Should we be moving away from Kayexalate® (Sodium Polystyrene Sulfonate)?

Shermaine Ngo, LMPS Pharmacy Resident
Preceptor: Joanie Tulloch, Emergency Medicine Rotation
May 2017
Learning Objectives

• Describe the evidence supporting efficacy of sodium polystyrene sulfonate
• List the safety concerns for sodium polystyrene sulfonate
• Describe an approach to deciding who should or should not be using sodium polystyrene sulfonate
Background
Hyperkalemia

**Definition:** serum $K^+$ level $\geq 5.5$ mmol/L

**Severe:** $K^+ > 6.5$ mmol/L or $K^+ > 6$ mmol/L + ECG changes/sxs

**Causes:**
- Impaired renal excretion of $K^+$
  - acute/chronic renal failure
- Drugs
  - ACEI/ARB
  - Aldosterone antagonists
  - NSAIDs

**Complications:**
- **Cardiac** conduction abnormalities
  - Ventricular fibrillation
  - Bradyarrhythmia
  - Sinus arrest
  - Asystole
- **Muscle** weakness or paralysis
- Death

Pharmacist’s Letter: Vetassa (Patiromer) and Management of Hyperkalemia

Dynamed: Hyperkalemia [cited 2017 May]
Goals of Therapy

- Prevent mortality
- Prevent complications of hyperkalemia
- Normalize serum K⁺ levels
- Prevent hypokalemia with treatment
- Minimize adverse drug reactions
Treatment Strategies

• Identify and remove cause (e.g. hypovolemia, drugs)

• Protect and stabilize myocardium against hyperkalemia (when there is ECG evidence of cardiotoxicity)
  – Calcium gluconate

• Shift K\(^+\) intracellularly
  – Insulin and Glucose
  – \(\beta_2\)-adrenergic agonists

• Remove K\(^+\) from the body
  – Sodium Polystyrene Sulfonate
  – Loop diuretics
  – Dialysis
**Sodium Polystrene Sulfonate (SPS)**

- **Brand Names:** Kayexalate®, Solystat®
- **Indication:** Hyperkalemia
- **Mechanism:** cation-exchange resin
  - Exchanges Na+ ions for K+ ions in the intestine
- **Doses:** 15g PO 1-4x/day, 30-50g PR q6h
- **Costs:** $3 per 15g (powder), $10 per 15g (suspension)
- **SEs:**
  - GI: anorexia, constipation, diarrhea, nausea, vomiting
  - LYTES: ↓Ca, ↓K, ↓Mg, ↑Na
- **Pharmacokinetics:**
  - Onset: 2 – 24 hours
  - Absorption: None

Lexicomp Monograph: Sodium Polystyrene Sulfonate
Monograph: Kayexalate ®
Approval of SPS

- Approved in 1958
  - For treatment of hyperkalemia
- Approved in Canada since 1961

Efficacy – Scherr, et al. (1961)

Management of Hyperkalemia with a Cation-Exchange Resin

Lawrence Scherr, M.D. †, David A. Ogden, M.D. †, Allen W. Mead, M.D., Norton Spritz, M.D. §, and Albert L. Rubin, M.D. ¶

<table>
<thead>
<tr>
<th>P</th>
<th>(N = 32) acute or chronic renal disease with serum K+ between 4.2-9.2 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>20 to 60g PO SPS or 10-40g PR SPS (with no sorbitol) • All had potassium-restricted diets</td>
</tr>
<tr>
<td>C</td>
<td>• No restrictions on other hyperkalemic treatments (e.g. Insulin/glucose, sodium bicarbonate)</td>
</tr>
<tr>
<td>O</td>
<td>After 24 hrs, mean ↓ in serum K+ • PO: 0.9 ± 0.1 mmol/L • PR: 0.8 mmol/L</td>
</tr>
</tbody>
</table>

Efficacy – Flinn, et al. (1961)

Treatment of the Oliguric Patient with a New Sodium-Exchange Resin and Sorbitol — A Preliminary Report

Robert B. Flinn, M.D.†, John P. Merrill, M.D.‡, and Walter R. Welzant, M.D.§

| P | (N = 10) oliguric pts
  • serum K+ between 6-7.3 mmol/L
  • all pts received 500-700mL of fluid daily |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Group 1: 5 - 15g SPS with 70% sorbitol QID x 5 days</td>
</tr>
<tr>
<td></td>
<td>Group 2: 200 mL enema with 40g SPS and 25% sorbitol daily x 5 days</td>
</tr>
<tr>
<td>C</td>
<td>Group 3: 10-20mL of 70% sorbitol syrup orally q2h until a loose bowel movement was produced daily x 5 days</td>
</tr>
</tbody>
</table>
| O | Day 5: mean serum K⁺ - Group 1: 5.2 mmol/L, Group 3: 4.6 mmol/L
  “Serum K+ showed similar reductions with combo tx vs. sorbitol alone”
  **Authors’ conclusion:** SPS with sorbitol was effective for treating hyperkalemia in oliguric patients |
# Efficacy – Mistry, et al. (2016)

## Evaluation of Sodium Polystyrene Sulfonate Dosing Strategies in the Inpatient Management of Hyperkalemia

Miilen Mistry, BScPhm, ACPR\(^1,2\), Amanda Shea, BSP, ACPR\(^3\), Pierre Giguère, BPharm, MSc\(^3\), and My-Linh Nguyen, BScPhm, ACPR\(^3\)

<table>
<thead>
<tr>
<th>D</th>
<th>Retrospective Chart Review</th>
</tr>
</thead>
</table>
| P | (N = 118) Adults admitted to the Ottawa Hospital who had received any dose of SPS (Jan 1, 2010 – Mar 23, 2014)  
Excluded:  
• concomitant therapy for treatment of hyperkalemia (except loop diuretics)  
• received > 2L of IV fluids |
| I | • PO 15g, 30g, 60g SPS (no sorbitol)  
• PR 30g SPS (no sorbitol) |
| O | **Primary:** Δ in serum K+ level  
**Secondary:**  
• Proportion remaining hyperkalemia  
• Proportion with post-dose hypokalemia |
Results

Efficacy:
• Dose-related ↓ in K+
• ↓ % of patients remaining hyperkalemic with ↑ doses
  – All patients receiving PR doses remained hyperkalemic

Safety:
• No patients experienced post-dose hypokalemia

PR 30g: ↓ 0.22 mmol/L
Efficacy – Batterink, et al. (2015)

Effectiveness of Sodium Polystyrene Sulfonate for Short-Term Treatment of Hyperkalemia

Josh Batterink, Jane Lin, Sarah Hin Mui Au-Yeung, and Tara Cessford

<table>
<thead>
<tr>
<th>D</th>
<th>Retrospective observational study</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>(N=138) Adults admitted to the internal medicine service of St Paul’s Hospital (Jan 2011 – May 2012) • K+ level between 5.0 and 5.9 mmol/L during hospital stay</td>
</tr>
<tr>
<td></td>
<td><strong>Exclusion</strong>: chronic or acute renal failure, recent changes in medication (incl. Initiation/discontination of insulin/dextrose, high-dose SABA, loop diuretics) or diet that would affect serum K+ levels</td>
</tr>
<tr>
<td>I</td>
<td>(N = 66) Treatment with a dose of oral SPS (contains sorbitol)</td>
</tr>
<tr>
<td>C</td>
<td>(N = 72) No treatment</td>
</tr>
<tr>
<td>O</td>
<td>• Mean Δ in serum K+ (6-24 hrs after the index potassium measurement)</td>
</tr>
</tbody>
</table>

Can J Hosp Pharm. 2015;68(4):296-303
Doses in Treatment Group

N = 66

<table>
<thead>
<tr>
<th>Doses</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 g</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>15 g</td>
<td>32 (48)</td>
</tr>
<tr>
<td>30 g</td>
<td>31 (47)</td>
</tr>
<tr>
<td>45 g</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>60 g</td>
<td>1 (1.5)</td>
</tr>
</tbody>
</table>
Results

Efficacy:

• Δ in serum K+ (mmol/L, mean ± SD):

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.58 ± 0.39</td>
<td>-0.44 ± 0.29</td>
<td>0.14</td>
<td>p = 0.036</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SPS 15g</th>
<th>SPS 30g</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.51 ± 0.38</td>
<td>-0.66 ± 0.40</td>
<td>0.15</td>
<td>p = 0.13</td>
</tr>
</tbody>
</table>

Safety:

• Screened for documented GI adverse events
  – 1 patient in treatment group had a documented nonfatal obstruction, unlikely related to SPS
Summary of Efficacy

• Efficacy with ↓ in serum $K^+$ levels
  – Supported by weak evidence
    • *Limitations*: non-randomized trials, small sample size, no control group, potential confounding factors
  – Lacking evidence on clinical outcomes
• $K^+$ reduction
  – ↓ 0.4 mmol/L$^{15gPO}$ to 0.9 mmol/L$^{60gPO}$
  – In mild hyperkalemia: difference of 0.14 mmol/L vs. no tx
  – Questionable clinical significance
  – Suggests oral formulations are more efficacious than rectal
Safety
Formulations

• When SPS first came onto market...
  – Suspension in water

• Safety concerns:
  – Constipation
  – Life-threatening intestinal impaction

• Sorbitol added to ↓ these safety concerns and ↑ stool 
  $K^+$ excretion

Gastroenterology 108: 752–760, 1995
FDA Warning

• Intestinal Necrosis:
  – Cases of intestinal necrosis...bleeding, ischemic colitis, perforation...have been reported in association with Kayexalate use
  – Majority of these cases reported the concomitant use of sorbitol

• Concomitant use of sorbitol is not recommended
  – Warning excludes pre-mixed suspension with 33% sorbitol
Is SPS blame-free?

• Proposed mechanism for SPS
  – Concretions of sodium polystyrene crystals adhere to mucosal surface ➔ direct injury
Multiple esophageal biopsies in this patient demonstrated only mucosal necrosis with Kayexalate crystals (arrows) in the inflammatory exudates.

Kayexalate injury (stomach)—erosive gastritis with angulated, basophilic crystal with mosaic pattern.

Human Pathology (2007) 38, 527 – 536
Availability

• Sodium Polystyrene Sulfonate:
  – Powder (no sorbitol)
  – Suspension (23.5% sorbitol)

Kayexalate ® - Sanofi-aventis Canada monograph
Rexall – Prescription Drugs: Kayexalate [cited 2017 May 27]
Clinical Question
## PICO

<table>
<thead>
<tr>
<th>P</th>
<th>Patients treated for hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Sodium Polystyrene Sulfonate</td>
</tr>
<tr>
<td>C</td>
<td>Placebo</td>
</tr>
<tr>
<td>O</td>
<td>Safety:</td>
</tr>
<tr>
<td></td>
<td>• Intestinal necrosis</td>
</tr>
<tr>
<td></td>
<td>• Gastrointestinal adverse events</td>
</tr>
<tr>
<td></td>
<td>• Mortality</td>
</tr>
</tbody>
</table>
## Search Strategy Results

<table>
<thead>
<tr>
<th>Database</th>
<th>Pubmed, Embase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Search Terms</strong></td>
<td>(sodium polystyrene sulfonate) OR (kayexalate) AND (gastrointestinal) OR (intestinal) OR (necrosis) OR (colon)</td>
</tr>
<tr>
<td><strong>Limits</strong></td>
<td>Humans, English, Available online</td>
</tr>
</tbody>
</table>
| **Results**    | • 1 Systematic Review  
                  • 6 Retrospective Studies  
                  • 2 Reviews  
                  • 31 Case Reports |
Gastrointestinal Adverse Events with Sodium Polystyrene Sulfonate (Kayexalate) Use: A Systematic Review

Ziv Harel, MD, MSc,a,b Shai Harel, MD, MS,a Prakesh S. Shah, MD, MSc,c,d,e Ron Wald, MDCM, MPH,a,b Jeffrey Perl, MD, SM,a,b Chaim M. Bell, MD, PhDb,d,e

aDivision of Nephrology, St Michael’s Hospital, University of Toronto, Ontario, Canada; bDepartment of Medicine and Keenan Research Centre, Li Ka Shing Knowledge Institute of St Michael’s Hospital, University of Toronto, Ontario, Canada; cDepartment of Pediatrics, University of Toronto, Ontario, Canada; dDepartment of Pediatrics, Mount Sinai Hospital, Toronto, Ontario, Canada; eDepartment of Health Policy, Management and Evaluation, University of Toronto, Ontario, Canada.
Harel, et al. (2013)

<table>
<thead>
<tr>
<th>Design</th>
<th>Systematic Review</th>
</tr>
</thead>
</table>
| Databases            | • 1948 to July 2011 (MEDLINE), 1980 to July 2011 (EMBASE), Cochrane Central Register of Controlled Trials (1993 to July 2011)  
  • Bibliographies of identified articles, websites of relevant drug agencies, professional associations in United States and Canada, Google scholar |
| Inclusion            | • Case reports of gastrointestinal adverse events (i.e. unfavourable or harmful consequence involving the gastrointestinal tract) associated with SPS |
| Exclusion            | • Patients < 18 years old  
  • Patients with normal endoscopic/histologic findings upon investigation  
  • Cases with a causality criteria of unlikely, conditional/unclassified, or unaccessible/unclassifiable according to the WHO causality assessment  
  • Case-series with missing information that could not be obtained from authors |
| Results              | 30 Reports describing:  
  • 58 cases (41 preparations with sorbitol, 17 without sorbitol) |
Patient Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age, years - mean ± SD</td>
<td>58 ± 17</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>29 (50)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Co-morbidities, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Kidney Disease</td>
<td>15 (26)</td>
</tr>
<tr>
<td>ESRD requiring dialysis</td>
<td>26 (45)</td>
</tr>
<tr>
<td>Prior solid organ transplant</td>
<td>9 (16)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current hospitalization, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative</td>
<td>16 (28)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>12 (21)</td>
</tr>
</tbody>
</table>

**Risk factors for GI AEs:**

- 71% – history of kidney disease
- 9% – admitting diagnosis for renal transplantation
- 16% – history of solid organ transplant
- 28% – post-operative
**SPS Treatment**

- **Majority of cases:**
  - Treatment of acute hyperkalemia
  - With concomitant sorbitol
  - By oral route

- **# of doses**
  - Not specified for 31% of cases
  - Most common: multiple dose

- **Dose of SPS**
  - Not specified in 34% of cases
  - Range: 15 g – 170 g

- **Sorbitol concentration**
  - 3 cases with 20% sorbitol
  - 1 case with 70% sorbitol

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<table>
<thead>
<tr>
<th>Indication, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hyperkalemia</td>
<td>51 (88%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># Doses, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose*</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Multiple dose*</td>
<td>28 (48)</td>
</tr>
<tr>
<td>Chronic doses</td>
<td>7 (12)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral route</td>
<td>58 (77)</td>
</tr>
<tr>
<td>Rectal route</td>
<td>15 (20)</td>
</tr>
<tr>
<td>Nasogastric</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Concomitant sorbitol</td>
<td>41 (71)</td>
</tr>
</tbody>
</table>

*A total of 33 cases reported single vs multiple doses*
Results

Non-chronic doses:
Time to symptoms (after 1st dose), in days, median (IQR) 2 (<1-5)

<table>
<thead>
<tr>
<th>Presenting symptoms, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain or tenderness</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td>Blood per rectum</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>GI involvement of injury, n (%)</td>
</tr>
<tr>
<td>Esophagus</td>
</tr>
<tr>
<td>Stomach</td>
</tr>
<tr>
<td>Small bowel</td>
</tr>
<tr>
<td>Cecum</td>
</tr>
<tr>
<td>Colon</td>
</tr>
<tr>
<td>Sigmoid/rectum/anus</td>
</tr>
</tbody>
</table>

- Treatment of acute hyperkalemia
  - 50% of cases: within 24 hours to 5 days
- Presenting symptoms
  - Most common: abdominal pain or tenderness
- Location of injury
  - Most common: lower GI tract
Results, cont.

- Histopathology of injury:
  - Most common:
    - Necrosis
    - Ulceration
  - SPS crystals commonly found in injured areas of GI tract

- Overall mortality rate: 33%
  - 94% of patients who died had colonic necrosis on biopsy

<table>
<thead>
<tr>
<th>Histopathology of injury, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrosis</td>
<td>36 (62)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>28 (48)</td>
</tr>
<tr>
<td>Perforation</td>
<td>5 (9)</td>
</tr>
<tr>
<td>SPS crystals</td>
<td>52 (90)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>33 (57)</td>
</tr>
<tr>
<td>Death</td>
<td>19 (33)</td>
</tr>
<tr>
<td>Not reported</td>
<td>6 (10)</td>
</tr>
</tbody>
</table>
# SPS with sorbitol vs. without sorbitol

<table>
<thead>
<tr>
<th></th>
<th>SPS + sorbitol (N = 41)</th>
<th>SPS - sorbitol (N = 17)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose*</td>
<td>4 (10)</td>
<td>1 (6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Chronic dose</td>
<td>0 (0)</td>
<td>7 (41)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Time to sxs, median (IQR) days</td>
<td>1.5 (&lt;1-3)</td>
<td>5 (&lt;1-25)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

**Histopathology of injury, n (%)**

<table>
<thead>
<tr>
<th></th>
<th>SPS + sorbitol (N = 41)</th>
<th>SPS - sorbitol (N = 17)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrosis</td>
<td>30 (73)</td>
<td>7 (41)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ulceration</td>
<td>12 (29)</td>
<td>9 (53)</td>
<td>0.09</td>
</tr>
<tr>
<td>Perforation</td>
<td>3 (7)</td>
<td>2 (13)</td>
<td>0.62</td>
</tr>
<tr>
<td>SPS crystals</td>
<td>38 (93)</td>
<td>14 (82)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**Outcome, n (%)**

<table>
<thead>
<tr>
<th></th>
<th>SPS + sorbitol (N = 41)</th>
<th>SPS - sorbitol (N = 17)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>22 (54)</td>
<td>11 (65)</td>
<td>0.43</td>
</tr>
<tr>
<td>Death</td>
<td>15 (36)</td>
<td>4 (24)</td>
<td>0.33</td>
</tr>
<tr>
<td>Not reported</td>
<td>4 (10)</td>
<td>2 (12)</td>
<td>1</td>
</tr>
</tbody>
</table>

- **Use of SPS without sorbitol**
  - More likely for chronic treatment of hyperkalemia
  - Wider IQR for time to symptoms for non-chronic doses

- **Use of SPS with sorbitol**
  - More likely to present with necrosis
Systematic Review’s Conclusion

• “sodium polystyrene sulfonate use, with and without sorbitol, may be associated with fatal gastrointestinal injury”
• “Although the risk to an individual patient may not be high, the widespread use of this medication may be exposing a large population to potential risk”
• “Until [rigorous assessment of optimal strategy, both in terms of safety and efficacy], physicians must be cognizant of the risk of these adverse events when prescribing sodium polystyrene sulfonate...”
Systematic Review Critique

STRENGTHS

• Search: extensive, multiple relevant databases
  – Published and unpublished

• Eligibility criteria: utilized WHO-UMC criteria for causality assessment
  – Included: certain, probable/likely and possible cases

• Compared SPS with and without sorbitol

LIMITATIONS

• Case reports and series
  – Missing information
  – Limited generalizability

• All cases
  – Possible causality: “Event with reasonable time relationship to drug intake; could also be explained by disease or other drugs”
Summary

• Suggests association of SPS with severe gastrointestinal adverse events
  – Majority of patients had risk factors for GI adverse events associated with SPS

• Cases reported with:
  – Single and *multiple* doses
  – *Acute* and chronic use
  – SPS *with* and without sorbitol
  – Upper and *lower* gastrointestinal injury
Original Investigation

Association of Prescription of Oral Sodium Polystyrene Sulfonate With Sorbitol in an Inpatient Setting With Colonic Necrosis: A Retrospective Cohort Study

Maura A. Watson, DO, MPH,¹ Thomas P. Baker, MD,² Annie Nguyen, PharmD,¹ Mary E. Sebastianelli, RN,³ Heather L. Stewart, MS,² David K. Oliver, RN,¹ Kevin C. Abbott, MD, MPH,¹ and Christina M. Yuan, MD¹
### Watson, et al. (2012)

| D | Retrospective cohort study (Sept 1, 2001 – Oct 31, 2010)  
|  | • Searched an anatomic pathology database for colonic tissue diagnoses and descriptions |
| P | Adults who received an outpatient or inpatient prescription at a tertiary medical center associated pharmacy |
| I | (N = 2,194 inpatients, N = 850 outpatients) SPS prescription |
| C | (N = 121,197) Prescription other than SPS |
| O | Tissue-confirmed diagnosis of colonic necrosis  
|  | • considered SPS-associated if SPS was prescribed 30 or fewer days before tissue accession date |
Results

- 98% – SPS with 33% sorbitol oral suspension
- Out-patient cases of colonic necrosis: Ø
- In-patient cases of colonic necrosis: 91

<table>
<thead>
<tr>
<th></th>
<th>SPS Rx</th>
<th>No SPS Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonic necrosis diagnosis</td>
<td>13</td>
<td>69</td>
</tr>
<tr>
<td>SPS within 30 days</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

- **3 cases** with colonic necrosis associated with SPS
  - Median dose: 45 (30-60g/d)

- 9-year cumulative incidence **with SPS**: 0.14% (0.03-0.40)
- 9-year cumulative incidence **without SPS**: 0.065% (0.052-0.081)
Study’s Conclusion

“Our results indicate that SPS-associated colonic necrosis risk is small and not significantly greater than background rate of colonic necrosis.”

- NNH = 1,395 (95% CI: 298-5100)
Trial Critique

STRENGTHS

• Methodology:
  – Substantial duration of 9 years
  – Large cohort size

• Sub-group analysis

• Objective outcome assessment
  – Tissue biopsies

LIMITATIONS

• Retrospective design
  – Missing information (dose, duration)
  – Confounding factors
  – ?Compliance of out-patients

• Limited generalizability
  – Single center

• Outcomes
  – Tissue biopsies
  – ?closer monitoring for in-patients (risk of detection bias)
  – Determination of association (prescription 30 days prior to biopsy)
Summary

• Sodium Polystyrene Sulfonate with 33% sorbitol associated with a low incidence of biopsy-confirmed colonic necrosis
  – 9-year cumulative incidence of: 0.14%
  ➔ 0.59% (incl. 10 cases with SPS Rx “not associated” with SPS)
  – Does not capture upper GI injury, ulcerations and other GI complications

dx.doi.org/10.1016/j.amjmed.2013.05.010
Canada Vigilance Adverse Reaction Database

- **Brand Name/Active Ingredient:** polystyrene sulfonate
- **Initial Received Date:** 1965-01-01 to 2016-12-31
- **Results:** 36 reports
Results – Gastrointestinal AEs

• **Reactions** (N = 36):
  – GI mucosal necrosis: 6 cases
  – Diarrhea, constipation, vomiting: 4 cases
  – Intestinal ischemia, perforation and crystal deposits: 1 case
  – Microscopic colitis: 1 case
  – GI tract irritation: 1 case

• **Doses**: 15 – 50 g
## Summary

<table>
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<tr>
<th>Goals of Therapy</th>
<th>Evidence</th>
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<tbody>
<tr>
<td><strong>EFFICACY</strong></td>
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<tr>
<td>Mortality associated with hyperkalemia</td>
<td>✗ Not shown to prevent mortality or complications of hyperkalemia</td>
</tr>
<tr>
<td>Clinical complications</td>
<td></td>
</tr>
</tbody>
</table>
| ↓ serum K+ levels         | ↓ 0.4 mmol/L\(^{15g PO}\) to 0.9 mmol/L\(^{60g PO}\)  
  • SS difference of 0.14 mmol/L\(^{15-30g PO vs.no tx}\) |
| **SAFETY**                |          |
| Drug-induced hypokalemia  | Low risk of hypokalemia |
| Gastrointestinal Adverse Events | Low risk of severe GI adverse events  
    • risks appear to be higher with combination with sorbitol  
    • unclear if risks higher due to higher use of combination  
    *Lexicomp Monograph*: <1%, gastrointestinal hemorrhage, gastrointestinal ulcer, intestinal necrosis, intestinal perforation, ischemic colitis  
    • Limited evidence with long-term use of SPS |
| Mortality associated with SPS | Low risk of mortality associated with SPS |
Who should we not be using SPS in?
Risk Factors for serious GI AEs

- Reduced GI motility
  - Drugs (e.g. Opiates)

- Any post-operative patients *until* resumption of normal bowel function

- Obstructive bowel disease

- Ileus

- Underlying bowel disease (e.g. ulcerative colitis)

- At risk for developing constipation or impaction

- Renal transplant patients

- Renal insufficiency/failure
  - Possible mechanism:
    \[ \text{↑ renin levels predispose pt to non-occlusive mesenteric ischemia via angiotensin-mediated vasoconstriction} \]

- Solid organ transplant
  - Especially patients with recent history

- Hypovolemia

- Critically ill or sepsis

Contraindications

Uptodate: treatment and prevention of hyperkalemia in adults

Management of Hyperkalemia

If ECG Δs associated with hyperkalemia:

- **Calcium gluconate 1g IV**

For potassium shift into cells:

- **Insulin regular 10units IV + Dextrose 50% 25g (50mL)** $\downarrow 0.5$-$1.2$meq/L
- **Nebulized or inhaled salbutamol** $\downarrow 0.5$-$1.5$meq/L

For potassium removal:

- **Loop diuretics (Furosemide 20-40mg IV)**
- **Sodium Polystyrene Sulfonate**
  - Consider spacing oral medications by at least 6 hours apart
  - Monitor: abdominal pain/tenderness, nausea/vomiting, diarrhea, blood per rectum
- **Dialysis**

Uptodate: Treatment and prevention of hyperkalemia in adults
How about Calcium Polystyrene Sulfonate?

- **Brand Name:** Calcium Resonium®
- **Formulations:** Powder for suspension (no sorbitol)
- **Safety:**
  - *Lexicomp monograph:* <1%, Bezoar formation, fecal impaction, GI necrosis, GI obstruction, GI ulcer, ischemic colitis, mesenteric ischemia, rectal, hemorrhage, intestinal stenosis
  - Several case reports suggesting association between calcium polystyrene sulfonate, alone and serious gastrointestinal AEs such as colonic necrosis
- **Similar pre-cautions and contraindications**
- **Costs:** $6 per 15 g dose

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