



Original Research

Hyperkalemia in women with acne exposed to oral spironolactone: A retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program[☆]



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ABSTRACT

Purpose: The necessity of serum potassium monitoring for healthy women who are prescribed spironolactone for acne has been debated. The aim of this study was to compare the incidence of hyperkalemia in women 18 to 45 years of age to that in women 46 to 65 years of age, when treated with oral spironolactone for acne.

Methods and materials: Data for all women 18 to 65 years of age who were prescribed oral spironolactone by a dermatologist for acne between January 2006 and October 2016 were extracted for analysis. Retrospective data were included for women who exhibited baseline serum potassium within the normal limits and who had repeat serum potassium monitoring within 12 months after initiation of spironolactone. The rate of incident hyperkalemia was determined.

Results: Of 618 women who received spironolactone for acne, 133 had serum potassium monitoring both before and after spironolactone initiation. Nine were excluded due to confounding comorbidities. Of the remaining 124 women, the mean age at initiation of spironolactone was 32 years (range, 18–57 years); 112 women were in the 18 to 45 years age group, and 12 were in the 46 to 65 years age group. All women had serum potassium within normal limits at baseline. Women in the 46 to 65 years age group had a significantly higher rate of incident hyperkalemia after spironolactone initiation compared with women 18 to 45 years of age (2 of 12 women [16.7%] vs. 1 of 112 women [$<1\%$]; $p = .0245$).

Conclusions: Although controversy surrounds the clinical utility of serum potassium monitoring in healthy women exposed to spironolactone for acne, based on the findings from this large patient population, monitoring of serum potassium is warranted for women over 45 years of age given an age-related greater risk of hyperkalemia.

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Introduction

Oral spironolactone has long been used as an efficacious, anti-androgen, off-label acne therapy in women (Charny et al., 2017). The necessity of serum potassium monitoring in the context of use for acne has been questioned. Plovovich et al. (2015) reported low utility of

serum potassium monitoring in healthy young women 18 to 45 years of age receiving spironolactone for acne. In their retrospective study population, the rates of hyperkalemia in women at baseline and during spironolactone therapy were reported as equivalent. However, whether women over the age of 45 years have a similar risk for hyperkalemia while taking spironolactone for acne remains unclear. This study aimed to compare the incidence of hyperkalemia in women in the 18 to 45 years age group with that of women in the 46 to 65 years age group when treated with oral spironolactone for acne.

Methods and materials

The Northwestern Medicine Enterprise Data Warehouse (NMEDW), a medical record data repository (>5 million patients;

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primarily residing in the Chicago metropolitan area), provided data for all women between 18 and 65 years of age who had a diagnosis of acne (International Classification of Diseases [ICD] 9 code 706.1; ICD 10 codes L70.0, L70.1, L70.2, L70.3, L70.5, and L70.8) and a dermatology clinic visit between January 2006 and October 2016. Data for all women who had serum potassium monitoring at baseline (occurring within 12 months before, or concurrent with, initiation of spironolactone) and at follow-up (occurring 1–12 months after initiation of spironolactone) were included for analysis. The outcome of interest was incident hyperkalemia at follow-up. Hyperkalemia was defined as ≥ 5.1 mEq/L, given the institutional normal reference range of 3.5 to 5.0 mEq/L. Women over 65 years of age and those with a diagnosis of hypertension (ICD 9 codes 401–405; ICD 10 codes I10–I16), renal failure (ICD 9 codes 584–586; ICD 10 codes N17–N19), or diabetes mellitus (ICD 9 code 250; ICD 10 codes E08–E11, E13) were excluded. The Fisher's exact test was used to compare the rates of incident hyperkalemia after spironolactone exposure by age group.

Results

Of 618 women diagnosed with acne and prescribed spironolactone by a dermatologist between January 2006 and October 2016, 133 (21.5%) met the inclusion criteria with serum potassium monitoring both at baseline and at follow-up (Fig. 1). After excluding 9 women with comorbidities (hypertension, renal disease, and diabetes mellitus), data for 124 women were included for analysis. At initiation of spironolactone, 112 women were in the 18 to 45 years age group, and 12 were in the 46 to 65 years age group (Fig. 1). All 124 women had baseline serum potassium values within normal limits. Three patients (ages 42, 47, and 47 years) had incident hyperkalemia at follow-up. The rate of incident hyperkalemia at follow-up was significantly higher for women in the 46 to 65 years age group compared with that observed for women in the 18 to 45 years age group (2 of 12 [16.7%] vs. 1 of 112 [$<1\%$]; $p = .0245$).

Discussion

This study demonstrated that hyperkalemia rarely occurs in younger women (age 18–45 years), consistent with previous reports (Kronic et al., 2008; Plovanich et al., 2015). Notably, incident hyperkalemia occurred significantly more often in older women (age 46–65 years). These data suggest that women over 45 years of age with no known hypertension, renal failure, or diabetes who are exposed to spironolactone for the treatment of acne have a significantly greater risk of incident hyperkalemia compared with younger women.

Given that renal function physiologically declines with advancing age, typically beginning in the fifth decade (>40 years of age), even in the absence of known comorbidities (Hoang et al., 2003), medication-related adverse effects are more likely to occur in older women. Therefore, hyperkalemia in the context of spironolactone use in otherwise healthy older women is not unexpected and warrants ongoing monitoring. This physiologic age-related decline in renal function and corresponding increased risk of medication-related adverse events underscore the need for age-specific guidelines in the full prescribing information for spironolactone.

The current full prescribing information for spironolactone specifies that serum potassium monitoring should be performed within 1 week of initiation or titration of spironolactone and regularly thereafter for the U.S. Food and Drug Administration–approved indications of heart failure, hypertension, edema, and primary hyperaldosteronism (Pfizer, 2018). Findings from this large population of adult women with acne exposed to oral spironolactone revealed that current clinical practice omits follow-up monitoring of serum potassium when the baseline level is within normal limits and patients have no known comorbidities. The majority of women (414 of 618 [67%]) who were prescribed spironolactone for acne had no serum potassium monitoring during follow-up (within 12 months of spironolactone initiation). Additionally, 248 of 618 women (40.1%) either had no serum potassium monitoring or had serum potassium monitoring >12 months before or after initiation of spironolactone for acne. Moreover, because the majority of patient data in this study existed prior to 2015, we do not attribute the lack of serum potassium surveillance to a clinical practice

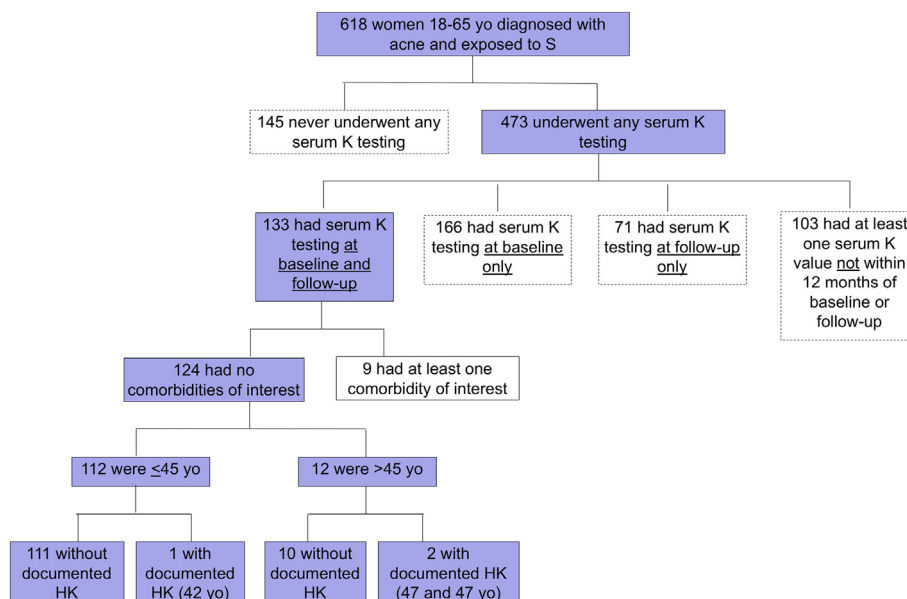


Fig. 1. Results of retrospective data collection. S = oral spironolactone; K = potassium; HK = hyperkalemia; yo = years old. The dashed line around the box signifies incomplete serum potassium testing. Baseline was defined as occurring within 12 months before or concurrent with initiation of spironolactone. Follow-up was defined as occurring between 1 and 12 months after initiation of spironolactone.

change based on publicity related to Plovanich et al. (2015). Variability in serum potassium monitoring may relate to differences in clinical practice patterns, clinician omission, or patient noncompliance. Observed inconsistencies in serum potassium monitoring reinforce the need for establishment and communication of guidelines for optimal serum potassium monitoring in the context of spironolactone use for acne.

Limitations of this study include the inability to verify medical record diagnostic coding. Laboratory data originating outside of the NMEDW system may not be integrated and evaluable. Given the low rate of observed hyperkalemia, stratification of risk by either spironolactone dose or duration of spironolactone exposure was not achievable.

Conclusions

Given that spironolactone continues to be widely used as an off-label treatment for acne, serum potassium monitoring recommendations warrant further delineation, specifically age-related dosing

guidelines. As corroborated by several published studies, hyperkalemia rarely occurs in otherwise healthy women <46 years of age who receive spironolactone for acne; therefore, serum potassium monitoring in this patient population appears to be unwarranted. In contrast, the increased rate of incident hyperkalemia observed in older women (>45 years of age) who received spironolactone for acne underscores the need for ongoing serum potassium monitoring in such patients.

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