Use of Salt Substitutes in the Treatment of Diuretic-Induced Hypokalemia

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To evaluate the safety, effectiveness, and patient acceptance of salt substitutes for use as a potassium replacement, a series of 10 patients who had controlled hypertension and who were taking a prescription potassium replacement product for diuretic-induced hypokalemia agreed to switch from their usual potassium product to the salt substitute for 6 weeks. Serum potassium values were monitored every 2 weeks while patients took the salt substitute. It was found that the salt substitute was very effective at maintaining patients' serum potassium in the normal range. A questionnaire completed at the end of the 6-week period showed that only three patients experienced any side effects from the salt substitute, none of which was severe enough to warrant discontinuation of the product. The questionnaire also revealed, however, that patients did not care for the salt substitute, and at the end of the study, eight out of the 10 subjects chose to return to their prescription potassium product despite a marked cost advantage in favor of the salt substitute. While this study shows that salt substitutes are an effective, safe, and economical alternative to prescription potassium products, poor patient acceptance of this agent is discouraging.

Hypokalemia secondary to diuretic use for hypertension is common. Nearly one third of all patients who are placed on thiazide diuretics will become hypokalemic, albeit usually only to a mild degree.[1] While there has been some suggestion that the mild hypokalemia seen in patients who are treated with diuretics is not dangerous and that treatment of this problem is not necessary,[2] other evidence suggests that the correction of mild hypokalemia may be beneficial in the treatment of high blood pressure.[3–5]

Among the approaches to treat diuretic-induced hypokalemia are the effervescent, liquid, or enteric-coated slow-release potassium preparations, the so-called potassium-sparing diuretics, and the high-potassium diet. All of these alternatives have drawbacks. Except for the high-potassium diet, these approaches are expensive. In addition, enteric-coated slow-release potassium is associated with gastrointestinal ulceration and bleeding.[6–9] On the other hand, while an increased potassium diet is a less expensive alternative and has been endorsed by many authors,[10–13] it has never been shown to be effective[2] and may result in increased caloric intake and weight gain that could increase blood pressure.

An attractive alternative to the above methods of potassium supplementation is the use of salt substitutes. These agents provide potassium chloride at a cost of 8% to 10% of the cost of the prescription potassium agents (Table 1).[14] Very little information is available about the effectiveness, safety, and patient acceptance of this regimen, however. This study assessed the effectiveness of salt substitutes in the control of diuretic-induced hypokalemia in a series of patients who were currently taking prescription potassium products. At the end of the 6-week trial, patient satisfaction with the salt substitute and any side effects associated with its use were evaluated with a patient questionnaire.

METHODS

Patients aged between 18 and 70 years who had stable hypertension and who were taking a potassium product for diuretic-induced hypokalemia were invited to participate in this study. Patients were eligible for the study if during

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TABLE 1. COST DIFFERENTIAL BETWEEN SALT SUBSTITUTES AND PRESCRIPTION POTASSIUM SUPPLEMENTS*

Potassium Product	Price ($) per 60 mmol† of Potassium
Salt substitutes	
Adolph's salt substitute	0.05
Morton's salt substitute	0.04
No Salt	0.04
Prescription supplements	
Kay Ciel Elixir	0.65
K-Lyte Tabs	0.58
Slow-K Tabs	0.48

** Based on Sopko and Freeman.[14]*
† 60 mmol equals 60 mEq.

the 6 months prior to the study there had been no change in either their antihypertensive medication or the amount of potassium supplementation they had been taking and if their serum potassium had remained in the normal range during this period. Patients whose serum creatinine level was greater than 176 μmol/L (2.0 mg/dL) or who were currently taking digitalis products were excluded from the study.

An initial electrolyte panel was performed on all subjects at the time of enrollment, and the potassium value at that time was considered the baseline value. Subjects then discontinued their potassium products for 2 weeks, after which time their serum potassium was reevaluated (washout value). Subjects were then given a 2-week supply of salt substitute (No Salt, Norcliff-Thayer). The salt substitute was provided to patients either in a preweighed vial (nine subjects) or, when it became commercially available, in unit dose packets (one patient). The salt substitute dose was calculated to match the subject's previous potassium product dose. Subjects were given written instructions to use the new potassium medication either mixed with fruit juice or sprinkled on their meals. All subjects were blinded to the identity of their new potassium medication.

For the next 6 weeks, subjects returned at 2-week intervals, at which time they returned the unused portion of their salt substitute and had their serum potassium tested. The results of the serum potassium determination were not conveyed to the patients, and no changes in the dosage of the salt substitute were made based on the results.

To determine the amount of salt substitute taken, the quantity of unused salt substitute was measured either by weighing the vial or counting the unit dose packets that were returned. Compliance with therapy was then calculated as the ratio of the amount of salt substitute actually taken to the quantity that would have been taken if the subject had followed the dosage instructions without missing any doses (that is, compliance would equal 1.0 if every dose was taken).

At the end of 6 weeks, subjects completed a multiple-choice questionnaire with five graded responses that addressed their satisfaction with the study, their general sense of well-being during the study period, and their opinion as to the taste of the salt substitute. Subjects were also asked whether they had any side effects attributable to the salt substitute and, if given the choice, whether they would choose the study product over their previous potassium supplement.

Data are expressed as the mean plus or minus one standard deviation. Serum potassium values were compared using the Wilcoxon rank sum test for matched pairs.

RESULTS

Through a review of active charts in the author's practice at the Riverside Methodist Hospital Family Practice Center in Columbus, Ohio, 12 patients were identified who met the entrance criteria for the study.

One patient declined to participate, and a second dropped out shortly after beginning the salt substitute phase of the trial. The remaining 10 patients completed the 6-week salt substitute trial, and 9 of these returned questionnaires following the study.

The mean age of patients was 51.6 ± 8.5 years (range 36 to 68 years). Five were men and five were women. Nine of the 10 subjects were insured with commercial insurance, whereas the tenth was on Medicaid. Seven of the patients had to pay for their own medication, two were reimbursed by their insurance company, and the remaining patient's medications were covered by Medicaid.

All 10 patients had hypertension; nine took a thiazide diuretic while another took furosamide. Five patients were treated with diuretics alone: two patients took hydrochlorothiazide (HCTZ) in combination with triamterene, two patients took HCTZ in combination with amiloride, and another patients took indapamine. Other patients were treated with chlorthalidone with atenelol (two patients), HCTZ/triamterene and prazosin (one patient), HCTZ/triamterene and methyldopa (one patient), and a combination of furosemide, atenolol, and captopril (one patient). Hypertension was complicated by type 2 diabetes mellitus in two patients, controlled hypothyroidism in one patient, and angina pectoris with idiopathic hypercalcemia in another patient.

Before the study, six of the patients took liquid potassium replacement products and four took slow-release potassium. The mean potassium requirement was 43.3 ± 17.1 mmol (range 20 to 75 mmol).

Table 2 shows the mean serum potassium for subjects at

TABLE 2. SERUM POTASSIUM VALUES OF STUDY SUBJECTS

Study Period	Serum Potassium (mmol/L)*
Baseline	3.68 ± 0.28
Washout	3.16 ± 0.15
With salt substitute	
After 2 weeks	3.58 ± 0.19
After 4 weeks	3.98 ± 0.27
After 6 weeks	3.87 ± 0.29

** 1 mmol/L equals 1 mEq/L.*

the baseline period, after the 2-week washout, and at the end of each 2-week study period. The baseline value of 3.68 ± 0.28 mmol/L (3.68 ±0.28 mEq/L) dropped to 3.16 ± 0.15 mmol/L (3.16 ± 0.15 mEq/L) after 2 weeks ($P<.01$). None of the 10 subjects had a normal potassium value at the conclusion of the washout period. Two weeks after starting the salt substitute, serum potassium levels rose to 3.58 ± 0.19 mmol/L (3.58 ± 0.19 mEq/L) ($P<.01$ with respect to the washout phase; $P>.05$ with respect to baseline). The potassium value after 4 weeks of salt substitute therapy was 3.98 ± 0.27 mmol/L (3.98 ± 0.27 mEq/L), and after 6 weeks was 3.87 ± 0.29 mmol/L (3.87 ± 0.29 mEq/L). Neither of these values was significantly different ($P>.05$) from the baseline potassium value.

Compliance with the salt substitute was found to be 0.89 ± 0.12 at 2 weeks of therapy (n = 7) and 0.86 ± 0.05 at 4 weeks of therapy (n = 6). As only three subjects returned their unused salt substitute at the conclusion of the study, compliance at 6 weeks was not calculated.

Nine of the 10 subjects completed the questionnaire administered at the conclusion of the study; the 10th subject did not return the questionnaire after multiple reminders. Eight of the nine subjects rated the taste of the salt substitute as worse or much worse than their usual potassium supplement. Three reported that their general sense of well-being was worse while on the salt substitute, while five reported no difference, and one felt better.

When asked their preference between the salt substitute and their previous potassium supplement, seven of the nine chose their prior medication. Only one subject preferred the salt substitute. The remaining subject expressed no preference. When informed that the salt substitute was less than one tenth the cost of their previous potassium agent, none of the subjects who preferred the prescription potassium supplement changed their preference, and all seven elected to return to their former medication. The patient who refused to return the study questionnaire also elected to return to her previous potassium supplement. Of the eight subjects who returned to their original potassium product, seven had to pay for their own medication; the eighth was on Medicaid. The single subject who expressed no preference for either medication selected the less-expensive salt substitute when notified of the price difference between the two products. Medication costs for this subject and the subject who preferred the salt substitute were covered by their insurance carriers.

Three patients reported side effects that they attributed to the salt substitute. All of these side effects were related to gastrointestinal upset shortly after taking the medication, and none was severe enough for them to discontinue the salt substitute.

Follow-up of the two patients who elected to continue the salt substitute showed that after 1 year they were both still taking this agent, and neither reported any side effects.

DISCUSSION

The effectiveness of salt substitutes for the treatment of diuretic-induced hypokalemia shown in this study is similar to that seen in two previous reports. Glazer and Weder[15] showed that salt substitutes could be used to correct diuretic-induced hypokalemia in hospitalized patients, but this report involved only two patients, and patient satisfaction with the regimen was not evaluated. In another report, salt substitute therapy was compared with prescription potassium supplements and potassium-sparing diuretics in 11 ambulatory patients with hypertension.[16] This study showed that after 1 month of therapy all three regimens were effective at correcting hypokalemia, but patients preferred the potassium-sparing diuretics. The use of potassium-sparing diuretics may not eliminate the need for potassium supplementation, however; in this study, five of the 10 subjects were taking a so-called potassium-sparing diuretic.

This study demonstrated that salt substitutes are an effective, safe, and economical alternative to prescription potassium supplements. Furthermore, subjects in this trial were very compliant with therapy. The compliance seen in this group of patients, however, may not reflect the usual medication-taking behavior of the average patient. The strict entrance criteria for this study resulted in selecting patients who in the past had been very compliant with their antihypertensive and potassium supplement medications. In addition, each patient knew that his or her serum potassium level would be tested every 2 weeks and that the medication was supposed to be returned. While this study demonstrated that a small group of subjects could be very compliant with salt substitute therapy for a short (6-week) period, it should not be assumed that the same would be true for all patients. In fact, questionnaire results showed that the subjects in this trial were generally dissatisfied with the taste of the salt substitutes, and most selected to

return to the more costly supplements rather than continue with the salt substitute. In patients who are less motivated and generally less compliant than this group of subjects, a similar level of dissatisfaction might hinder long-term compliance when using salt substitutes for potassium supplementation. A larger, more in-depth study would be helpful to assess whether these results can be generalized to other patient populations.

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