Efficacy of Sodium Polystyrene Sulfonate for the Treatment of Hyperkalemia

Yu-Chen Lin, B.Sc.(Pharm); Josh Batterink, B.Sc.(Pharm); Gregory Michael Legal, Pharm.D.; Tara Anne Cessford, M.D.; Hin Mui Au-Yeung

Background

- Hyperkalemia can induce fatal arrhythmias
- Sodium polystyrene sulfonate (SPS) commonly used for the treatment of hyperkalemia as potassium(K+)-binding resin
- Since FDA approval in 1958, only 2 small (n<10) randomized crossover studies and 1 retrospective cohort study evaluated the efficacy of SPS with mixed results
- SPS has been associated with colonic necrosis, mucosal lesions and aspiration pneumonitis

Objectives

- Primary: Evaluate the effect of oral SPS on mean change in serum K+ level 6-24 hours post-dose
- Secondary: Evaluate the potential relationship between the dose of SPS and the magnitude of serum K+ reduction

Methods

- Retrospective observational study at St. Paul's Hospital (SPH)
- Study period: January 2011 – May 2012
- Patients identified via Providence Health Care Laboratory
  - Intervention group: received oral SPS for treatment
  - Control group: did not receive SPS for treatment
- 50 pairs (100 patients) required to give 90% power to show equivalence between groups with minimal clinically important difference in serum K+ reduction ≥ 0.2 mmol/L with an alpha value of 0.05
- Patients in intervention group matched to control patients using kernel based propensity score matching

Inclusion

- Age 19 years or older
- Admitted to SPH medical or surgical wards
- Serum K+ level of 5.0-5.9 mmol/L
- For patients with multiple includable hyperkalemia episodes, only one treated and one untreated episode will be considered

Exclusion

- Admitted with hyperkalemia
- Did not have a serum K+ level within 24 hours after index K+
- Acute renal failure per RIFLE criteria
- Chronic renal failure (CrCl ≤ 15ml/min) or receiving dialysis
- Unclear/missing medication history or medication administration record
- Concurrent change in K+ content of diet
- Concurrent initiation or change to K+ altering medication/supplement

Propensity Score Matching – Kernel Method

Propensity score covariates: change in K+ level 24 hours prior to index level, index potassium level, eGFR, gender, heart failure, urea level, diabetes, ACEI/ARB, thiazides/loop diuretics, aldosterone antagonist/K+ sparing diuretics

Table 1. Patient Characteristics

Variables	Control (n=72)	Treatment (n=66)
Mean age (Year±SD)	69 ± 17	69 ± 16
Female gender no.(%)	24 (33)	26 (39)
Mean Index K+ Level (mmol/L)	5.1 ± 0.2	5.3 ± 0.2
Mean eGFR (ml/min)	59 ± 27	56 ± 32
Mean urea (mmol/L)	11 ± 7	13 ± 9
Disease States no. (%):		
Heart failure	11 (15)	12 (18)
Liver dysfunction	8 (11)	12 (18)
Diabetes	22 (31)	19(29)
Diet type no. (%):		
Regular	10 (14)	10 (15)
Low K+	1 (1)	1 (2)
Others	61 (85)	55 (83)
Concurrent medications no. (%):		
Increase serum K+		
Dalteparin	29 (40)	25 (38)
ACEI/ARB	14 (19)	18 (27)
Aldosterone antagonist/K+ sparing diuretics	8 (11)	6 (9)
TMP-SMX	3 (4)	5 (8)
High dose heparin	3 (4)	4 (6)
Non-selective beta-blockers	2 (3)	1 (2)
Others	2 (3)	2 (3)
Calcineurin inhibitors	0	1 (2)
Decrease serum K+		
Basal insulin/insulin sliding scale	17 (24)	15 (23)
Thiazide/loop diuretics	16 (22)	15 (23)
Salbutamol	10 (14)	13 (20)
Lithium	1 (1)	1 (2)
Others	1 (1)	0

Table 2. Time to follow up serum potassium level

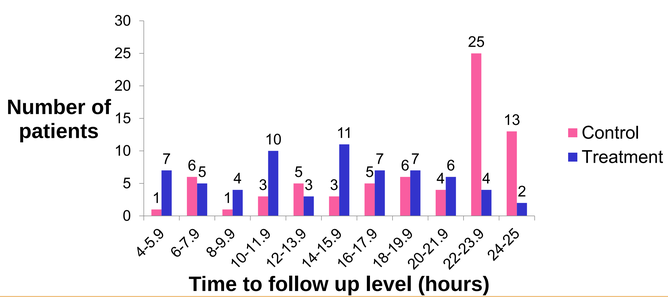
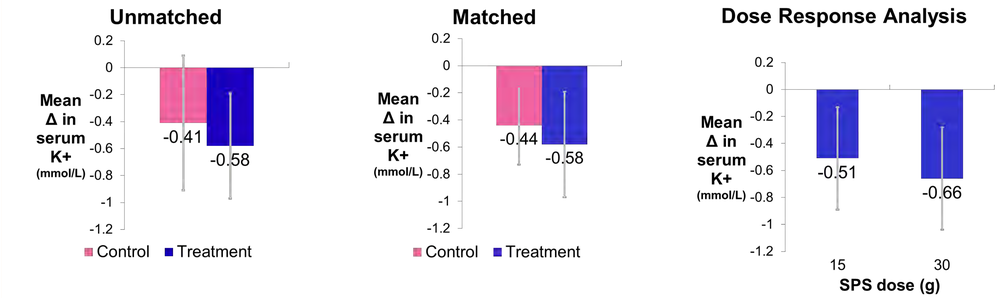


Table 3. Propensity Score Matching Result

Covariates	Unmatched/ Matched	Mean Treated	Mean Control	% Reduction Bias	p value
Change in K+ level 24hr prior to index level	Unmatched	0.43	0.56		0.108
	Matched	0.43	0.42	93.5	0.918
Index K	Unmatched	5.29	5.15		0.000
	Matched	5.29	5.28	91.7	0.759
eGFR	Unmatched	57.17	64.56		0.175
	Matched	57.17	60.24	58.4	0.600
Gender	Unmatched	0.39	0.33		0.463
	Matched	0.39	0.37	62.4	0.789
Heart Failure	Unmatched	0.18	0.15		0.650
	Matched	0.18	0.16	24.5	0.740
Urea Level	Unmatched	13.36	10.55		0.035
	Matched	13.36	13.11	91.1	0.874
Diabetes	Unmatched	0.29	0.31		0.822
	Matched	0.29	0.29	72.0	0.951
ACEI/ARB	Unmatched	0.27	0.19		0.280
	Matched	0.27	0.31	47.2	0.606
Thiazide/ Loop Diuretics	Unmatched	0.23	0.22		0.944
	Matched	0.23	0.20	-352.4	0.752
Dalteparin	Unmatched	0.38	0.40		0.775
	Matched	0.38	0.45	-194.9	0.413
Aldosterone Antagonist/ K+ Sparing Diuretics	Unmatched	0.09	0.11		0.697
	Matched	0.09	0.10	59.1	0.873

Results



Limitation

- Retrospective cohort study design so residual confounding a possibility
- Variable time to follow up K+ level

Conclusion

- Oral SPS therapy reduced serum K+ 0.14 mmol/L more than control (6 to 24 hrs post dose)
- No dose-response relationship was observed
- Prospective RCTs would be helpful to further evaluate the benefit of SPS