# Low Usefulness of Potassium Monitoring Among Healthy Young Women Taking Spironolactone for Acne

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Low Usefulness of Potassium Monitoring Among Healthy Young Women Taking Spironolactone for Acne

Molly Plovanich, MD; Qing Yu Weng, BS; Arash Mostaghimi, MD, MPA

Spironolactone is an androgen receptor antagonist that is an effective treatment for hormonally mediated acne.1-4 Although generally well tolerated, spironolactone use is associated with hyperkalemia among patients with heart failure taking additional drugs that interfere with potassium excretion.5 However, the prevalence of spironolactone-induced hyperkalemia among young women taking spironolactone for acne is unclear. To date, there have been 4 small-scale clinical studies,6-9 each fewer than 100 patients, that have measured serum potassium as a secondary outcome in patients taking spironolactone for acne. Three studies6-8 yielded zero cases of hyperkalemia, and one study9 showed a 13.7% rate of mild hyperkalemia, which was defined as a serum potassium measurement of 4.8 to 5.3 mEq/L (to convert potassium level to millimoles per liter, multiply by 1.0).

The rate of hyperkalemia in healthy young women taking spironolactone for acne is equivalent to the baseline rate of hyperkalemia in this population. Routine potassium monitoring is unnecessary for healthy women taking spironolactone for acne.

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of healthy young women taking spironolactone for acne or for an endocrine disorder with associated acne to determine whether potassium monitoring is clinically indicated in this population.10

Methods

All medical records from December 1, 2000, through March 31, 2014, at Brigham and Women’s Hospital and Massachusetts General Hospital (Boston) were evaluated using the Research Patient Data Repository, a clinical data registry that captures comprehensive information about patients seen within the Partners HealthCare system in Boston. Data in the repository include clinic visits, inpatient admissions, laboratory data, operative notes, and pathology reports.

Our search parameters identified patients who were female, 18 to 45 years old, diagnosed as having acne, given a prescription for spironolactone, and seen in an outpatient setting at Brigham and Women's Hospital or Massachusetts General Hospital. We excluded patients who had a history of heart failure, were using medications that affect the renin-angiotensin-aldosterone system (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β-blockers, amiloride hydrochloride, or triamterene), or had nephritis, nephrotic syndrome, renal failure, or chronic renal disease as defined by a glomerular filtration rate of less than 60 mL/min.

Each identified medical record was individually reviewed (by M.P. and Q.Y.W.) to confirm that inclusion criteria were met and to determine the primary clinical indication for spironolactone therapy, whether the serum potassium measurement was checked after the initiation of spironolactone, the total number of times the serum potassium measurement was checked, what specialty prescribed spironolactone (dermatology vs other), and the age at which the patient began spironolactone therapy. We collected all serum potassium data available in this cohort, including values obtained when taking and not taking spironolactone.

The normal range of serum potassium measurements was defined as 3.5 to 5.0 mEq/L, which is the standard reference range for the institutions at which this study was conducted. Hyperkalemia was classified as mild (5.1-6.0 mEq/L), moderate (6.1-6.9 mEq/L), or severe (≥7.0 mEq/L).11,12 All study protocols were reviewed and approved by the Partners HealthCare Human Research Committee. Informed consent was not required. All data analysis was performed using statistical software (SAS, version 9.4; SAS Institute Inc).

Results

Cohort Selection

The initial Research Patient Data Repository query identified 1559 patients, 394 of whom worked within the Partners HealthCare system and were excluded to preserve confidentiality. Of the remaining 1165, an additional 191 patients were excluded because of inability to validate that they had taken spironolactone for acne or for an endocrine disorder with associated acne (Figure 1). Of the remaining 974 patients who had a diagnosis of acne and had been prescribed spironolactone, 676 were taking spironolactone for a primary diagnosis of acne, and 298 were taking spironolactone for an endocrine disorder with acne as a secondary feature. Common endocrine disorders encountered include polycystic ovary syndrome, hirsutism, alopecia, and hyperandrogenism.

Practice of Potassium Monitoring

We evaluated the current practice of potassium monitoring for patients with a new prescription for spironolactone (Table). The serum potassium measurement was checked in 56.4% of patients with acne as a primary diagnosis. In contrast, the serum potassium measurement was checked in 74.9% of patients with an endocrine disorder who had acne as a secondary feature ($P < .01$).

There was substantial variation in how often serum potassium was measured in patients whose potassium was monitored, with a range of 1 to 22 tests (mean, 3 tests). In patients with a sole diagnosis of acne, the mean (SD) number of serum potassium measurements per person was 2.54 (2.71), with a 95% CI of 2.26 to 2.81. In patients with acne as a secondary diagnosis, the mean (SD) number of serum potassium measurements per person was 3.96 (3.78), with a 95% CI of 3.46 to 3.96.

Table. Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acne Primary Diagnosis (n = 676)</th>
<th>Acne Secondary Diagnosis (n = 298)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with serum potassium measurement, %</td>
<td>56.4</td>
<td>74.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of serum potassium measurements per patient, mean (SD)</td>
<td>2.54 (2.71)</td>
<td>3.96 (3.78)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>27.5 (6.4)</td>
<td>26.2 (6.0)</td>
<td>.01</td>
</tr>
<tr>
<td>Prescriber, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatologist</td>
<td>79.3</td>
<td>20.8</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6.4</td>
<td>53.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Unclear</td>
<td>14.3</td>
<td>26.2</td>
<td></td>
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Dermatologists were the overwhelming majority of prescribers for patients with acne as a primary diagnosis. In this cohort, 79.3% of prescribers were dermatologists, 6.4% were trained in other fields, and 14.3% were prescribers who could not be definitively identified. In contrast, in patients with an endocrine disorder, only 20.8% of prescribers were dermatologists, and 53.0% were from other specialties, particularly endocrine and primary care. In this cohort, 26.2% of prescribers could not be definitively identified.

Incidence of Hyperkalemia

In total, 1802 serum potassium measurements were obtained when patients were taking spironolactone for acne or for an endocrine disorder with associated acne. Of these, 13 measurements were between 5.1 and 6.0 mEq/L, indicating a 0.72% rate of mild hyperkalemia (Figure 2). In 6 patients, the elevated values prompted successive testing within 1 to 3 weeks, revealing normal values in all cases, suggesting that the original measurements may have been erroneous. Spironolactone therapy was not discontinued for any of the patients in the interim. Of the remaining 7 patients, successive testing was not pursued. None of the patients received additional monitoring such as electrocardiography for adverse events related to hyperkalemia. All patients with hyperkalemia were asymptomatic, and there were no reported adverse clinical events.

To determine the baseline rate of hyperkalemia in our population, we calculated the rate of hyperkalemia using all serum potassium measurements available to us, including values obtained when taking and not taking spironolactone. This yielded a rate of 0.76% (32 of 4209), which is comparable to the 0.72% (13 of 1802) rate of hyperkalemia in patients taking spironolactone.

Discussion

Before this study, the rate of hyperkalemia in healthy young women receiving spironolactone for acne was unknown. We identified a low rate of mild hyperkalemia in patients taking spironolactone for acne that was similar to the baseline rate of hyperkalemia in this population, suggesting that spironolactone does not significantly alter the rate of clinical hyperkalemia in our population.

When a subset of 13 patients with elevated serum potassium measurements underwent repeat testing, all values were within normal limits, suggesting that the original measurements were erroneous or that the mild hyperkalemia was transient and quickly self-resolved. In either case, there were no adverse clinical events, indicating that any mild hyperkalemia was clinically insignificant. Patients with acne as a secondary diagnosis did not have higher rates of hyperkalemia, despite their underlying endocrine disorder.

For the first time to date, we also report an estimate of how frequently the serum potassium measurement is checked by physicians in clinical practice. Dermatologists had the lowest rates of potassium monitoring, whereas internal medicine specialists, whose patient panel was enriched with endocrine disorders, had higher rates. It is unclear whether this effect is influenced by the patients’ comorbidities or reflects easier access to laboratory monitoring.

What are the implications of our results for clinical practice? Given our inability to identify any instances of persistent and clinically meaningful hyperkalemia in 14 years of clinical data, we suggest that potassium monitoring should no longer be conducted in healthy young women taking spironolactone for acne. Abandoning frequent potassium monitoring can decrease unnecessary office visits and reduce health care spending.

Spironolactone is an inexpensive, generic drug, with a monthly cost of $4.00 when obtained through major retailers in the United States. The cost of a single serum potassium measurement is $6.27 as determined by the 2014 clinical laboratory fee schedule by the Centers for Medicare & Medicaid Services. However, a serum electrolyte panel costing $43.51 is frequently ordered in conjunction with the potassium measurement. Within our study population, the latter panel equates to up to $78 405.02 in spending that does not appear to yield clinically significant information for the studied population. Furthermore, these estimates do not take into account patient-specific costs such as time and lost work productivity. It is likely that patients and physicians have restricted the use of spironolactone because of concerns regarding hyperkalemia and the feasibility of the recommended potassium monitoring frequency. The ability to prescribe spironolactone safely without drug monitoring will allow for expanded use of this inexpensive and efficacious drug for young women with acne.

Our results are limited by the fact that the study was performed at just 2 hospitals, which may reflect only a subset of national prescribing patterns. Although the retrospective nature provides insight into how frequently prescribers check serum potassium measurements, a substantial subset of patients did not have their potassium level checked, and potential cases of hyperkalemia may not have been captured. A small percentage of patients were being prescribed spironolactone by physicians from an outside specialty.
hospital or clinic, from which we could not capture potassium data. This could have resulted in falsely low estimates of how often physicians check serum potassium measurements.

Moving forward, it will be important to educate multiple specialties about our results and their implications for clinical practice. In addition, it will be necessary to replicate our results in similar populations at other institutions.

### Conclusions

In conclusion, our results suggest that routine potassium monitoring is unnecessary for healthy young women taking spironolactone for acne. The low rate of hyperkalemia may encourage more health care professionals to consider the use of this highly effective drug in their clinical practice.