Recent Advances in the Management of Hyperkalemia

The Role of Newer Treatment Strategies to Improve Patient Outcomes

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Disclosures

Biff F. Palmer, MD, has no financial interests/relationships or affiliations in relation to this activity.
Hyperkalemia 101
The Burden and Current Standards of Care
Hyperkalemia is a serious medical problem. Patients are usually asymptomatic and do not realize they have it. Hyperkalemia may lead to:

1. Life-threatening arrhythmias
2. Sudden cardiac death

References:
Variability in What Defines “Hyperkalemia”¹⁻³

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum K⁺, mEq/L</th>
<th>Risks</th>
</tr>
</thead>
</table>
| Mild      | >5.0-5.9        | • ↑ risk of renal AE  
               |                  | • ↑ mortality with chronic illnesses patients                      |
| Moderate  | 6.0-7.0         | • Cardiac arrhythmias                                               |
| Severe    | >7.0            | • Cardiac arrhythmias                                               |

Serum K⁺ levels of 5.0, 5.5, or 6.0 mEq/L are commonly used cutoffs for ULN

K⁺: potassium; ULN: upper limit of normal.
Prevalence of Hyperkalemia

**General population**
Prevalence is 2% to 3% in the general population.\(^1\)

**All hospitalized patients**
- 1% to 10% depending on the definition of hyperkalemia
- 8% to 10% when hyperkalemia is defined as ≥6 mmol/L

**Patients with CKD**
Prevalence in patients with stage ≥3 CKD ranges from 5% to 50% and increases as kidney function declines.\(^2\)

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CKD: chronic kidney disease.
Hyperkalemia: Effect on Healthcare Costs¹,²

- Average Medicare length of stay was 3.2 days; mean charges of $24,085 per stay
- One-third of patients were discharged to another short-term hospital, institution, or home healthcare
- In 2011, estimated total annual hospital charges for Medicare admissions with hyperkalemia as primary diagnosis were ~$697 million

What Causes Elevated Serum K⁺?¹,²

**K⁺ redistribution**
- Strenuous exercise
- Burns, crush injury
- Hemolysis
- Tumor lysis syndrome
- Hyperglycemia

**Exogenous sources of K⁺**
- Medications
- Blood
- Diet and K⁺ supplements
- Pseudohyperkalemia

**Reduced K⁺ excretion**
- Impaired renal function
- Diabetes mellitus
- Heart failure
- Obstructive uropathy
- Hypoaldosteronism
- RAAS inhibitors

RAAS: renin–angiotensin–aldosterone system.
# Medications Associated With Hyperkalemia

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Mechanism</th>
<th>Example(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEis</td>
<td>Inhibit conversion of angiotensin I to angiotensin II</td>
<td>Captopril, lisinopril, etc</td>
</tr>
<tr>
<td>ARBs</td>
<td>Inhibit activation of angiotensin II receptor by angiotensin II</td>
<td>Losartan, irbesartan, etc</td>
</tr>
<tr>
<td>Aldosterone antagonists</td>
<td>Block aldosterone receptor activation</td>
<td>Spironolactone, eplerenone</td>
</tr>
<tr>
<td>β-adrenergic receptor blockers</td>
<td>Inhibit renin release</td>
<td>Propranolol, metoprolol, atenolol</td>
</tr>
<tr>
<td>Digitalis glycoside</td>
<td>Inhibits Na⁺-K⁺-ATPase; necessary for K⁺ secretion</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Heparin</td>
<td>Reduces production of aldosterone</td>
<td>Heparin sodium</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Inhibit synthesis of prostaglandin E and prostacyclin, inhibiting renin release</td>
<td>Ibuprofen, etc</td>
</tr>
<tr>
<td>K⁺-sparing diuretics</td>
<td>Block collecting duct apical Na⁺ channel, decreasing gradient for K⁺ secretion</td>
<td>Amiloride, triamterene</td>
</tr>
<tr>
<td>Other</td>
<td>Block collecting duct apical Na⁺ channel, decreasing gradient for K⁺ secretion</td>
<td>Trimethoprim, pentamidine</td>
</tr>
</tbody>
</table>

ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; NSAID: nonsteroidal anti-inflammatory drug.

Populations at Risk\(^1,2\)

- **Advanced Stage of CKD (Stage ≥3)**: Reduced excretion
- **Aged >65 Years**
  - Hyporeninemic hypoaldosteronism
- **Diabetes**
  - Renin deficiency in diabetic nephropathy
- **Heart Failure**
  - Decreased delivery of Na\(^+\) to the distal nephron
- **Taking Certain Medications**
  - ACEis, ARBs, NSAIDs, etc

Na\(^+\): sodium.
Adjusted Mortality by Serum K$^+$ Level, Age, and Comorbid Illness Status$^1$

Increases in mortality remained after adjustments for demographic characteristics and comorbidities.

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$^a$ Shading represents 95% confidence limits.

All-Cause Mortality Associated With Hyperkalemia

Spline analysis adjusted for covariates, showing serum K$^+$ as a continuous variable with all-cause mortality over the distribution of K$^+$ values (2.5-8.0 mEq/L) in heart failure, CKD, DM, and combined cohort compared with controls.

EMR data analysis from geographically diverse US population (N = 911,698) receiving medical care; relationship with mortality over 18-month period.

Hyperkalemia: Typically Occurs in Patients With CKD

Real-World Observational Studies

<table>
<thead>
<tr>
<th>Patient Population (eGFR, mL/min/1.73m²)</th>
<th>Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CKD</td>
<td>8.9</td>
</tr>
<tr>
<td>Stage 3 (30-59)</td>
<td>20.7</td>
</tr>
<tr>
<td>Stage 4 (15-29)</td>
<td>42.1</td>
</tr>
<tr>
<td>Stage 5 (&lt;15)</td>
<td>56.7</td>
</tr>
</tbody>
</table>

Veteran's Health Administration National Cohort (N = 245,808)

Incidence per 100 Patient-Months

- No CKD
  - No RAASi: 1.77
  - RAASi: 7.67

- CKD
  - No RAASi: 8.22
  - RAASi: 2.30

*P < .0001 vs no CKD.
Association Between MRA Therapy and Risk of Readmission for Hyperkalemia

Hyperkalemia Readmission Among Patients With HFrEF

Cumulative Incidence, %

Days After Discharge

MRA Therapy
- No
- Yes

Gray Test $P < .001$

HFrEF: heart failure with reduced ejection fraction; MRA: mineralocorticoid receptor antagonists.
Hyperkalemia: Causes and Clinical Manifestation

Development of hyperkalemia requires a defect in one or more of the mechanisms that maintain $K^+$ homeostasis

- Decreased renal elimination (the most common cause)
- Increased $K^+$ load (dietary)
- Intracellular to extracellular shifts (uncommon)

Hyperkalemia is often asymptomatic and discovered on routine laboratory tests

Clinical manifestations of acute and chronic hyperkalemia are related to neuromuscular changes and cardiac arrhythmias

- Muscular weakness or flaccid paralysis
- Ileus
- Characteristic ECG changes

Serum K⁺ Levels and Associated ECG Changes

<table>
<thead>
<tr>
<th>Serum K⁺, mEq/L</th>
<th>Major ECG Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5 to 6.5</td>
<td>Tall peaked T waves</td>
</tr>
<tr>
<td>6.5 to 7.5</td>
<td>Loss of P waves</td>
</tr>
<tr>
<td>7 to 8</td>
<td>Widened QRS complexes</td>
</tr>
<tr>
<td>8 to 10</td>
<td>Sine wave, ventricular arrhythmias, asystole</td>
</tr>
</tbody>
</table>

Conventional Options for Hyperkalemia Management

- Membrane stabilization
- K⁺ redistribution

**Insulin**
- K⁺ elimination
- Removal/reduction of drugs that increases serum K⁺

**β2-adrenergic agonists**

**Ca²⁺ gluconate or chloride salt**

**Dialysis**

**RAASi reduction**

**Loop diuretics**

**Sodium bicarbonate**

**SPS**

**Low K⁺ diet**

**Emergent**

**Intermediate**

**Maintenance**

Treatment options for hyperkalemia

RAASi: RAAS inhibitor; SPS: sodium polystyrene sulfonate.
Standard Treatment Options for Hyperkalemia Are Limited

<table>
<thead>
<tr>
<th>Acute Therapies&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td>• Do not remove excess K&lt;sup&gt;+&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary K&lt;sup&gt;+&lt;/sup&gt; Restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>• K&lt;sup&gt;+&lt;/sup&gt; is common ingredient in many foods</td>
</tr>
<tr>
<td>• Limits healthy food choices</td>
</tr>
<tr>
<td>• Met by nonadherence</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sodium Polystyrene Sulfonate (SPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Uncertain efficacy (no rigorous clinical trials)</td>
</tr>
<tr>
<td>• Poor tolerability</td>
</tr>
<tr>
<td>• High rate of serious intestinal toxicity</td>
</tr>
<tr>
<td>• May not be effective without sorbitol; however, sorbitol has been reported to cause intestinal complications, including bowel necrosis and perforation in immunocompromised patients</td>
</tr>
</tbody>
</table>

<sup>a</sup> IV calcium, sodium bicarbonate, insulin and dextrose, nebulized β-adrenergic agonists.
## SPS: Warnings and Precautions Highlighted in FDA-Approved Label

<table>
<thead>
<tr>
<th>Approval Date</th>
<th>1958</th>
</tr>
</thead>
</table>
| **Warning**   | Intestinal necrosis, which may be fatal, and other serious GI AEs (bleeding, ischemic colitis, perforation) have been reported in association with SPS use  
  - Concomitant use of sorbitol with SPS has been implicated in cases of colonic intestinal necrosis |
| **Precaution**| SPS exchanges K⁺ for Na⁺, leading to Na⁺ volume overload  
  • Use caution when administering SPS to patients who cannot tolerate even a small increase in Na⁺ loads (eg, severe congestive heart failure, severe hypertension, marked edema) |

SPS Associated With High Risk of Hospitalization for Serious GI Adverse Events


HR = 1.94 (95% CI: 1.10-3.41)
Take-Home Points

Hyperkalemia

- A complex clinical challenge, $K^+$ kills
- Comorbidities (CKD, diabetes, heart failure) place patients at high risk of hyperkalemia
  - In part, because the therapy (ie, RAASi) needed to treat the comorbidities increases the risk of hyperkalemia
- Therapeutic interventions in the ED to manage hyperkalemia aim at
  - Stabilization of cell membrane
  - Shifting $K^+$ intracellularly
  - Removal of $K^+$ from the body
Recent Advances in Hyperkalemia

The Role of Newer Treatment Strategies to Improve Patient Outcomes
# Ideal Attributes of a K⁺ Binder

## Clear and Sustained Efficacy
- Substantially lowers serum K⁺ levels
- Works in diverse populations (CKD, diabetes, heart failure, elderly, and combinations of these)
- Works in a matter of hours and maintains its efficacy long term (months to years)

## Good Tolerability and Long-Term Safety
- Palatable drug with good patient acceptance of dose form
- Compatible with commonly used drugs in target population
- Low AE rates and clear long-term safety
Novel Methods of $K^+$ Elimination

- **Patiromer**
  - FDA approved in 2015

- **Sodium zirconium cyclosilicate (ZS-9)**
  - FDA approved in 2018

**Limitation of use:** These agents should not be used as emergency treatment for life-threatening hyperkalemia due to delayed onset of action.
Patiromer

- Orally administered
- Homogenous, spherical beads
- Nonabsorbed, cation exchange polymer that contains a Ca\(^{2+}\) counterion
- Increases fecal K\(^+\) excretion through binding of K\(^+\) in the GI tract, predominantly in lumen of colon, where concentration of K\(^+\) is highest
  - Binds K\(^+\) in exchange for Ca\(^{2+}\)

Ca\(^{2+}\): calcium.
OPAL-HK: Change in Serum K⁺ With Patiromer During Initial Period

- Secondary efficacy endpoint: 76% of patients had serum K⁺ in target range (3.8 to <5.1 mEq/L) at week 4

OPAL-HK: Controlling Hyperkalemia With Patiromer Enables Patients to Remain on RAASi Therapy

Randomized Withdrawal Phase Results

- Recurrence of hyperkalemia ($K^+ \geq 5.5$ mEq/L) occurred in 60% of placebo patients vs 15% of patients on patiromer ($P < .001$)

![Bar chart showing the percentage of patients requiring any adjustment of RAASi (down titration or discontinuation) for hyperkalemia at any time during Part B and receiving any dose of a RAASi at the end of Part B.]

AMETHYST-DN: Study Design

Open-label, randomized, dose-ranging, dose titration, 52-week (1-year) study (N = 306)

Patients with normokalemia who have T2DM and CKD with/without hypertension on ACEi, ARB (or both)

Primary endpoint: Mean change in serum K⁺ from baseline to week 4 or before initiation of dose titration

Compliance throughout the entire study ranged from 86.7% to 95.9% across dose groups and strata.
### Adverse Reactions Reported in ≥2% of Patients in Patiromer Clinical Trials

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Patients, % (N = 666)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypomagnesemia (serum Mg$^{2+}$ &lt;1.4 mg/dL)</td>
<td>9.3</td>
</tr>
<tr>
<td>Constipation</td>
<td>7.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.8</td>
</tr>
<tr>
<td>Hypokalemia (serum K$^+$ &lt;3.5 mEq/L)</td>
<td>4.7</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.3</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>2.0</td>
</tr>
<tr>
<td>Flatulence</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Mg$^{2+}$: magnesium.

### Patiromer Warnings and Precautions

<table>
<thead>
<tr>
<th>Approval Date</th>
<th>Precaution</th>
<th>Boxed Warning</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 2015</td>
<td>• Worsening of GI motility</td>
<td>• Patiromer binds to many orally administered medications, which could decrease their absorption and reduce their effectiveness</td>
</tr>
<tr>
<td></td>
<td>• Hypomagnesemia</td>
<td>• Choose patiromer or the other oral medication if adequate dosing separation is not possible</td>
</tr>
<tr>
<td></td>
<td>• Administer other oral medications (ie, metformin, levothyroxine, ciprofloxacin) at least 3 hours before or 3 hours after patiromer²</td>
<td></td>
</tr>
</tbody>
</table>

DIAMOND Study: Patiromer for Management of Hyperkalemia in Patients With Heart Failure Receiving RAASi Therapy

A Phase 3b Multicenter, Double-Blind, Placebo-Controlled Randomized Trial

Key eligibility criteria
- Hospitalization for heart failure (with or without CKD) within 12 months
- HFrEF (LVEF <40%)
- eGFR ≥30 mL/min/1.73m²
- History of current hyperkalemia at screening or history of hyperkalemia in the past year that led to a reduction/discontinuation of RAASi
- N = ~2,400 patients
- Top-line results are expected in 2022

Primary endpoint: time to first occurrence of cardiovascular death or cardiovascular hospitalization

eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction.
Sodium Zirconium Cyclosilicate (ZS-9): Novel First-in-Class Compound Designed to Trap $K^+${1}

- Orally administered, tasteless, odorless
- Non-absorbed, inorganic crystalline zirconium silicate compound
- Exchanges $K^+$ for $H^+$ and $Na^+$ in the intestine
  - High $K^+$ specificity attributable to chemical composition and diameter of the micropores
  - 125 times more selective for $K^+$ compared with SPS

Phase 3 ZS-9: Change in Serum K⁺ During Initial Period

- Normokalemia maintained in patients who received 5 g or 10 g of ZS-9
- K⁺ levels increased to hyperkalemic levels in placebo group
- When ZS-9 was discontinued, hyperkalemia redeveloped within 1 week

Phase 3 ZS-9: Change in Serum K⁺ During Initial Period (Cont’d)¹

Dose-Dependent Serum K⁺ Reduction Over 48 Hours in Patients With Heart Failure on RAASi

a P < .05.
HARMONIZE: Early Effects of ZS-9 on Serum K⁺

- Mean starting K⁺: 5.55 mEq/L
- 0.2-, 0.4-, 0.5-mEq/L K⁺ decline at 1, 2, 4 hours, respectively ($P < .001$)
- Median time to K⁺ normalization: 2.2 hours
- 84% of patients normalized by 24 hours
- 98% of patients normalized by 48 hours

ZS-9 Adverse Reactions\(^1\)

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Patients, % (N = 353)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral edema</td>
<td>7.7</td>
</tr>
<tr>
<td>Edema requiring treatment with diuretics</td>
<td>4.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7.0</td>
</tr>
<tr>
<td>Hypokalemia (serum K(^+) 3.0-3.5 mEq/L)</td>
<td>2.5</td>
</tr>
<tr>
<td>Doubling of serum creatinine</td>
<td>0.7</td>
</tr>
<tr>
<td>GI AEs</td>
<td>&lt;5.0</td>
</tr>
</tbody>
</table>

ZS-005 Study: Long-Term Safety-Efficacy of ZS-9 for Hyperkalemia

Open-Label, Single Arm, Two-Part Phase 3 Study

Key eligibility criteria
- Mean age: 64 years
- Mean eGFR: 47 mL/min/1.73m²
- No dietary/medication restrictions
- 65% of patients were on RAASi

Correction Phase (24-72 hours)
ZS-9 30 g/day
Mean serum K⁺ 4.8 mEq/L
(n = 751)

Maintenance Phase (12 months)
ZS-9 5 g/day, titrated (mean 7.2 g/day)
Mean serum K⁺ 4.7 mEq/L
(n = 746)

Primary endpoint: restoration of normal serum K⁺ values (3.5-5.0 mEq/L) during the correction phase and maintenance of serum K⁺ of 5.1 mEq/L during the maintenance phase

ZS-005 Study: Long-Term Management of Hyperkalemia With ZS-9

- ZS-9 achieved normokalemia during correction phase
- ZS-9 maintained normokalemia without substantial RAASi changes for ≤12 months

# Summary of SPS, Patiromer, and ZS-9

<table>
<thead>
<tr>
<th></th>
<th>SPS</th>
<th>Patiromer</th>
<th>ZS-9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of action</strong></td>
<td>Nonspecific cation binding in exchange for Na⁺</td>
<td>Nonspecific cation binding in exchange for Ca²⁺</td>
<td>Selective K⁺ binding in exchange for Na⁺ and H⁺</td>
</tr>
<tr>
<td><strong>Time to normokalemia</strong></td>
<td>Unconfirmed efficacy</td>
<td>Achieves normokalemia within 48 hours</td>
<td>84% of patients are normokalemic within 24 hours</td>
</tr>
<tr>
<td><strong>Drug–drug interactions</strong></td>
<td>Interactions with antacids, laxatives, digitalis, sorbitol, lithium, and thyroxine</td>
<td>Potential to alter other drug absorption (metformin, levothyroxine, and ciprofloxin); administer 3 hours before or after other medications</td>
<td>Median time to normalization is 2.2 hours³</td>
</tr>
<tr>
<td><strong>Location of K⁺ binding</strong></td>
<td>Colon</td>
<td>Colon</td>
<td>Colon</td>
</tr>
<tr>
<td><strong>Safety/tolerability</strong></td>
<td>Poor tolerability/adherence, associated with colonic necrosis, hypokalemia, electrolyte disturbances, and GI effects</td>
<td>Well tolerated but may cause constipation and possible hypomagnesemia</td>
<td>Well tolerated but may cause edema and mild to moderate GI effects</td>
</tr>
</tbody>
</table>

Transitions of Care

Potential source of error and miscommunication

Issues best avoided by upfront, mutually agreed upon structure and process

Should involve all who might administer care
- Family physicians, emergency physicians
- Hospitalists and internists
- Cardiologists
- Critical care specialists
- Nephrologists
Take-Home Points

Role of Novel Agents in Managing Hyperkalemia

• Both patiromer and ZS-9 are
  – Effective in reducing serum $K^+$ to normokalemic levels in patients with hyperkalemia
  – Well tolerated over 1 year without the risk of bowel necrosis that is associated with SPS
  – Effective and well tolerated in patients with heart failure; enable long-term use of RAASi
• Novel $K^+$-lowering strategies have the potential to improve the clinical management of hyperkalemia
• Preventing and managing hyperkalemia requires a multidisciplinary approach that entails
  – Reducing high-$K^+$ foods
  – Adjusting hyperkalemia-inducing medications
  – Adding medications that reduce hyperkalemia including novel $K^+$ binders
• Long-term monitoring and control can reduce $K^+$-related mortality
Clinical Case

Application of Newer Therapies in a Real-World Setting
Case Presentation: 66-Year-Old Man

History of T2DM, hypertension, and CKD

Presents with generalized weakness, nausea, vomiting, and dyspnea on exertion

Vital signs: heart rate, 100 BPM; BP, 170/110 mmHg; RR, 26 breaths/min; temperature, 35°C

Current Medications
- Hydralazine 100 mg three times a day; isosorbide mononitrate 60 mg once a day; lisinopril 5 mg; furosemide 40 mg twice a day; metoprolol SR 100 mg once a day; atorvastatin 80 mg once a day; insulin glargine 40 U/mL once a day; glimepiride 2 mg once a day
Considerations During Initial Presentation

What is the expected electrolyte abnormality?

What risk factor does this person have for hyperkalemia?
Case Presentation: Physical Examination

- Patient is uncomfortable but awake
- Crackles over the lower third of chest
- S3 on cardiac auscultation
- Generalized edema
- Diabetic with hypertensive retinopathy
Management Considerations

How would you manage the patient now?

What tests do you want to perform?
## Case Presentation: Laboratory Results

### Laboratory Results

- **K^+**: 5.6 mEq/L
- **Creatinine**: 2.2 mg/dL
- **eGFR**: 36 mL/min/1.73m²
- **HbA1c**: 7.8%
- **BNP**: 824
- **ECHO**: Diastolic dysfunction with an EF of 44% (1 month earlier)

- Discussed a low K^+ diet with patient and provided a handout on food to avoid or limit
- Changed diuretic to long-acting torsemide at 20 mg once a day for better BP
- Started patient on patiromer 8.4 g once a day to be taken at breakfast for 2 days for K^+ control, and then increased lisinopril to 20 mg once a day

**BNP**: brain natriuretic peptide; **ECHO**: echocardiogram.
Case Presentation: Next Steps

5 Days Later
- K⁺: 4.9 mEq/L
- Creatinine: 2.2 mg/dL
- eGFR: 35 mL/min/1.73m²
- BP: 140/90 mmHg

Started spironolactone 12.5 mg once a day

1 Week Later
- K⁺: 4.9 mEq/L
- eGFR: 33 mL/min/1.73m²
- Creatinine: 2.4 mg/dL
- BP: 128/80 mmHg (improved)

Patient reported only constipation

4 Months Later
- Repeated ECHO, EF 65%
- K⁺: 4.7 mEq/L
- eGFR: 33 mL/min/1.73m²
- Creatinine: 2.2 mg/dL
- BP: 128/80 mmHg (improved)

Patient had much better physical stamina and no dyspnea or weakness
AMBER Study: Patiromer to Enable Spironolactone Use in Patients With Resistant Hypertension and CKD¹

A Phase 2 Multicenter, Double-Blind, Placebo-Controlled Randomized Trial

Key eligibility criteria

- Age ≥18 years
- eGFR 25 to ≤45 mL/min/1.73m²
- Serum K⁺ 4.3-5.1 mEq/L
- Resistant hypertension: SBP of 135-160 mmHg during screening despite taking ≥3 antihypertensive drugs, including a diuretic, ACEi, or ARB

- Primary endpoint: patients who remained on spironolactone at week 12
- Secondary endpoints: systolic automated office BP at baseline and week 12; change in SBP from baseline

Spironolactone + 
patiromer
(n = 147)

Spironolactone + 
placebo
(n = 148)

AMBER Study: Patiromer to Enable Spironolactone Use in Patients With Resistant Hypertension and CKD (Cont'd)\(^1\)

Patiromer enabled more patients with resistant hypertension and CKD to continue treatment with spironolactone with less hyperkalemia

Predictors of Hyperkalemia Before Starting Therapy Derived From Trials\textsuperscript{1,2}

- eGFR $< 45$ mL/min/1.73m$^2$
- Serum K$^+$ $> 4.5$ mEq/L
- eGFR $< 45$ mL/min/1.73m$^2$ plus serum K$^+$ $> 4.5$ mEq/L

Team-Based Approach: Identifying Patients at Risk for Hyperkalemia

- Know the risk factors and educate the patient
- Slow dose titration of RAASi agents
- Monitor $K^+$ closely when initiating therapy and after each dose adjustment
- Coordinate care
Standard Care for Chronic Hyperkalemia\textsuperscript{1,2}


- Review medication history
- Titrate or discontinue RAASi
- Diuretic therapy
- K\textsuperscript{+} binder therapy
Patient Counseling for Hyperkalemia

- Low K+ diet
- Signs and symptoms of hyperkalemia
- Stay hydrated
- Avoid NSAIDs—for pain, use non-NSAIDs
- Medication adherence with K+ binders
## Low K⁺ Diet Is the First Step in Chronic Management¹,²

### Fruits
- Apricot, raw (2 medium) dried (5 halves)
- Avocado (1/4 whole)
- Banana (1/2 whole)
- Cantaloupe
- Dates (5 whole)
- Dried fruits
- Figs, dried
- Grapefruit juice
- Honeydew
- Kiwi (1 medium)
- Mango (1 medium)
- Nectarine (1 medium)
- Orange (1 medium)
- Orange juice

### Vegetables
- Acorn squash
- Artichoke
- Bamboo shoots
- Baked beans
- Butternut squash
- Refried beans
- Beets, fresh then boiled
- Black beans
- Broccoli, cooked
- Brussels sprouts
- Chinese cabbage
- Carrots, raw
- Dried beans and peas
- Greens, except kale

### Other Foods
- Bran/bran products
- Chocolate (1.5-2 ounce)
- Granola
- Milk, all types (1 cup)
- Molasses (1 tablespoon)
- Nutritional supplements
- Nuts and seeds (1 ounce)
- Peanut butter (2 tablespoons)
- Salt substitutes/lite salt
- Salt-free broth
- Yogurt

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Clinical Take-Home Points

What Can We Do to Prevent Recurrent Hyperkalemia?

- Educate patient about low K⁺ diet
- Use appropriate diuretics for the level of kidney function
- If serum K⁺ >4.8 mEq/L and cannot use RAAS blockade where clearly indicated, use a K⁺ binder in initial low doses to facilitate its use
- Both can be used daily and do not interfere with almost all other agents being given
- Perform routine follow-up with the patient to ensure adherence and access to the drugs
Audience Q&A
Please remember to complete and submit your Post-Test and Evaluation for CME credit.

Missed anything?

Visit us at: www.peerview.com/hyperkalemiaFamily

- Download slides and Practice Aids
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Thank you and have a good day.