Frequent potassium monitoring is associated with hyperkalemia that is clinically insignificant in females taking spironolactone for dermatologic conditions

Dear Editor,

Spironolactone is used as an off-label treatment for acne, hair loss, and hirsutism. Hyperkalemia risk by patient demographics and daily dosages requires clarification. We aimed to measure hyperkalemia prevalence and risk factors in women taking spironolactone for dermatologic conditions.

After institutional review board approval, demographics and potassium measurements were collected from female patients taking spironolactone for ≥2 weeks for acne, hair loss, or hirsutism from 2006 to 2021. Hyperkalemia was defined as ≥5.2 mEq/L.[1] R Version 4.2.2 was used, with Fisher's Exact and Wilcoxon rank sum tests with significance $p<0.05$.

Overall, 1,489 patients taking at least one course of spironolactone were included [Table 1]; 5.6% (n = 83, 81/83 during the first course) experienced hyperkalemia, with 97.6% mild (≤6.0 mEq/L) and none severe (≥7.0 mEq/L). On average, patients with elevated versus normal potassium measurements had more frequent potassium monitoring (4.38 vs. 2.23, $p<0.001$, Table 1). Using logistic regression, age, and maximum daily spironolactone dose were statistically significant hyperkalemia predictors. The odds of hyperkalemia increased by 2.36%/year of age and by 0.81%/mg. Race, ethnicity, and spironolactone indication were not hyperkalemia predictors (all $p>0.05$) [Table 1]. Only nine (10.7%) of hyperkalemic courses caused therapy discontinuation [Table 2].

Older patients and those taking higher spironolactone doses more often developed hyperkalemia, and race, ethnicity, and indication did not increase risk. Hyperkalemia was uncommon and most often mild, consistent with retrospective studies of 974 (Plovanich *et al*.) and 195 (Plante *et al*.) women taking spironolactone for dermatologic conditions with hyperkalemia rates of 0.72% and 3.3%, respectively, and all cases mild.[1,2] In our study, >70% of hyperkalemic patients took ≥100 mg/day, consistent with Plante *et al*.'s study, with all hyperkalemic patients taking 100 mg/day.[2] Older women in our cohort more often experienced hyperkalemia, similar to a retrospective study of 124 women taking spironolactone for acne (16.7% of those aged 45–65 vs. <1% 18–45 [$p = 0.0245$]).[3,4]

More frequent potassium monitoring was associated with clinically insignificant hyperkalemic since >70% of patients with elevated potassium had no change in treatment or potassium normalisation. Similarly, in a retrospective study of 1,863 acne patients taking isotretinoin, there were rare and clinically insignificant triglycerides (grade 3 <1%), total cholesterol (no grade 3), aminotransferase (grade 3 <0.5%), complete-blood-count (none) abnormalities, infrequently changing management and with normalisation.[5] Potassium measurements are subject to haemolysis. Increased hyperkalemia prevalence with more frequent monitoring may indicate high false positive rates, given that >20% of our patients with hyperkalemia were normalised. Therefore, minimising potassium monitoring in low-risk groups may reduce costs and time burden associated with false positive hyperkalemia.

Limitations include single-centre, retrospective design, majority whites, incomplete race/ethnicity data, lack of control for diet, medication adherence, other treatments, and lack of information about comorbid endocrine disorders.

In sum, hyperkalemic measurements with spironolactone were associated with more frequent monitoring, which more often occurred in older women and patients taking higher daily dosages. Therefore, potassium monitoring in healthy young women taking spironolactone for dermatologic conditions is unwarranted, given cost, time, and patient discomfort considerations that will unlikely change management.

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Table 1: Patient characteristics by hyperkalemia status

	Hyperkalemia Status			
	Overall, N = 1,489	**Negative, N = 1,408**	**Positive, N = 81**	**p-value[1]**
# of courses, n (%)				0.12
1	1,432 (96%)	1,357 (96%)	75 (93%)	
2	53 (3.6%)	48 (3.4%)	5 (6.2%)	
3	4 (0.3%)	3 (0.2%)	1 (1.2%)	
Age on course start date				0.11
Median (IQR)	30 (25,36)	29 (25,36)	32 (25,40)	
Mean (SD)	32 (10)	32 (10)	35 (13)	
Range	18,78	18, 78	18, 72	
Age group, n (%)				**0.022**
<25	329 (22%)	309 (22%)	20 (25%)	
25–34	728 (49%)	699 (50%)	29 (36%)	
35–44	258 (17%)	244 (17%)	14 (17%)	
45-54	116 (7.8%)	104 (7.4%)	12 (15%)	
55 or older	58 (3.9%)	52 (3.7%)	6 (7.4%)	
Race groups, n (%)				0.4
American Indian/Alaska Nation	1 (<0.1%)	1 (<0.1%)	0 (0%)	
Asian	115 (7.7%)	105 (7.5%)	10 (12%)	
Black/African American	80 (5.4%)	76 (5.4%)	4 (4.9%)	
Declined	263 (18%)	255 (18%)	8 (9.9%)	
Nat. Hawaiian/Other Pacific Islander	2 (0.1%)	2 (0.1%)	0 (0%)	
Other Combination	175 (12%)	162 (12%)	13 (16%)	
White	853 (57%)	807 (57%)	46 (57%)	
Self-reported race or ethnicity, n (%)				0.8
Declined/Unknown	340 (23%)	325 (23%)	15 (19%)	
Hispanic/Latin/Spanish Origin	152 (10%)	144 (10%)	8 (9.9%)	
Multiracial	2 (0.1%)	2 (0.1%)	0 (0%)	
Not Hispanic/Non-Latin/Spanish Origin	995 (67%)	937 (67%)	58 (72%)	
Indication, n (%)				0.2
Acne	938 (63%)	896 (64%)	42 (52%)	
Androgenetic Alopecia	58 (3.9%)	55 (3.9%)	3 (3.7%)	
Hair Loss	178 (12%)	164 (12%)	14 (17%)	
Hirsutism	101 (6.8%)	95 (6.7%)	6 (7.4%)	
Multiple Indications*	214 (14%)	198 (14%)	16 (20%)	
Maximum daily dose (mg) group, n (%)				**0.007**
≤50	528 (35%)	509 (36%)	19 (23%)	
75–100	800 (54%)	754 (54%)	46 (57%)	
125–200	160 (11%)	144 (10%)	16 (20%)	
>200	1 (<0.1%)	1 (<0.1%)	0 (0%)	
Number of Monitoring Values				**<0.001**
Median (IQR)	1.00 (1.00, 3.00)	1.00 (1.00, 3.00)	3.00 (2.00, 6.00)	
Mean (SD)	2.35 (2.38)	2.23 (2.22)	4.38 (3.75)	
Range	1.00, 31.00	1.00, 31.00	1.00, 20.00	

[1]*Fisher's exact test; Wilcoxon rank sum test*

Note: Patients with hypertension, renal disease, heart failure, taking medications affecting renin-angiotensin-aldosterone and/or missing data were excluded. Eighty-three patients experienced hyperkalemia while taking a course of spironolactone. However, this summary is prepared looking at the first spironolactone course only, filtered by course start date. Since most of the cases of hyperkalemia (81/83) occurred during the first course, statistical consideration of the summary and analysis based on the first course of spironolactone is recommended. Furthermore, for the purposes of computing p-values, declined responses in Race and Ethnicity were coded as missing. In Race, American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander and Other combination were all combined into one 'Other' category. In Ethnic groups, multiracial was combined with the Hispanic/Latin category. Maximum daily dose of >200 (one patient) was combined with the 125–200 category, while Number of courses = 3 was combined with two courses.

*includes a combination of acne, androgenic alopecia, hair loss/hair thinning, and/or hirsutism, n, N: refers to a count, Bold font: indicates statistical significance, IQR = interquartile range, SD = standard deviation.

Table 2: Outcomes of spironolactone courses after hyperkalemia

	n (%)
Spironolactone therapy stopped because of hyperkalemia	9 (10.7%)
Spironolactone therapy stopped because of other symptoms* or illness	3 (3.6%)
Spironolactone therapy stopped at the patient request	2 (2.4%)
The therapeutic dose of spironolactone was lowered because of hyperkalemia, and continued medication at a lower dose	10 (11.9%)
Repeat labs were ordered and potassium level was normalised, continued spironolactone therapy	20 (23.8%)
Repeat labs ordered but not performed, continued spironolactone therapy	3 (3.6%)
No change in spironolactone therapy and no additional labs were performed	37 (44.0%)

*Breast pain, menstrual irregularities

Potassium measurements are recommended in older patients and those taking high daily dosages.

Ethical approval

The research/study was approved by the Institutional Review Board at Weill Cornell Medicine Institutional Review Board, number 19-11021077, dated 5/25/2021.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of AI-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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References

1. Plovanich M, Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. JAMA Dermatol 2015;151:941–4.
2. Plante J, Robinson I, Elston D. The need for potassium monitoring in women on spironolactone for dermatologic conditions. J Am Acad Dermatol 2022;87:1097–9.
3. Thiede RM, Rastogi S, Nardone B, Sadowsky LM, Rangel SM, West DP, *et al*. Hyperkalemia in women with acne exposed to oral spironolactone: A retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. Int J Womens Dermatol 2019;5:155–7.
4. Wang Y, Lipner SR. Retrospective analysis of adverse events with spironolactone in females reported to the United States food and drug administration. Int J Womens Dermatol 2020;6:272–6.
5. Barbieri JS, Shin DB, Wang S, Margolis DJ, Takeshita J. The clinical utility of laboratory monitoring during isotretinoin therapy for acne and changes to monitoring practices over time. J Am Acad Dermatol 2020;82:72–9.