Management of Hyperkalemia in Hemodialysis Patients

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Disclosures

• Advisory Board: Relypsa
• Speaker Honoraria: Sanofi Aventis
Case Presentation

- A 69 y/o woman with ESKD 2/2 SLE, on 3x/wk hemodialysis. After finishing HD, she complained of cramps and tingling in her legs and few seconds after collapsed. Her husband called 911, and she was brought to the local hospital. In ED was found to be in ventricular tachycardia. She was treated with 300 mg of amiodarone, and corrected to normal sinus rhythm. While in the ED became unconscious again, and had another episode of VT. She received lidocaine 100 mg IV, and Magnesium IV, and admitted to the ICU.
- She has a known history of QT prolongation, attributed to hydroxychloroquine and fluoxetine.

Labs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Ca</td>
<td>8.3</td>
</tr>
<tr>
<td>Mg</td>
<td>1.5</td>
</tr>
<tr>
<td>Phos</td>
<td>4.1</td>
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<tr>
<td>Albumin</td>
<td>2.0</td>
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[Heart rate monitoring graphs]
Recent history of her dialysate and serum K values are shown below.

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What could have been done to prevent sudden cardiac arrest in this patient?

Outline

- Impact of hyperkalemia and SCD in CKD patients
- Factors affecting potassium balance in HD patients.
- Serum potassium levels and risk in HD patients
- Current Dialytic Strategies to Manage Hyperkalemia
- New Approaches to optimize potassium homeostasis and minimize risk
Outline

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What is the Impact of SCD in CKD?

Annual rates of sudden cardiac death

- ESRD
  - Prevalent 5%
  - Incident (first year) 7%
- Heart Failure
  - 4%
- Pre-Dialysis CKD
- General Population
  - Approx 1.5%
- NoCKD, CKD3-4, CKD5, ESRD-HD

Chan et al. 2011 CJASN
Pun et al. 2009 KI
Conventional CHD-related Risk Factors

ESKD-HD patients

CKD Patients

Cardiomyopathy (Decreased EF)

Arrhythmic Triggers (Ischemia)

Unique CKD-related Risk factors

Conventional CHD-related Risk Factors

Unique CKD-related Risk factors

Abnormal Electrolytes

Autonomic Instability

Dialysis Reactions

Volume shifts

Risk Factors for SCA in CKD

Hyperkalemia is a significant contributor to SCD in preHD CKD

22,009 patients undergoing cardiac catheterization

N=6,181 with eGFR<60

- Relative Risk of Hyperkalemia in CKD 3/4: 3.3 fold higher
- 2-fold increase in risk of SCA with hyperkalemia (no association with hypokalemia); independent of cardiac disease risk factors
- Population attributable SCA risk of Hyperkalemia: 2.5 fold higher in CKD vs GFR>60

Pun et. al. Abstract presented at ASN 2015
Pun et. al. Kidney International Reports 2017
Frequency of Hyperkalemia in the Hemodialysis Population

2001-2006
N=111,651 HD patients

Serum K Concentration (Time-averaged; mEq/L)

Torien K et al. CJASN (2012) 7: 1272-1235

Sudden Death is the Leading Cause of Death in Dialysis Patients

25.3% SCD

USRDS ADR 2014
SCD risk is tied to the dialysis schedule

Mortality and CV events on Days of the Dialysis Week

Foley et. al. NEJM 2011: 365: 1099

High Risks During Intradialytic AND Pre-Dialytic Period

• High risk within 12 hours of dialysis start
• High risk in 12 hours preceding HD over dialysis free weekend

Dialysis = Arrhythmic Trigger

Renal Replacement Therapy: Dialysis

- Principle: Remove solutes in the blood by diffusion across a semi-permeable membrane
What’s good about dialysis?

- “Renal Replacement” Therapy
  - Maintain body composition
    - Removal of Potassium
    - Removal of Salt/Water
    - Remove metabolic waste products and “uremic” toxins

- Risks in Interdialytic Period
  - Hyperkalemia → Arrhythmias
  - Fluid Overload → CHF
  - Uremia

What might be bad about dialysis?

- Overly rapid shifts in:
  - Electrolytes (Potassium)
  - Fluid

- Risks During/After Dialysis treatment
  - HypoK → Arrhythmias
  - Hypotension → Ischemia
Our Goal: Improve CV Outcomes By Reducing HD Risk Exposures

Potentially due to rapid shifts in (or insufficient removal of) potassium

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• Impact of hyperkalemia and SCD in CKD patients
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• Dialysate potassium levels and risk in HD patients
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Determinants of Potassium Homeostasis: Normal

Dietary Intake 120 mEq → GI Secretion 5-10 mEq → Renal Secretion 105-110 meq

ICF 3000 meq → ECF ~70 meq

Acidemia → Alkalemia
Hyperglycemia → Insulin
Beta adrenergic

Determinants of Potassium Homeostasis: CKD5D

Dietary Intake 50-80 mEq → GI Secretion 20-30 mEq

ICF 3000 meq → ECF ~70 meq

Acidemia → Alkalemia
Hyperglycemia → Insulin
Beta adrenergic

Minimal

Determinants of Potassium Homeostasis: CKD5D

- Dietary Intake: 50-80 mEq
- GI Secretion: 20-30 mEq
- Alkalemia
- Hyperglycemia
- Acidemia

ICF: 3000 meq
ECF: ~70 meq

Hemodialysis: 70-100 mEq per treatment = 30-50/day

Dialytic factors involved in potassium removal

- Diffusion: 85%
  - Driven by serum/dialysate gradient
  - Modulated by dialysate potassium concentration (which is fixed)
  - Gradient falls during course of HD
Typical serum potassium curve during and after 4 hour dialysis session

Effect of Different Serum-Dialysate Gradients on SK Levels

Blumberg et al NDT 1997 (12) 1629-1634
Outline:

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What is the Ideal Serum Potassium Level in Hemodialysis patients?
Potassium and SCA Risk

- Study of 500 witnessed peridialytic SCA vs. 1600 matched controls
- Risk linked to extremes of plasma potassium (K)
- Lowest risk at K ~ 5.1

Pre-Dialysis Plasma Potassium and SCA Risk

Plasma potassium level and all cause mortality:
74,000 MHD patients followed over 3 years

All cause mortality
Cardiovascular Mortality

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Kovesdy C P et al. CJASN 2007;2:999-1007
Take Home Points: Pre-Dialysis Serum Potassium Levels and Outcomes

- Hemodialysis patients are more “tolerant” of mild hyperkalemia; Predialysis potassium level of ~5-5.5 not associated with increased risk
- Increased mortality and arrhythmic risk with K>5.5
- K~ <4 also associated with increased risk, but may not be directly related to potassium levels

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What is the Ideal Dialysate Potassium Prescription in Hemodialysis patients?

Variability in worldwide dialysate potassium

Karaboyas et. al. AJKD 2017:69(2)266
Safety of Low Potassium Dialysate

“Only one patient had high-grade ventricular ectopy. It was seen with each of the three potassium concentrations, but was most severe with the potassium-free dialysate.”


Low Dialysate Potassium and Peridialytic SCD

- 20% of SCA pts on very low K dialysate at time of event (mostly 1K)
- Mean Predialysis plasma K was in the normal range (4.9 meq/L)

What about Low K bath for hyperkalemia?

- Difference in risk between low and high K dialysate decreases as plasma K increases
- No indication of benefit for low K dialysate at any level of plasma K


Serum-Dialysate Potassium Gradient and Outcomes

- 62,388 HD patients 2010-2011
- Serum-Dialysate gradient vs. Risk of Same-day/Next day hospitalization.
- No 0 K dialysate
- Dose response relationships between gradient and outcomes
- No association with mortality

Brunelli et. al. NDT 2017
What about High Potassium Bath?

Increased Mortality Risk of Dk>3 Among Hyperkalemic Patients

Plasma K ≥5.0 mEq/L

Kovesdy C P et al. CJASN 2007;2:999-1007

N=81,013

aHR=1.36 (1.02-1.86)

Take home points: Dialysate K

- No randomized controlled studies to guide therapy, only observational data which could be confounded.
- Observational studies consistently identify harm with low Dk<2 with normal or low predialysis potassium
- Managing hyperkalemia with low dialysate K is associated with increased hospitalization and ER visit
- But using high dialysate K >3 is also associated with harm especially with normal or high predialysis potassium
Managing Hyperkalemia on HD = Sailing between Scylla and Charybris

Low K Bath → Large K shifts → Arrhythmias and SCD

High K Bath → Hyperkalemia → Arrhythmias and SCD

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1. Dialytic Approaches: Potassium Modeling


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Decreased ventricular ectopy during and after dialysis with Potassium modeling

Dialytic Approaches: Extended/Frequent Dialysis

- 4 hr vs. 8 hr
- Pair matched for total UF, dialysate K and dialysate volume
- Slower rate of potassium fall
- 15% overall increase in total potassium removal
- Identical end-of treatment serum K

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2. Modulating Colonic Secretion

- RAAS inhibitors may have effects on [K+] in anuric patients via colonic AT1 receptors [Knoll et. Al Am J Med 2002 (112)]
- Fludrocortisone not effective in decreasing [K] in a RCT. [Kaisar et al. AJKD 2006 (47)]
- Polystyrene-based potassium binding resins reduce K in HD patients but utility limited by poor long-term adherence and tolerability [Chaban et. Al. Renal Failure 2013: 35]
- Treatment with daily bisacodyl is associated with significant reduction in K (5.9 to 5.5 meq/L) [Mathialahan et. Al NDT 2003:18 341-347]
- Novel Potassium Binding agents: No large scale studies in HD patients, but data from CKD trials and small HD studies promising. [Bakris et. al JAMA 2015:314: 151; Packham et. al NEJM 2015(372):222]
Patiromer Decreases Serum Potassium and Phosphate Levels in Patients on Hemodialysis (N=6)

- Generally very well tolerated in CKD populations
- Sodium free
- Potassium binders could allow for use of higher K baths ➔ smaller fluctuations in serum K ➔ decreased arrhythmias?

3. Protocol Approach to Avoid Dialysate Mismatch

Risks associated with Hyperkalemia management
- Hyperkalemia: Bad (greatest risk K>5.5)
- Low K Bath/High Serum-Dialysate gradient: Probably Bad
- Mismatched Serum/Dialysate Assignment: Worst!

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3. Protocol Approach to Avoid Dialysate Mismatch

- Involve Renal Dieticians in reviewing serum/dialysate potassium levels for potential mismatches
  - Established an adjustment protocol based on serum K values

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<th>Recommendation</th>
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<td>&lt;4 mmol/L</td>
<td>Increase dialysate K by 1 mmol/L to a maximum of 4 mmol/L</td>
</tr>
<tr>
<td>4.1–5.5 mmol/L</td>
<td>Increase dialysate K by 1 mmol/L to a maximum of 3 mmol/L</td>
</tr>
<tr>
<td>5.6–6.4 mmol/L</td>
<td>Consider 2mmol/L K dialysate</td>
</tr>
<tr>
<td>&gt;6.5</td>
<td>Consider longer time, or daily HD</td>
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- Distinguish typical vs. atypical changes in potassium— one-off change in bath treatment vs. permanent change
- After initial adjustments in first 3 months, new steady state was reached and only 4% of patients required bath adjustment.

Summary/Recommendations

- Dialysis patients are more tolerant of hyperkalemia— increased risk begins at serum levels ~ >5.5 mEq/L
- Usual dialytic management of hyperkalemia by lowering K bath < 2 mEq/L is associated with risk, particularly in those with normal/mildly elevated potassium
- Avoiding serum/dialysate K mismatches via careful review of trends, patient history, frequent monitoring/adjustment algorithms could have highest yield in reducing dialysis-associated arrhythmias and sudden death
- Attention to concomitant dialytic factors (Mg, HCO3, dialysis time) and manipulating colonic K secretion could reduce fluctuations in potassium and reduce dialytic risk in persistently hyperkalemic patients