HYPOKALEMIA: ARE ELDERLY FEMALES MORE VULNERABLE?

Morris Kleinfeld, MD, Sonia Borra, MD, Sobha Gavani, MD, and Anthony Corcoran, MD
Brooklyn, New York

This study was undertaken to evaluate the relationship between prevalence of hypokalemia and the age and sex of patients. Serum potassium concentrations of 872 patients were measured, and the prevalence of hypokalemia was compared between age and sex groups. Hypokalemia was more common in patients 65 years or older than in younger groups ($P<.001$), with a significantly higher frequency in female patients ($P<.003$). The finding was more common in elderly female patients than in elderly males ($P<.002$). No statistically significant difference was noted in the frequency of hypokalemia in elderly male patients compared with younger patients of either sex. The predominance of hypokalemia in elderly groups was chiefly attributable to a marked preponderance in elderly female patients over all other groups. Neither younger females nor elderly males were at increased risk. The preponderance in elderly females was not dependent on diuretic usage. It may have been due to age- and sex-associated differences in body mass composition, which result in a physiologically low total exchangeable body potassium in elderly females, placing this group at greater risk for developing hypokalemia. (*J Natl Med Assoc.* 1993;85:861-864.)

Key words • hypokalemia • elderly women

It is widely believed that elderly patients are more prone to develop hypokalemia than younger patients.[1] However, few systematic studies have been performed to support this belief. One study[2] discovered a strong association of hypokalemia with female sex in hospitalized patients, with no constant relationship between patient age and the occurrence of hypokalemia in this population. Other investigators have suggested that a high prevalence of hypokalemia exists in female geriatric outpatients[3] and nursing home patients[4] treated with diuretics compared with similarly treated male geriatric outpatients and nursing home patients. The purpose of the present study was to determine whether any significant correlation exists between the prevalence of hypokalemia and the age and sex of adult patients admitted to an acute hospital service.

PATIENTS AND METHODS

Identification of study subjects was performed prospectively during a 4-week period in June 1990. All adult hospital admissions to the medical and surgical services in an urban community hospital were categorized into two groups according to age: those 65 years and older, and those younger than 65 years. Patients within each group were categorized according to sex.

All determinations of serum potassium concentrations obtained by the laboratory during the study period were reviewed, and patients exhibiting a decrease in the level of serum potassium, defined as a potassium level <3.5 mmol/L, were identified. Low serum potassium levels so identified were, therefore, either present at the time of admission or developed during the course of hospitalization. All patients noted to have a low serum potassium were included in the study.

The chart of each patient was reviewed and notation was made of age, sex, history and physical findings, primary and secondary diagnosis, quantity of sodium and potassium in the diet, and medications administered. Pertinent clinical events such as the presence of diarrhea, vomiting, and gastrointestinal drainage and their duration and severity were noted. Special attention

From the Departments of Long-Term Care Medicine and Nephrology, Kingsbrook Jewish Medical Center; and SUNY Health Science Center, Brooklyn, New York. Requests for reprints should be addressed to Dr Morris Kleinfeld, DMRI Bldg, Kingsbrook Jewish Medical Center, 585 Schenectady Ave, Brooklyn, NY 11203-1891.

TABLE 1. FREQUENCY OF HYPOKALEMIA CORRELATED WITH AGE AND SEX

Group	No. of Patients: Study Population	No. of Patients: With Hypokalemia	Frequency (%)
Total	872	110	12.61
Males	356	27	7.58
Females	516	83	16.09
≥65 years	533	86	16.12
Males	188	18	9.57
Females	345	68	19.71
<65 years	339	24	7.08
Males	168	9	5.36
Females	171	15	8.77

was given to the dose and duration of treatment with diuretics, laxatives, digitalis, corticosteroids, insulin, and catecholamines because these drugs are known to influence the handling or distribution of potassium in the body and can contribute to the development of hypokalemia.[5] The use of antibiotics with the potential to induce potassium wasting by the kidney, such as aminoglycosides and penicillin and its derivatives, also was noted.

All patients underwent routine laboratory screening on admission to the hospital. Tests included assays for serum sodium, chloride, potassium, bicarbonate, blood urea nitrogen, creatinine, and glucose concentrations. A complete blood cell count also was obtained. In patients who were found to have a low serum potassium level, a serum magnesium level, urine pH and urine sodium, and potassium concentrations were measured. Arterial blood gases were determined as clinically indicated. All testing was repeated, if necessary, on clinical indication.

In patients found to have a low serum potassium level, the most likely cause of the disorder was determined by clinical review of patient charts by one of the authors to identify the presence of specific factors known to predispose to the development of hypokalemia. If no likely cause could be identified, the cause was classified as unknown. Statistical significance of findings was evaluated using chi square analysis with and without correction for continuity.

RESULTS

Table 1 shows the incidence of hypokalemia correlated with age and sex. Table 2 compares the incidence of hypokalemia between age and sex groups. Eight hundred seventy-two patients were admitted to the hospital during the study period; 110 patients (12.61%) exhibited hypokalemia at the time of admission (81 patients) or developed it during the course of hospitalization (29 patients). Stratification according to age revealed 533 patients fell into the 65 years and older group, and 339 fell into the younger than 65 years group. The mean age of all patients was 66.6 years (range: 18 to 99), while the mean age of hypokalemic patients was 76.5 years (range: 19 to 94). Eighty-six of these patients were 65 years or older and 24 were younger than 65 years.

The difference in sex incidence of hypokalemia for all patients (male = 7.58% versus female = 16.09%) and for the groups aged 65 years and older (male = 9.57% versus female = 19.71%) was statistically significant ($P<.003$ and $P<.004$, respectively). There was no significant difference in sex incidence in the group younger than 65 years. The difference in age incidence for all patients (≥65 years = 16.12% versus <65 years = 7.08%) and for female patients (≥65 years = 19.71% versus <65 years = 8.77%) was statistically significant ($P<.001$ and $P<.002$, respectively). There was no significant difference in age incidence in male patients.

Sufficient data were available to identify the likely cause of hypokalemia in 105 patients (Table 3). These causes included altered distribution of potassium (as a result of metabolic alkalosis or the administration of insulin or catecholamines), inadequate dietary intake of potassium, extrarenal loss of potassium (due to vomiting, diarrhea, or gastrointestinal drainage), and renal loss of potassium (due to diuretic use, renal disease, or nephrotoxic drugs). The number of patients in each category was insufficient to detect any significant differences in the prevalence of particular causes between male and female and between younger and elderly patients.

DISCUSSION

Hypokalemia occurred in 12.6% of patients in an adult hospitalized population. Paice et al,[2] evaluating 58 167 hospitalized patients, found the incidence of hypokalemia to be 21%. The apparently higher occurrence in the latter study may be attributable to a high frequency of cancer (17.4%) as a primary diagnosis in the hypokalemic study subjects and to the frequent incidence in that study of hypokalemia secondary to insufficient potassium replacement in patients on intravenous fluids (18%).

The results of our study are more in agreement with those of Krakauer et al,[3] who noted a prevalence of 15% in 178 geriatric outpatients on diuretics (65% of whom also had prescriptions for potassium supplements) as

TABLE 2. COMPARISON OF THE FREQUENCY OF HYPOKALEMIA AMONG VARIOUS AGE AND SEX GROUPS

Group	Frequency of Hypokalemia (%)	Group	Frequency of Hypokalemia (%)	*P* Value
Total females	16.09	Total males	7.58	<.03
Total ≥65 years	16.12	Total <65 years	7.08	<.001
Females ≥65	19.71	Males ≥65	9.57	<.004
Females ≥65	19.71	Females <65	8.77	<.002
Females ≥65	19.71	Males <65	5.36	<.001
Females <65	8.77	Males <65	5.36	>.20
Females <65	8.77	Males ≥65	9.57	>.50
Males ≥65	9.57	Males <65	5.36	>.10

TABLE 3. CAUSES OF HYPOKALEMIA CORRELATED WITH AGE AND SEX*

Cause of Hypokalemia	<65 Years†		≥65 Years‡	
	Females	Males	Females	Males
Altered distribution	5	1	10	3
Nutritional	0	0	3	0
Extrarenal losses	4	4	13	3
Renal losses				
Diuretic use	5	3	13	5
Other causes	1	1	24	7
Unknown	0	0	5	0
Total	**15**	**9**	**68**	**18**

*The number of patients in each category was not sufficient to determine statistically significant differences in the frequency of individual causes.
†n = 24.
‡n = 86.

well as those of Clark et al,[4] who discovered a prevalence of 13.7% in 161 geriatric nursing home patients. An additional study[6] found evidence of hypokalemia in 14% of blood samples drawn from 1243 outpatients.

A significant correlation of the prevalence of hypokalemia with increased age ($P<.001$) and with female sex ($P<.03$) was observed. The increased prevalence in elderly patients was primarily accounted for by an increased prevalence in females of that group compared with younger females ($P<.002$), with younger males ($P<.001$), and with elderly males ($P<.004$). No statistically significant differences emerged when the prevalence of hypokalemia in elderly males was compared with the prevalence in younger males or younger females, although a trend was noted toward increased prevalence in elderly males compared with younger males.

Prior studies have found correlations of the presence of hypokalemia of various etiologies with female sex[2] and of diuretic-associated hypokalemia with female sex in elderly populations.[3,4] The question of whether the female predominance of hypokalemia extends to age groups other than the elderly has not been addressed previously, and this investigation does not support such an extension. In the present study, the prevalence in elderly females (19.71%) exceeded the prevalence in younger females (8.77%) by an extent similar to that by which it exceeded the prevalence in elderly males (9.57%) (Table 2). These data indicate that increased female prevalence occurs primarily in elderly but not in younger populations.

A second unanswered question relates to the degree to which the female preponderance of hypokalemia is dependent on diuretic use as an etiology of the condition. In this study, diuretic use does not appear to have predominated over other causes of hypokalemia. Although renal losses were the cause in 37 elderly females, diuretics were responsible in only a minority of that number (Table 3). Therefore, it is likely that the predominance of hypokalemia in elderly females is not dependent on diuretic therapy or, indeed, on any specific underlying etiology, but holds true for hypokalemia irrespective of proximate cause.

Both of the above findings (ie, the increased predominance of hypokalemia primarily in elderly

females and the independence of this predominance of specific etiologies of hypokalemia) are supported by the results of pioneering studies performed in the mid-1950s by Sagild.[7] Using injections of a radioactive isotope of potassium, K^{42}, and employing dilution techniques, this investigator measured the exchangeable body potassium per kilogram body weight in normal human subjects stratified by age and sex. He found the highest values (mean: 49.3 mEq/kg) in males under 30 years and the lowest values (mean: 27.9 mEq/kg) in females over 60 years. A general decrease in value was observed to occur through the following age groups: men aged 18 to 30 years, men aged 31 to 60 years, men aged 61 to 80 years, women aged 18 to 30, women aged 31 to 60 years, and women aged 61 to 80 years.

It is noteworthy that the age/sex groups in Sagild's study who exhibited higher levels of exchangeable potassium are essentially the same as those in the present study that exhibit a lower prevalence of hypokalemia; moreover, the Sagild groups with the lowest level of exchangeable potassium are the same as the group in our study with the highest prevalence of hypokalemia. Sagild proposed that the observed decrease in exchangeable body potassium with age results from the trend in man toward an age-related absolute and relative increase in fat and absolute and relative decrease in lean body mass. The lower exchangeable body potassium in females of all age groups could be attributable to "physiological fatness" and relatively smaller lean body mass in women compared with men. More recently, an 18-year longitudinal study measuring total body potassium in healthy volunteers confirmed Sagild's finding that loss of total body potassium is greater in elderly females than in other age groups.[8]

CONCLUSION

The results of the present study indicate that the model originally proposed by Sagild has more than merely theoretical relevance. It stratifies the risk for developing hypokalemia into groups extending from younger males—at low risk because of an abundant reserve of exchangeable potassium—to elderly females—at a disproportionately higher risk because of an already physiologically depleted reserve of exchangeable potassium. In practice, the risk of incurring a clinically significant hypokalemia probably attaches only to individuals in whom the exchangeable body potassium is depleted beyond a critical value, ie, elderly females. Therefore, elderly females with cardiovascular disease and, particularly, those receiving digoxin would, in this model, merit careful monitoring of serum potassium levels to minimize the development of dangerous arrhythmogenic effects.

Literature Cited

1. Judge TG. Hypokalemia in the elderly. *Gerontol Clin.* 1968;10:102-107.

2. Paice BJ, Paterson KR, Onyanga-Omara F, Donnelly T, Gray JMB, Lawson DH. Record linkage study of hypokalemia in hospitalized patients. *Postgrad Med J.* 1986;62:187-191.

3. Krakauer R, Lauritzen M. Diuretic therapy and hypokalemia in geriatric outpatients. *Dan Med Bull.* 1978;25:126-129.

4. Clark BG, Wheatley R, Rawlings JL, Vestal RE. Female preponderance in diuretic-associated hypokalemia: a retrospective study in seven long-term care facilities. *J Am Geriatr Soc.* 1982;30:316-321.

5. Steen B. Hypokalemia—clinical spectrum and etiology. *Acta Med Scand.* 1989;647(suppl):61-66.

6. Walters EG, Barnes IC. A survey of hypokalemia in patients of general practitioners. *Br J Clin Pract.* 1988;42:192-195.

7. Sagild U. Total exchangeable potassium in normal subjects with special reference to changes with age. *Scand J Clin Lab Invest.* 1956;8:44-50.

8. Flynn MA, Nolph GB, Baker AS, Martin MM, Krause G. Total body potassium in aging humans: a longitudinal study. *Am J Clin Nutr.* 1989;50:713-717.