Diuretic Induced Hypokalemia in the Elderly

Robert P. Navarro, PharmD, Daniel K. O'Brien, MD, Pamela Nuffort, RN, and David L. Spencer, MD
Minneapolis, Minnesota, and Springfield, Illinois

The effects of four commonly prescribed diuretics on serum potassium were assessed. One hundred sixteen elderly clinic patients, independently living, (mean age 74.3 years, range 60 to 99 years) were taking hydrochlorothiazide (HCTZ) (n = 40; mean daily dose, 53.9 mg), a combination of hydrochlorothiazide-triamterene (HCTZ-TMTR) (n = 38; mean daily dose, 1.28 capsules), furosemide (n = 20; mean daily dose, 38.0 mg), or chlorthalidone (n = 18; mean daily dose, 55.6 mg). Patients did not take more than one diuretic. No patients received potassium supplementation or had diseases affecting potassium balance. The study design was a nonblinded, noncrossover retrospective chart audit with chi-square analysis. All patients were counseled about reducing excessive sodium intake and using potassium-rich foods and salt substitutes, although compliance concerning these dietary factors was not assessed. Even though some comparisons of diuretics showed statistical significance, these differences probably are not clinically significant because all serum potassium values were above 3.0 mEq/L and no patient was symptomatic. This study supports the use of HCTZ as an initial antihypertensive diuretic; it is as efficacious as the other diuretics in this study, is less expensive, and usually does not cause clinically significant hypokalemia more often than do the other diuretics.

Diuretics constitute 10 percent of prescriptions written for elderly patients, making this category of drugs one of the most widely prescribed in this age group.[1] Approximately 30 percent of the patients receiving diuretics also receive potassium supplementation and/or potassium sparing diuretics to prevent or treat hypokalemia. This adverse effect requires treatment in only 10 percent of patients receiving diuretics.[2] The conclusion shared by many authors is potassium supplements and potassium sparing diuretics are overused.[3-16]

The purpose of this observational, retrospective study was to assess the serum potassium in

From the Department of Family Practice and Community Health, School of Medicine, and the College of Pharmacy, University of Minnesota, Minneapolis, Minnesota, and the Department of Family Practice, School of Medicine, Southern Illinois University, Springfield, Illinois. Requests for reprints should be addressed to Dr. Robert P. Navarro, Smiley's Point Clinic, 2200 Riverside Avenue South, Minneapolis, MN 55454.

0094-3509/82/040685-05$01.25

Table 1. Mean and Range of Serum Potassium Values (mEq/L)

Drug	Serum Potassium	
	Mean	Range
HCTZ (n = 40)	3.86	3.1-4.8
HCTZ-TMTR (n = 38)	4.24	3.4-5.4
Furosemide (n = 20)	4.23	3.4-5.3
Chlorthalidone (n = 18)	3.76	3.3-4.8

HCTZ, hydrochlorothiazide; TMTR, triamterene

elderly patients who were taking one of four commonly prescribed diuretics without potassium supplementation.

Methods

A retrospective chart audit of 116 patients (29 male, 87 female) receiving diuretics without potassium supplementation was conducted. All patients received the diuretics for hypertension, although some also had a diagnosis of heart failure. No patients had obvious edema. All patients were ambulatory residents of a high-rise apartment complex who obtained health care from Smiley's Point Clinic, a family practice residency teaching clinic. The mean age was 74.3 years (range 60 to 99 years). All patients included in this study received daily diuretics and had reported in the chart at least one determined serum potassium value which was taken at least two weeks after drug initiation or dosage change. The study patients did not have any of the following problems reported in their chart: diabetes mellitus; renal, gastrointestinal or endocrine diseases; recent vomiting or diarrhea; or any indication of severely altered nutritional intake. The patients included in this research project were receiving only one of four diuretics: hydrochlorothiazide (HCTZ), a combination of 25 mg of HCTZ and 50 mg of triamterene (Dyazide), represented here as HCTZ-TMTR, furosemide (Lasix), and chlorthalidone (Hygroton). No patient was taking potassium supplementation. All patients received a list of potassium-rich foods and were encouraged to avoid very salty foods and to use a salt substitute, but compliance in these dietary factors was not assessed. Chi-square analysis was used to detect statistical significance of different potassium values resulting from the use of different diuretics. The patients and treating physicians were unaware of the study. No patient crossed over from one diuretic group to another.

Results

The distribution of patients taking diuretics, mean daily dosages, and resulting potassium values (mean and range) are found in Tables 1 and 2. The mean potassium value for all groups was within the "normal" range (3.5 to 5.5 mEq/L). At least one patient in each group exhibited laboratory hypokalemia. Table 2 shows the number and percent of patients falling in specific, discrete serum potassium ranges.

In this clinic, HCTZ is usually the diuretic of choice because of its efficacy, incidence of adverse effects similar to other diuretics, and low cost. Because of this interest in HCTZ, the effect

Table 2. Distribution of Potassium Values Resulting from the Use of Each Diuretic (n = 116)

Drug	Mean Daily Dose (mg)	Ranges of Serum Potassium Values (mEq/L) ≤2.9 No.	3.0 to 3.4 No. (%)	3.5 to 3.9 No. (%)	4.0 to 4.4 No. (%)	4.5 to 4.9 No. (%)	5.0 to 5.4 No. (%)	≥5.5 No.
HCTZ (n = 40)	53.9	0	9 (23)	13 (32)	14 (35)	4 (10)	0 (0)	0
HCTR-TMTR (n = 38)	1.28 caps*	0	1 (3)	13 (34)	11 (29)	9 (24)	4 (10)	0
Furosemide (n = 20)	38.0	0	1 (5)	5 (25)	7 (35)	6 (30)	1 (5)	0
Chlorthalidone (n = 18)	55.6	0	1 (6)	14 (77)	2 (11)	1 (6)	0 (0)	0
Total		0	12 (10)**	45 (39)**	34 (29)**	20 (17)**	5 (5)**	0

HCTZ, hydrochlorothiazide; TMTR, triamterene
*HCTZ 32 mg and TMTR 64 mg (mean daily dose)
**Percent of all subjects within each serum potassium value range

Table 3. HCTZ: Serum Potassium Values Resulting from Different Dosages (n = 40)

Serum Potassium (mEq/L)	Dosages 25 mg/day	50 mg/day	100 mg/day
≥5.0	0	0	0
4.5-4.9	1	3	1
4.0-4.4	3	9	4
3.5-3.9	0	9	1
3.0-3.4	0	7	2
2.5-2.9	0	0	0
Total	4	28	8

$\chi^2 = 5.36$, 6 *df*, P ~ .5 (not significant)

of different dosages of HCTZ on serum potassium is shown in Table 3. Although the number of subjects in each group was small, chi-square analysis shows the correlation of dose and resulting serum potassium values was not significant (P ~ .5). Also, potassium values resulting from HCTZ (as the standard) were compared with values resulting from the use of other diuretics (Tables 4 through 6). Although statistically significant differences were found with HCTZ vs HCTZ-TMTR ($P < .05$) and HCTZ vs chlorthalidone ($P < .02$), these differences do not appear to be clinically significant. Tables 5 and 7 compare the potassium values resulting from HCTZ vs furosemide and HCTZ-

Table 4. Comparison of Serum Potassium Values Resulting from the Use of HCTZ and HCTZ-TMTR

Serum Potassium (mEq/L)	HCTZ (n = 40)	HCTZ-TMTR (n = 38)
≥5.0	0	4
4.5-4.9	4	9
4.0-4.4	14	11
3.5-3.9	13	13
3.0-3.4	9	1
2.5-2.9	0	0

HCTZ, hydrochlorothiazide; TMTR, triamterene
$\chi^2 = 12.75$, 4 *df*, $P<.05$

Table 5. Comparison of Serum Potassium Values Resulting from the Use of HCTZ and Furosemide

Serum Potassium (mEq/L)	HCTZ (n = 40)	Furosemide (n = 20)
≥5.0	0	1
4.5-4.9	4	6
4.0-4.4	14	7
3.5-3.9	13	5
3.0-3.4	9	1
2.5-2.9	0	0

HCTZ, hydrochlorothiazide
$\chi^2 = 8.03$, 4 *df*, $P\sim.10$ (not significant)

Table 6. Comparison of Serum Potassium Values Resulting from the Use of HCTZ and Chlorthalidone

Serum Potassium (mEq/L)	HCTZ (n = 40)	Chlorthalidone (n = 18)
≥5.0	0	0
4.5-4.9	4	1
4.0-4.4	14	2
3.5-3.9	13	14
3.0-3.4	9	1
2.5-2.9	0	0

HCTZ, hydrochlorothiazide
$\chi^2 = 9.89$, 3 *df*, $P<.02$

TMTR vs furosemide, respectively, and both tests revealed no significant differences.

Discussion

Although chi-square analysis comparing some diuretics in this study yielded statistically different serum potassium values, any differences probably are not clinically significant for the following reasons:

1. Mean potassium values of all four diuretic groups was within the "normal" range.
2. All diuretic groups had at least one patient who had laboratory-determined hypokalemia. In all cases, however, the potassium value was not low enough to require treatment, and the patients were not symptomatic.
3. No patient in any of the four groups exhibited laboratory-determined hyperkalemia.
4. Serum potassium is at best a crude measurement of total body potassium, which is affected by physiologic factors (intracellular vs extracellular ratio, blood pH, serum glucose, diurnal variation).

It is important to make the distinction between laboratory-determined hypokalemia (serum potassium less than 3.5 mEq/L) and clinical hypokalemia requiring treatment. Most patients tolerate a serum potassium level in the 3.0 to 3.5 mEq/L range without symptoms and do not require treatment. Serum potassium levels rarely fall below this at Smiley's Point Clinic. An exception is the patient receiving digitalis, who is maintained well within the normal range (3.5 to 5.5 mEq/L).

Presenting these data at the clinic resulted in an increase in the use of HCTZ and a reduction in the prophylactic use of potassium supplements and potassium-sparing diuretics. The latter two products are expensive and usually unnecessary, and potassium supplements (except wax matrix, slow-release products) are associated with poor compli-

Table 7. Comparison of Serum Potassium Values Resulting from the Use of HCTZ-TMTR and Furosemide

Serum Potassium (mEq/L)	HCTZ-TMTR (n = 38)	Furosemide (n = 20)
≥5.0	4	1
4.5-4.9	9	6
4.0-4.4	11	7
3.5-3.9	13	5
3.0-3.4	1	1
2.5-2.9	0	0

HCTZ, hydrochlorothiazide; TMTR, triamterene
$\chi^2 = 1.36$, 4 *df*, $P > .50$ (not significant)

ance because of lack of palatability.[16-18] After initiating HCTZ (or furosemide when significant edema is present) the serum potassium predictably decreases slightly, but most patients remain within the "normal" range. The serum potassium soon stabilizes and is not expected to decrease further if potassium intake is maintained and factors influencing potassium excretion are not present (vomiting, diarrhea). Serum potassium should be monitored occasionally, especially following acute illnesses or diuretic dosage increases. It is less expensive to check the serum potassium periodically (every 6 months or more) than to use supplementation or potassium-sparing diuretics prophylactically. Hyperkalemia is potentially a problem with the use of supplements and/or potassium-sparing diuretics, especially in elderly patients. The Boston Collaborative Drug Surveillance Program reported the danger of hyperkalemia is more a concern than is diuretic induced hypokalemia.[5,6,19] Spironolactone, a potassium-sparing diuretic, is probably more likely to produce hyperkalemia than is triamterene.[19]

In conclusion, normal dosages of HCTZ or furosemide (the two diuretics used primarily in this study) generally do not produce clinically significant hypokalemia. Expensive potassium-sparing diuretics and/or supplements should be used only when indicated, such as when the serum potassium is less than 3.0 mEq/L and the patient is symptomatic or is receiving digitalis. Encouraging patients to replace salty foods with potassium-rich foods and to use a salt substitute (which may contain 10 to 20 mEq potassium per teaspoonful) may be helpful in maintaining a stable serum potassium level.[20,21] As a result, it is possible to use fewer, less expensive drugs, eliminate unpalatable supplements in most patients, obtain therapeutic results, and not experience a higher incidence of electrolyte abnormalities.

References

1. Kellenberger TE: Report on Drug Use. St. Paul, Department of Public Welfare, State of Minnesota, 1980
2. McMahon FG: Management of essential hypertension. New York, Futura, 1978, pp 83-104
3. Dargie HJ, Boddy K, Kennedy AC, et al: Total body potassium in long-term furosemide therapy: Is potassium supplementation necessary? Br Med J 4:316, 1974
4. McKenna TJ, Donahue JF, Brien TC, et al: Potassium-sparing agents during diuretic therapy in hypertension. Br Med J 2:739, 1971
5. Kassirer JP, Harrington JT: Diuretics and potassium metabolism: A reassessment of the need, effectiveness and safety of potassium therapy. Kidney Int 11:505, 1977
6. Lawson DH, Boddy K, Gray JMB, et al: Potassium supplements in patients receiving long-term diuretics for oedema. Q J Med 65:469, 1976
7. Lawson DH: The clinical use of potassium supplements. J Maine Med Assoc 66:166, 1975
8. Edmonds CJ, Jasani B: Total-body potassium in hyperactive patients during prolonged diuretic therapy. Lancet 2:8, 1972
9. Kosman ME: Management of potassium problems during long-term diuretic therapy. JAMA 230:743, 1974
10. Davidson C, McLachlan MJF, Burkinshaw L, Morgan DB: Effect of long-term diuretic treatment on body potassium in heart disease. Lancet 2:1044, 1976
11. Maronde RF, Milgrom M, Dickey JM: Potassium loss with thiazide therapy. Am Heart J 78:16, 1969
12. Gifford RW Jr: A guide to the practical use of diuretics. JAMA 235:1890, 1976
13. Rovner DR: Use of pharmacologic agents in the treatment of hypokalemia and hyperkalemia. Ration Drug Ther 6(2):1, 1972
14. Finnerty FA, Maxwell MH, Lunn J, Moser M: Long-term effects of furosemide and hydrochlorothiazide in patients with essential hypertension. Angiology 28:125, 1977
15. Michal R, Gehlbach SH: An evaluation of potassium usage in ambulatory hypertensive patients. J Fam Pract 10: 621, 1980
16. Lawson DH: Adverse reactions to potassium chloride. Q J Med 63:433, 1974
17. MacLeod SM: The rational use of potassium supplements. Postgrad Med 57:123, 1975
18. Lawson DH: Clinical use of potassium supplements. Am J Hosp Pharm 32:708, 1975
19. Greenblatt DJ, KochWeser J: Adverse reactions to spironolactone. JAMA 225:40, 1973
20. Sopko JA, Freeman RM: Salt substitutes as a source of potassium. JAMA 238:608, 1977
21. McRae MP: Foods high in potassium. Hosp Pharm 14:731, 1979