary excretion of sodium and potassium (Table 4). At the end of the TS 1 or TS 2 period 24-h urinary excretion of sodium did not differ from that found during the control period. Urinary excretion of potassium was clearly increased with the use of both TS 1 and TS 2. The sodium/potassium molar ratio in the 24-h urine collection was decreased while the test salts were being used.

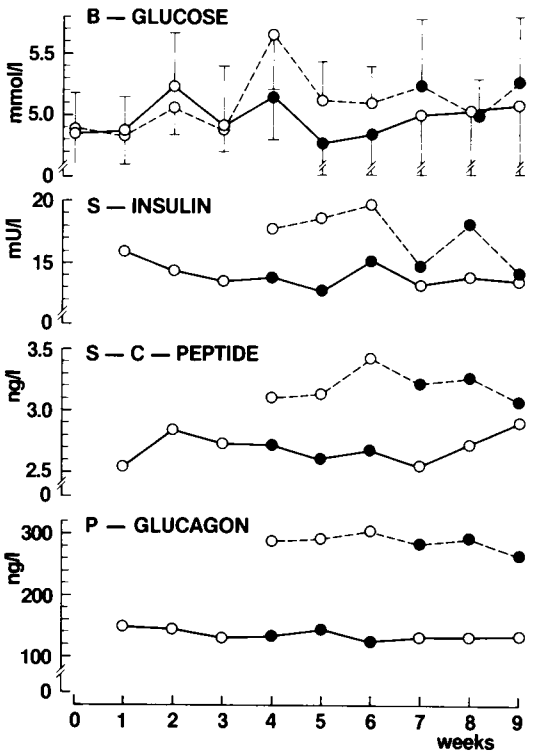

FIG. 5. Blood glucose, serum insulin, serum C-peptide, and plasma glucagon levels in two groups of elderly hospitalized patients. Open circles indicate values during use of common table salt (NaCl), and solid circles during use of the Na^+-K^+-Mg^{2+} salt mixture. The number of patients was nine in both groups. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods.

Blood pressure, heart rate, and body weight (Table 5). Average systolic blood pressure was lowered with the use of both TS 1 and TS 2. The fall in diastolic pressure, although statistically significant, was very small. The average heart rate did not change during the study. The decrease in body weight while the test salts were being used was minor.

Serum sodium, potassium, calcium, and urate levels and blood glucose level (Table 6). Serum sodium levels were slightly increased with the use of both TS 1 and TS 2. A significant increase in serum potassium concentration was also observed. A detailed analysis of this finding revealed that the serum potassium level rose from 3.72 mmol/L to an average of 4.14 mmol/L with TS 1 and to 4.12 mmol/L with TS 2 in patients who had low serum potassium levels (<4.0 mmol/L) during the control period ($p < 0.001$, $n = 31$). The average serum potassium level did not change significantly with use of the test salts in patients whose serum potassium level was ≥4.0 mmol/L during the control period.

A minor decrease in serum calcium level occurred while the test salts were being used. Average serum urate levels did not change significantly with TS 1 use, and the decrease with TS 2 use, although reaching statistical significance, was also very small.

Average blood glucose levels fell with the use of both TS 1 and TS 2. A closer analysis of this result revealed that the blood glucose level decreased from an average of 6.1 mmol/L during the control period to 5.5 mmol/L with TS 1 ($p < 0.01$), and to an average of 5.2 mmol/L ($p < 0.001$) with TS 2 in patients who had high blood glucose levels (>5.7 mmol/L) during the control period ($n = 18$).

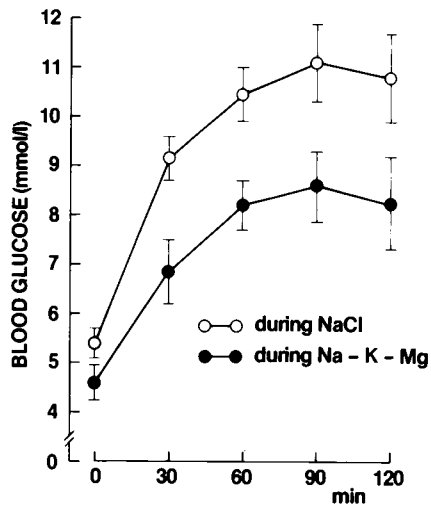

FIG. 6. Oral glucose tolerance during the use of common table salt (NaCl) and after use of the Na^+-K^+-Mg^{2+} salt mixture for 3 weeks in eight elderly hospitalized patients. Verticle bars indicate SEM. The exact composition of the Na^+-K^+-Mg^{2+} salt is given in Methods.

TABLE 4. *Urinary excretion of sodium and potassium and sodium/potassium molar ratio in treated hypertensive patients before and during use of Na^+-K^+-Mg^{2+} salt mixtures (TS 1 and TS 2)*[a]

Variable	Control	TS 1	TS 2
24-h Na (mmol)	222 ± 9	223 ± 8	223 ± 10
24-h K (mmol)	87 ± 2.6	101 ± 3.1[b]	103 ± 3.8[b]
Na/K ratio	2.72 ± 0.15	2.35 ± 0.10[c]	2.34 ± 0.11[c]

[a] Means ± SE are given. n = 85. The exact compositions of the test salts (TS 1 and TS 2) are given in Methods.
[b] $p < 0.001$, [c] $p < 0.05$.

DISCUSSION

In all the present studies the Na^+-K^+-Mg^{2+} salts were well accepted by the patients. This finding is in agreement with a previous report that the taste of the salt mixture with a composition of 65% NaCl, 25% KCl, and 10% $MgSO_4 \cdot 7H_2O$, which is the commercially available Na^+-K^+-Mg^{2+} salt in some countries (*see above*), could not be distinguished from that of common table salt (25). In the studies on hospitalized patients the only salt added in the hospital kitchen was Na^+-K^+-Mg^{2+} salt. Therefore there is no doubt that the patients were receiving this salt. In the outpatients the excretion of potassium was markedly increased during the Na^+-K^+-Mg^{2+} salt periods, and this finding strongly suggests that these patients also were using Na^+-K^+-Mg^{2+} salt.

The main objective of these studies was to examine the safety of Na^+-K^+-Mg^{2+} salt. No metabolic or other side effects could be detected in any of the trials, even with the use of a mixture in which 55% of the NaCl was replaced by potassium and magnesium salts. This was the case in spite of the fact that many of the patients were elderly and had impaired renal function. A large proportion of the patients were receiving potassium-sparing diuretics, but even in such patients hyperkalemia or hypermagnesemia did not develop.

Several favorable changes were observed while Na^+-K^+-Mg^{2+} salt was being used. The rise in previously low serum potassium and magnesium levels was an expected finding, since such an effect of potassium (26) or magnesium (19) supplements had been previously demonstrated. In the study on drug-treated hypertensive patients the average increase in daily potassium intake appeared to be approximately 15 mmol/day as suggested by the increase in the urinary excretion of this cation. In the studies using potassium supplements alone much higher amounts of potassium have been needed to achieve a corresponding rise in low serum potassium levels (26). In the present experiments the increase in the intake of magnesium may have contributed to the restoration of normal potassium levels. Such a synergistic effect of potassium and magnesium is suggested by the finding that the addition of magnesium is effective and even necessary in the correction of resistant potassium deficiency (17,20).

In drug-treated hypertensive patients the use of Na^+-K^+-Mg^{2+} salt was associated with a significant fall in blood pressure. In agreement with this finding an antihypertensive effect of the commercially available Na^+-K^+-Mg^{2+} salt has been reported in Japanese subjects (27). In spontaneously hypertensive rats Na^+-K^+-Mg^{2+} salt also inhibited the development of hypertension (28). In our study it cannot be excluded that the fall in blood pressure was brought about merely by the follow-up of the patients. However, this possibility is diminished by the fact that all the patients had been under regular blood pressure control for at least 1 year and on average for 6 years before this study. Moreover, no changes in the medication of the patients were made during the study. In other studies both potassium (9–12) and magnesium (22) supplements have been proved to lower blood pressure. Hence it is likely that at least part of the antihypertensive effect was specifically due to the Na^+-K^+-Mg^{2+} salt.

While Na^+-K^+-Mg^{2+} salt was being used a marked fall in previously raised blood glucose levels was seen, whereas normal blood glucose levels were not changed. Oral glucose tolerance was also improved with the use of Na^+-K^+-Mg^{2+} salt. Previous studies have shown that potassium supplements partly normalize elevated blood glucose levels (29). Impaired oral glucose tolerance due to

TABLE 5. *Blood pressure, heart rate, and body weight of treated hypertensive patients before and during use of Na^+-K^+-Mg^{2+} salt mixtures (TS 1 and TS 2)*[a]

Variable	Control	TS 1	TS 2
Systolic blood pressure (mm Hg)	141 ± 1.4	135 ± 1.3[b]	134 ± 1.2[b]
Diastolic blood pressure (mm Hg)	91 ± 0.8	90 ± 0.8[d]	89 ± 0.8[c]
Heart rate (beats/min)	68 ± 1.2	68 ± 1.1	68 ± 1.2
Body weight (kg)	81.8 ± 1.4	80.8 ± 1.4	80.1 ± 1.4[b]

[a] Means ± SE are given. n = 85. The exact compositions of the test salts (TS 1 and TS 2) are given in Methods.
[b] $p < 0.001$, [c] $p < 0.01$, [d] $p < 0.05$.

TABLE 6. *Serum sodium, potassium, calcium, and urate levels and blood glucose level in treated hypertensive patients before and during use of Na^+-K^+-Mg^{2+} salt mixtures (TS 1 and TS 2)*[a]

Variable	Control	TS 1	TS 2
Sodium (mmol/L)	141 ± 0.4	143 ± 0.3[b]	143 ± 0.3[b]
Potassium (mmol/L)	4.15 ± 0.04	4.31 ± 0.04[b]	4.33 ± 0.04[b]
Calcium (mmol/L)	2.49 ± 0.01	2.46 ± 0.01[d]	2.46 ± 0.01[d]
Urate (μmol/L)	379 ± 9	372 ± 9	364 ± 9[d]
Glucose (mmol/L)	5.2 ± 0.07	5.0 ± 0.08[c]	5.0 ± 0.06[c]

[a] Mean ± SE is given; n = 85. The exact compositions of the test salts (TS 1 and TS 2) are given in the text.
[b] $p < 0.001$, [c] $p < 0.01$, [d] $p < 0.05$.

the use of diuretics was also corrected by potassium supplementation (30). Therefore, the decrease in raised blood glucose levels and improvement in oral glucose tolerance in the present experiments may be explained by the additional potassium derived from the Na^+-K^+-Mg^{2+} salt. However, the extra magnesium derived from the Na^+-K^+-Mg^{2+} salt might also have contributed to the normalization of blood glucose. Diabetics are known to be especially prone to magnesium deficiency, which may predispose to organ damage (31) and even severe diabetic ketoacidosis (32).

The improvement in glucose metabolism did not seem to be mediated by increased secretion of insulin, since fasting insulin levels were not affected by the use of Na^+-K^+-Mg^{2+} salt. The lack of a change in the secretion of insulin is also suggested by the fact that the levels of C-peptide also remained unchanged. C-peptide is secreted at the same time and in equimolar concentrations as insulin, but the half-life of C-peptide is much longer than that of insulin. The fasting levels of glucagon also remained unchanged. It is therefore possible that the improvement in the potassium and magnesium balance with the use of the Na^+-K^+-Mg^{2+} salt may have facilitated the cellular transport of glucose.

Hence, our results demonstrate that the use of Na^+-K^+-Mg^{2+} salt instead of common table salt is safe. Since in the planning of these experiments emphasis was put on the safety aspects, the other findings should be considered preliminary and therefore interpreted with caution. However, the changes observed are in good agreement with the results of other studies in which the use of potassium or magnesium supplements and a reduction in sodium intake have been examined. Therefore further studies on the effects of the replacement common table salt by Na^+-K^+-Mg^{2+} salt are warranted.

Acknowledgment: The studies described here were supported in part by grants from the Yrjö Jahnsson Foundation.

REFERENCES

1. U.S. Senate Select Committee on Nutrition and Human Needs. *Dietary goals for the United States*. Washington, DC: U.S. Government Printing Office, 1977.
2. National Academy of Sciences. *Recommended dietary allowances*. Washington, DC: Food and Nutrition Board, National Research Council, 1980.
3. World Health Organization. Arterial hypertension: report of a WHO Expert Committee. *WHO Tech Rep Ser* 1978:628.
4. Ram CVS, Garrett BN, Kaplan NM. Moderate sodium restriction and various diuretics in the treatment of hypertension: effects of potassium wastage and blood pressure control. *Arch Intern Med* 1981;141:1015–9.
5. Meneely GR, Battarbee HD. High sodium–low potassium environment and hypertension. *Am J Cardiol* 1976;38: 768–85.
6. Sasaki N. Relation of urinary findings, especially sodium potassium ratio, to blood pressure levels in farmers in northeast Japan. *Med Biol* 1956;39:182–7.
7. Langford HG, Watson RL. Electrolytes, environment and blood pressure. *Clin Sci Mol Med* 1973;45:111–3.
8. Pietinen PI, Wong O, Altschul AM. Electrolyte output, blood pressure, and family history of hypertension. *Am J Clin Nutr* 1979;32:997–1005.
9. Iimura O, Kijima T, Kikuchi K, et al. Studies on the hypotensive effect of high potassium intake in patients with essential hypertension. *Clin Sci* 1981;61(suppl):77s–80s.
10. Holly JMP, Goodwin FJ, Evans SJW, Vandenburg MJ, Ledingham JM. Re-analysis of data in two *Lancet* papers on the effect of dietary sodium and potassium on blood pressure. *Lancet* 1981;2:1384–7.
11. Skrabal F, Auböck J, Hörtnagl H. Low sodium/high potassium diet for prevention of hypertension: probable mechanisms of action. *Lancet* 1981;2:895–900.
12. MacGregor GA, Smith SJ, Markandu ND, Banks RA, Sagnella GA. Moderate potassium supplementation in essential hypertension. *Lancet* 1982;2:567–70.
13. Dyckner T, Wester PO. The relation between extra- and intracellular electrolytes in patients with hypokalemia and/or diuretic treatment. *Acta Med Scand* 1978;204:269–82.
14. Dyckner T, Wester PO. Effect of magnesium infusions in diuretic induced hyponatraemia. *Lancet* 1981;1:585–6.
15. Karppanen H. Epidemiological studies on the relationship between magnesium intake and cardiovascular diseases. *Artery* 1981;9:190–9.
16. Marier JR. Nutritional and myocardial aspects of magnesium in drinking-water. *Magnesium Bull* 1981;1a:48–54.
17. Lim P, Jacob E. Magnesium deficiency in patients on long-term diuretic therapy for heart failure. *Br Med J* 1972;3: 620–2.
18. Wester PO, Dyckner T. Diuretic treatment and magnesium losses. *Acta Med Scand* [*Suppl*] 1981;647:145–52.

19. Sheehan J, White A. Diuretic-associated hypomagnesaemia. *Br Med J* 1982;285:1157–9.
20. Dyckner T, Wester PO. Ventricular extrasystoles and intracellular electrolytes before and after potassium and magnesium infusions in patients on diuretic treatment. *Am Heart J* 1979;97:12–8.
21. Whang R, Chrysant S, Dillard B, Smith W, Fryer A. Hypomagnesemia and hypokalemia in 1,000 treated ambulatory hypertensive patients. *J Am Coll Nutr* 1982;1:317–22.
22. Dyckner T, Wester PO. Effect of magnesium on blood pressure. *Br Med J* 1983;286:1847–9.
23. Karppanen H. *Rationale of "new salt" (mineral salt)*. Helsinki: Vientipaino Oy Exportprint, 1979.
24. Mudge GH. Agents affecting volume and composition of body fluids. In: Gilman AG, Goodman LS, Gilman A, eds. *The pharmacological basis of therapeutics*. 6th ed. New York: Macmillan, 1980:848–84.
25. Pietinen P, Ruotsalainen P, Tanskanen A, Puska P. Sodium intake reduction in volunteer families by using a salt substitute and nutrition counselling. *Ann Nutr Metab* 1981; 25:371–80.
26. Morgan DB, Davidson C. Hypokalaemia and diuretics: an analysis of publications. 1980;1:905–8.
27. Yamori Y, Kihara M, Nara Y, Ooshima A. Effects of sodium reduction on Na/K ratio and blood pressure. In: *Proceedings of a Nordic meeting on "salt and hypertension."* Stockholm: Cederroths, 1982:155–71.
28. Dietz R, Schömig A, Rascher W, Strasser R, Ganten U, Kübler W. Partial replacement of sodium by potassium in the diet restores impaired noradrenaline (NA) inactivation and lowers blood pressure in SHR-SP. [Abstract]. In: *Abstracts of Eighth scientific meeting of the International Society of Hypertension*. Milan: International Society of Hypertension, 1981:108.
29. McFarland KF, Carr AA. Changes in the fasting blood sugar after hydrochlorothiazide and potassium supplementation. *J Clin Pharmacol* 1977;17:13–7.
30. Rapoport MI, Hurd HF. Thiazide-induced glucose intolerance treated with potassium. *Arch Intern Med* 1964; 113:405–8.
31. McNair P, Christiansen C, Madsbad S, et al. Hypomagnesemia, a risk factor in diabetic retinopathy. *Diabetes* 1978;27:1075–7.
32. Moles KW, McMullen JK. Insulin resistance and hypomagnesaemia: case report. *Br Med J* 1982;285:262.