Post-discharge outcomes among hyperkalemic patients treated with and without SPS in the inpatient setting

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Introduction

- Hyperkalemia, defined as abnormally high serum potassium (>5.0 mEq/L), is an established complication of reduced renal function in patients with chronic kidney disease (CKD) or acute kidney injury[1]
- Patients with hyperkalemia have an average of 0.44 all-cause inpatient admissions per year[2]
- Previous research found that about 20% of patients with an inpatient stay with hyperkalemia were readmitted to inpatient care within 30 days of discharge[3]
- Sodium polystyrene sulfonate (SPS) is a long-standing treatment option for hyperkalemia in the inpatient setting. However, the inpatient management and post-discharge outcomes of patients with hyperkalemia treated with SPS during the inpatient setting are not well characterized

Objectives

1. To describe and compare the management of patients with hyperkalemia treated with SPS and not treated with SPS in the inpatient setting
2. To assess if subsequent inpatient admissions and hyperkalemia recurrence following an inpatient stay differ between patients with hyperkalemia treated with SPS and not treated with SPS during an inpatient stay

Methods

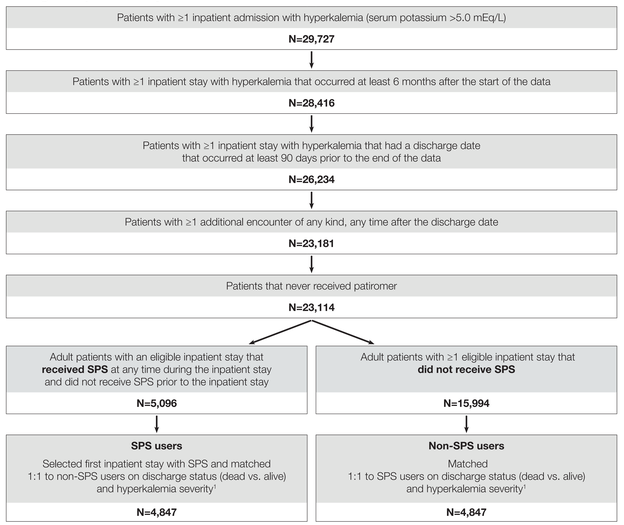
Data source

- Electronic medical record data from two health systems located in Louisiana that were part of the Research Action for Health Network (REACHnet) were used in this study from 2012–2018
  - REACHnet contains data for over 5 million patients of different age, sex and race/ethnicity backgrounds
  - Available variables include limited de-identified information, such as patient demographics, vital signs, lab test results, prescriptions, procedures, and diagnoses
- This study was approved by the New England Institutional Review Board on June 25, 2018

Sample Selection

- Patients with hyperkalemia receiving SPS during an inpatient stay were selected and matched 1:1 on discharge status (dead vs. alive) and hyperkalemia severity (most severe potassium lab during the inpatient stay) to patients with hyperkalemia that did not receive SPS (**Figure 1**)

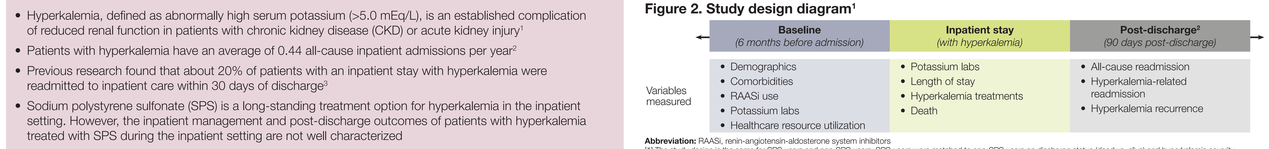
Figure 1. Sample selection of patients with hyperkalemia treated with and without SPS during an inpatient stay



[1] Hyperkalemia severity was defined by the most severe potassium lab value during the inpatient stay

Study Design

Figure 2. Study design diagram[1]



Abbreviation: RAASi, renin-angiotensin-aldosterone system inhibitors
[1] The study design is the same for SPS users and non-SPS users. SPS users were matched to non-SPS users on discharge status (dead vs. alive) and hyperkalemia severity
[2] Post-discharge outcomes were evaluated 30, 60, and 90 days post-discharge

Statistical Analyses

- SPS users and non-SPS users were compared using Wilcoxon signed-rank tests for continuous variables and McNemar's tests for categorical variables
- Multivariable logistic regression models examined all-cause inpatient readmission, hyperkalemia-related inpatient readmission (≥1 potassium lab value >5.0 mEq/L during an inpatient stay), and hyperkalemia recurrence (≥1 potassium lab value >5.0 mEq/L in any setting) within 30, 60 and 90 days post-discharge
  - All models were adjusted for demographics (age, sex, and race), hyperkalemia severity (based on first high potassium lab during the inpatient stay), comorbidities (acute kidney injury, CKD, heart failure, hypertension, type II diabetes, Charlson comorbidity index), treatments during baseline (RAASi, dialysis, diuretics), healthcare resource utilization (all-cause inpatient/outpatient/emergency department visits, any inpatient visits related to CKD/heart failure/hyperkalemia/ hypertension/type II diabetes), baseline potassium labs (number of labs, severity of baseline potassium lab closest to the inpatient stay), and reason for inpatient admission (e.g. hyperkalemia related)
- P-values <0.05 were considered statistically significant and are denoted with an *

Results

Patient and Clinical Characteristics during the 6 Months Prior to the Inpatient Stay (see Table 1 for details)

- SPS users were older than non-SPS users (65.7 vs. 62.1 years) and had a higher burden of comorbidities, including CKD (79.1% vs. 57.2%) and heart failure (49.8% vs. 37.7%)
- SPS users had more potassium labs >5 mEq/L (1.2 vs. 0.6 labs) and had more hyperkalemia-related inpatient admissions (7.3% vs. 2.7%) during baseline than non-SPS users

Table 1. Comparison of patient and clinical characteristics during the 6 months prior to the inpatient stay among SPS and non-SPS users

	SPS users N=4,847	Non-SPS users N=4,847	*P*-value
Demographics			
Age (years), mean ± SD	65.7 ± 16.0	62.1 ± 16.9	< 0.001 *
Female, n (%)	2,175 (44.9%)	2,163 (44.6%)	0.82
Race, n (%)			
White	2,622 (54.1%)	2,669 (55.1%)	0.35
Black	2,097 (43.3%)	2,012 (41.5%)	0.08
Other	71 (1.5%)	74 (1.5%)	< 0.01 *
Unknown	57 (1.2%)	92 (1.9%)	< 0.01 *
Comorbidities[1], n (%)			
Acute kidney injury	3,393 (70.0%)	2,375 (49.0%)	< 0.001 *
CKD stage 3-5	3,832 (79.1%)	2,773 (57.2%)	< 0.001 *
Stage 3	1,514 (31.2%)	1,265 (26.1%)	< 0.001 *
Stage 4	952 (19.6%)	494 (10.2%)	< 0.001 *
Stage 5, without dialysis	614 (12.7%)	388 (8.0%)	< 0.001 *
Stage 5, with dialysis	752 (15.5%)	626 (12.9%)	< 0.001 *
Heart failure	2,415 (49.8%)	1,828 (37.7%)	< 0.001 *
Hypertension	4,329 (89.31%)	3,951 (81.5%)	< 0.001 *
Type 2 diabetes	2,591 (53.5%)	2,177 (44.9%)	0.24
CCI	2.5 ± 2.5	2.0 ± 2.3	< 0.001 *
Treatments, n (%)			
Any RAASi use[2]	1,477 (30.5%)	1,168 (24.1%)	< 0.001 *
Potassium labs			
≥ 1 Potassium lab during baseline, n (%)	3,395 (70.0%)	3,252 (67.1%)	< 0.001 *
Potassium value (mEq/L),[3,5] mean ± SD	4.5 ± 0.6	4.3 ± 0.6	< 0.001 *
Any labs >5 mEq/L,[4,5] n (%)	813 (23.9%)	375 (11.5%)	< 0.001 *
Number of labs >5 mEq/L,[3,4] mean ± SD	1.2 ± 2.3	0.6 ± 1.4	< 0.001 *
Healthcare resource utilization, n (%)			
All-cause inpatient admissions	1,919 (39.6%)	1,609 (33.2%)	< 0.001 *
Hyperkalemia-related inpatient admissions[6]	356 (7.3%)	131 (2.7%)	< 0.001 *
All-cause emergency department visits	1,419 (29.3%)	1,220 (25.2%)	< 0.001 *
All-cause outpatient visits	3,778 (77.9%)	3,685 (76.0%)	< 0.05 *

Abbreviations: CCI, Charlson comorbidity index; N, number; RAASi, renin-angiotensin-aldosterone system inhibitors; SD, standard deviation
[1] All comorbidities were measured during the baseline period or during the inpatient stay except for CCI, which was measured during the baseline period only
[2] RAASi included aldosterone receptor antagonists, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and direct renin inhibitors
[3] The potassium value closest to the inpatient admission was reported
[4] *Potassium value (mEq/L), any labs >5 mEq/L, and number of labs >5 mEq/L* were calculated among patients with ≥1 potassium lab during baseline
[5] The p-values for *potassium value (mEq/L), any labs >5 mEq/L, and number of labs >5 mEq/L* were calculated using a Chi-squared test for categorical variables and a Wilcoxon rank-sum test for continuous variables
[6] A hyperkalemia-related inpatient admissions was defined as an inpatient stay with at least one diagnosis for hyperkalemia

Characteristics during the Inpatient Stay (see Table 2 for details)

- During the inpatient stay, 23.2% of SPS and non-SPS users had mild hyperkalemia, 36.8% had moderate hyperkalemia, and 40.0% had severe hyperkalemia
- About 1 in 9 patients (11.7%) died during the inpatient stay, with SPS users dying later during the inpatient stay than non-SPS users (9.8 vs. 7.7 days)
- The use of temporizing agents was common for SPS and non-SPS users (58.2% vs. 43.5%)
- Among SPS users, only 17 patients (0.4%) received SPS at discharge

Table 2. Comparison of characteristics during the inpatient stay among SPS and non-SPS users

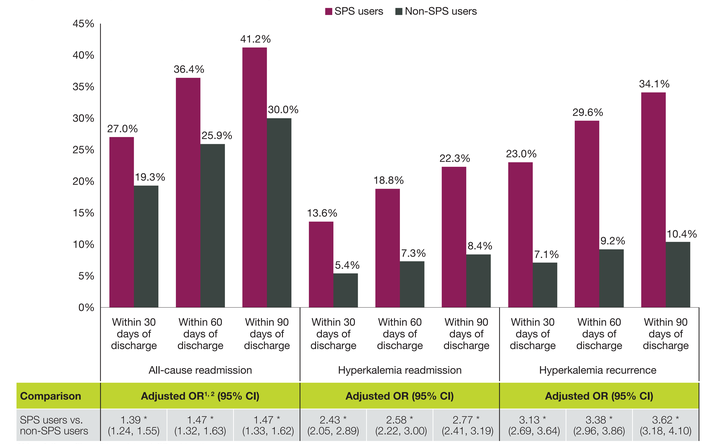
	SPS users N=4,847	Non-SPS users N=4,847	*P*-value[1]
Hyperkalemia severity during inpatient stay,[2] n (%)			
Mild (>5.0 - 5.5 mEq/L)	1,125 (23.2%)	1,125 (23.2%)	-
Moderate (>5.5 - 6.0 mEq/L)	1,783 (36.8%)	1,783 (36.8%)	-
Severe (>6.0 mEq/L)	1,939 (40.0%)	1,939 (40.0%)	-
Inpatient stay information			
Length of inpatient stay (days), mean ± SD	9.0 ± 7.3	9.1 ± 7.4	0.54
Potassium lab value returned to ≤5 mEq/L during stay,[3,4] n (%)	3,966 (83.0%)	3,979 (86.2%)	< 0.001 *
Death during inpatient stay			
Patients who died during stay, n (%)	567 (11.7%)	567 (11.7%)	-
Days between admission and death, mean ± SD	9.8 ± 8.7	7.7 ± 8.4	< 0.001 *
Treatments, n (%)			
Any temporizing agent use	2,822 (58.2%)	2,109 (43.5%)	< 0.001 *
Albuterol (nebulizer or IV)	1,188 (24.5%)	524 (10.8%)	< 0.001 *
IV calcium	1,950 (40.2%)	1,455 (30.0%)	< 0.001 *
IV insulin + glucose[5]	1,739 (35.9%)	821 (16.9%)	< 0.001 *
Sodium bicarbonate (oral or IV)	1,160 (23.9%)	1,123 (23.2%)	0.36
SPS at discharge	17 (0.4%)	-	-

Abbreviations: IV, intravenous; N, number; SD, standard deviation
[1] P-values were not shown for variables used to match SPS and non-SPS users
[2] The most severe potassium lab measured during the inpatient stay was used to define hyperkalemia severity
[3] Calculated among patients with ≥2 potassium labs during the inpatient stay (SPS users: 4,781; non-SPS users: 4,617)
[4] The p-value for *potassium lab value returned to ≤5 mEq/L during stay* was calculated using a Chi-squared test
[5] IV insulin + glucose was indicated by separate records for insulin and glucose occurring on the same day

Post-Discharge Outcomes (see Figure 3 for details)

- SPS users had more all-cause and hyperkalemia-related inpatient readmissions and hyperkalemia recurrence within 30, 60, and 90 days post-discharge than non-SPS users
- The difference between SPS and non-SPS users persisted in multivariable regression models

Figure 3: Comparison of post-discharge outcomes 30, 60 and 90 days after the inpatient stay



Comparison	Adjusted OR[1, 2] (95% CI)			Adjusted OR (95% CI)			Adjusted OR (95% CI)		
SPS users vs. non-SPS users	1.39 * (1.24, 1.55)	1.47 * (1.32, 1.63)	1.47 * (1.33, 1.62)	2.43 * (2.05, 2.89)	2.58 * (2.22, 3.00)	2.77 * (2.41, 3.19)	3.13 * (2.69, 3.64)	3.38 * (2.96, 3.86)	3.62 * (3.18, 4.10)

Abbreviations: CI, confidence interval; OR, odds ratio
[1] Odds ratios and 95% confidence intervals were estimated using a binomial generalized linear model with a logit link
[2] The sample size for all regressions is 7,992. Patients who died during their inpatient stay were removed from this analysis

Discussion

- Despite SPS being a mainstay treatment for hyperkalemia, Palaka et al. (2018) highlighted the limited evidence to determine the efficacy and safety of SPS[4]
  - One retrospective study found that SPS lowered serum potassium levels, but the authors noted that the difference may not be clinically important[5]
  - Other studies found that SPS is associated with certain serious adverse events (e.g. colonic necrosis) which may limit its use among patients[6, 7]
- In this study, SPS users had higher odds of all-cause and hyperkalemia-related readmission and hyperkalemia recurrence than non-SPS users. It is important to note that SPS users appeared to be in worse clinical condition than non-SPS users. Although the multivariable regression models comprehensively adjusted for confounders and the cohorts were matched on discharge status (alive vs. dead) and hyperkalemia severity, residual confounding is possible and other intrinsic differences between the populations may be driving the subsequent observed differences in post-discharge events
- More SPS users than non-SPS users had a record for a temporizing agent during the inpatient stay and very few SPS users received SPS at discharge, yet almost one quarter of SPS users had their hyperkalemia recur within 30 days of discharge
  - Potential reasons for the low use of SPS at discharge may be due to patients' low tolerance for long-term SPS medication usage, provider preferences, limitations in insurance coverage, and limited medication access post-discharge
- Results from this study highlighted the high burden of readmission and hyperkalemia recurrence among patients discharged from hyperkalemia-related inpatient stay despite treatment with SPS
- A limitation of this study is that patient encounters occurring outside of the healthcare systems were not available in the data; therefore, some baseline and post-discharge outcomes may not have been captured in the data

Conclusion

- Despite treatment with SPS in the inpatient setting and greater comorbidity burden in SPS users, very few patients received SPS at discharge, and there was a high burden of readmission and hyperkalemia recurrence among patients with hyperkalemia
- Additionally, despite the high use of emergency temporizing agents in hyperkalemic patients treated with SPS in the inpatient setting, the high burden of readmission and hyperkalemia recurrence remained, potentially indicating the temporary effect of these agents, and highlighting the need for tolerable, effective, and easy to administer therapies and prevention of hyperkalemia recurrence and readmission

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Disclosures

- EC, FM, KAB, EB, ELW and LY are employees of Analysis Group, which received payment from AstraZeneca for the conduct of this analysis
- JD and DA are employees of AstraZeneca
- RI is a past employee of AstraZeneca
- HZ is on the advisory board and speaker's bureau at AstraZeneca
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