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Hyperkalemia & Management Solutions

ANNOUNCER:
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This medical industry feature titled, "**Hyperkalemia and Management Solutions**," is sponsored by AstraZeneca. This program is intended for healthcare providers (HCPs).

Your host is Dr Charles Turck.

DR TURCK:
High potassium, or hyperkalemia, can be a life-threatening condition that is often treated as an acute event.[1,2] More recent potassium binders that have been studied for up to one year, may be an effective way to manage patients with hyperkalemia.[2,3]

This is ReachMD, and I'm Dr Charles Turck. Joining me to discuss hyperkalemia, treatment gaps and solutions, is Dr. Anjay Rastogi, lead author of "New Agents in Treatment of Hyperkalemia: An Opportunity to Optimize Use of RAAS Inhibitors for Blood Pressure Control and Organ Protection in Patients with Chronic Kidney Disease".

Dr Rastogi, an investigator in clinical trials for AstraZeneca, UCLA Professor and Clinical Chief of Nephrology, is the Director of the Nephrology Clinical Research Program and Medical Director of the ESRD Dialysis Program. He is also the founder and director of UCLA's CORE Kidney program, dedicated to spreading awareness on kidney disease and providing resources for patients, doctors, and the general public.

Dr Rastogi, thanks for being here today.

DR RASTOGI:
Thanks for having me Dr Turck.

DR TURCK:
Dr Rastogi, let's begin with a high-level overview of hyperkalemia. What is the current clinical definition of this condition, and what are some concerns and risk factors associated with it?

DR RASTOGI:
Well Dr Turck, hyperkalemia is defined as serum potassium levels above the normal range and can vary from mild to severe.[1,4] A normal range for many labs is 3.5 to 5.0 mEq/L.[4]

Hyperkalemia can present itself with various symptoms such as muscle weakness, tingling, nausea, heart palpitations, arrythmia, or even paralysis.[1] In many cases, it's silent.[1]

Patients with chronic kidney disease, heart failure or diabetes have a higher risk of hyperkalemia.[1] Additionally, some of the medications that treat these other conditions, like RAAS inhibitors which include ACEi, ARB, MRA, ARNi, also predispose patients to hyperkalemia. [3,4]

DR TURCK:
Based on the information you have provided and your experience with patients with hyperkalemia, how might these risk factors impact the management of this condition?

DR RASTOGI:
That's a very important question, Dr Turck. For many providers, a common option for management has been to discontinue or reduce the dose of RAAS inhibitor therapy that may cause recurrent hyperkalemia.[2,3] However, this may deprive patients from the benefits of RAAS inhibitors and may not resolve their hyperkalemia.[2,3]

Hyperkalemia can be recurrent for many patients,[5] and I think there needs to be a continued effort in treating it as a chronic condition rather than just an acute episode.

DR TURCK:
In addition to these risk factors that impact management, what are some of the treatment challenges in managing hyperkalemia as a recurrent condition?

DR RASTOGI:
So Dr Turck, HCPs may often recommend a low potassium diet to their patients to manage hyperkalemia.[3] However, as patients try to adhere to this diet, they may deprive themselves of nutritious fruits and vegetables.[3] Compliance with a low potassium diet can also be challenging, especially if these patients have been placed on additional dietary restrictions for other conditions.[3,6]

Medications such as diuretics are also used quite frequently to manage hyperkalemia but can have their own adverse effects.[3,7]

DR TURCK:
For those just tuning in, you're listening to ReachMD.

I'm Dr Charles Turck, and I'm speaking with Dr Anjay Rastogi about the burden of hyperkalemia and management solutions. Now that we've talked about hyperkalemia management and treatment gaps, let's shift over to potassium binders as a potential solution to treat hyperkalemia.

Dr Rastogi, the recent KDIGO 2020 Guideline for Diabetes Management in Chronic Kidney Disease now includes K^+ binders as a treatment option for hyperkalemia associated with ACEi or ARB therapy in patients with diabetes, albuminuria and hypertension.[8] How is this beneficial for these patients?

DR RASTOGI:
So, thanks for bringing this up Dr Turck. The KDIGO guideline provides several options for managing ACEi or ARB-associated hyperkalemia in these patients, including K^+ binders. K^+ binders should be considered to control hyperkalemia after other measures have failed, rather than decreasing or discontinuing ACEi or ARB treatment.[8] I think this gives providers great options that could potentially change how we treat our patients.

DR TURCK:
What is the importance of including K^+ binders for the treatment of hyperkalemia as a recurrent condition in patients?

DR RASTOGI:
K^+ binders are important because they may play a key role in lowering potassium levels to treat and manage hyperkalemia.[3] Hyperkalemia, in my opinion, can be a significant inconvenience to the patient and the healthcare provider. Because it can be silent in many cases, patients may be unaware of their potassium levels making it necessary to check potassium levels with labs regularly as part of their management.[1]

LOKELMA, sodium zirconium cyclosilicate – 10 grams for oral suspension – is a modern K^+ binder brought to the market in 2018 and is indicated for the treatment of hyperkalemia in adults.[9] I do want to caveat that LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.[9]

DR TURCK:
Can you share with us potential ways a K^+ binder like LOKELMA could address the unmet needs of patients with hyperkalemia?

DR RASTOGI:
Absolutely. LOKELMA may be beneficial to patients managing hyperkalemia because it increases potassium fecal excretion through the selective binding of potassium in the lumen of the gastrointestinal tract. LOKELMA preferentially captures potassium in the small and large intestines, according to an in-vitro study in simulated intestinal fluid and exchanges it for hydrogen and sodium.[9-11]

In addition to understanding its mechanism, we've been able to study LOKELMA's effectiveness in clinical trials in which LOKELMA

demonstrated a rapid reduction of K^+ as early as 1 hour and sustained normokalemia for up to 1 year with continued treatment in adult patients with hyperkalemia who were not on dialysis. In Study 1, patients were given a 10 g dose of LOKELMA 3 times daily for 48 hours which started to work as early as 1 hour and demonstrated a greater reduction in serum potassium levels compared to patients given placebo at 48 hours. Again, it is important to keep in mind that LOKELMA should not be used for emergency treatment of life-threatening hyperkalemia. In study 2, patients with hyperkalemia who achieved normal potassium levels in the 48-hour initial phase entered a 28-day maintenance phase. A greater proportion of patients on LOKELMA maintained serum potassium levels in a normal range compared to those who switched to placebo. Finally, the patients that continued into the open label, 11-month extension phase, sustained normal potassium levels with continued LOKELMA treatment.[9,12-14]

DR TURCK:
Earlier, we touched on the challenge of RAAS inhibitor therapy for patients managing hyperkalemia. How could LOKELMA help to address this challenge?

DR RASTOGI:
So, Dr Turck, as a nephrologist, RAAS inhibitor therapy in my patients while also managing hyperkalemia is one of the most important therapeutic goals. In a retrospective analysis of a 12-month open-label study evaluating LOKELMA in 520 patients with hyperkalemia and not on dialysis. Of the 483 patients who were on RAAS inhibitor therapy at baseline, 74% had no change in their therapy, 13% were able to increase their RAAS inhibitor therapy dose, and 14% decreased their dose. Overall, 89% of the adult patients with hyperkalemia taking LOKELMA were able to continue RAAS inhibitor therapy.[14]

LOKLEMA was shown to be generally well tolerated. The most common adverse reactions listed in the LOKELMA PI are edema reported at 4.4%, 5.9%, and 16.1% of patients receiving 5 g, 10 g and 15 g, respectively vs. 2.4% of patients receiving placebo, and hypokalemia, reported in 4.1% of LOKELMA-treated patients with a serum K^+ value of <3.5 mEq/L.[11-14]

Please do listen to the Warnings and Precautions including gastrointestinal AEs in patients with motility disorder and edema and additional Important Safety Information at the end of this discussion.

DR TURCK:
Dr Rastogi, before we end, are there any final thoughts you'd like to share?

DR RASTOGI:
Yes, Dr Turck. In the past 5 years, there has been a paradigm shift in how we manage hyperkalemia as a recurrent condition, including the use of recent K^+ binders such as LOKELMA. This paradigm shift may help in addressing treatment gaps and unmet patient needs.

DR TURCK:
That's a great way to round out our discussion on hyperkalemia. I want to thank my guest for helping us better understand management of hyperkalemia. Dr. Rastogi, it was great speaking with you today.

DR RASTOGI:
Great speaking with you today as well, Dr. Turck. Thank you very much for having me.

DR TURCK:
I'm Dr. Charles Turck.

Before we close, let's take a moment to review some important safety information and where to find the full prescribing information for LOKELMA.

ANNOUNCER:
IMPORTANT SAFETY INFORMATION FOR LOKELMA® (sodium zirconium cyclosilicate)

WARNINGS AND PRECAUTIONS:

- **Gastrointestinal Adverse Events in Patients with Motility Disorders:** Avoid LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders. LOKELMA has not been studied in patients with these conditions and it may be ineffective and may worsen gastrointestinal conditions
- **Edema:** Each 5-g dose of LOKELMA contains approximately 400 mg of sodium, but the extent of absorption by the patient is unknown. In clinical trials of LOKELMA in patients who were not on dialysis, edema was observed and was generally mild to moderate in severity and was more commonly seen in patients treated with 15 g once daily. Monitor for signs of edema, particularly in patients who should restrict their sodium intake or are prone to fluid overload (eg, heart failure or renal disease).

Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed.
In a clinical trial of LOKELMA in patients on chronic hemodialysis in which most patients were treated with doses of 5 g to 10 g once daily on non-dialysis days, there was no difference in the mean change from baseline in interdialytic weight gain (a measure of fluid retention) between the LOKELMA and placebo groups.

- **Hypokalemia in Patients on Hemodialysis:** Patients on hemodialysis may be prone to acute illness that can increase the risk of hypokalemia on LOKELMA (eg, illnesses associated with decreased oral intake, diarrhea). Consider adjusting LOKELMA dose based on potassium levels in these settings.
- **Diagnostic Tests:** LOKELMA has radio-opaque properties and, therefore, may give the appearance typical of an imaging agent during abdominal X-ray procedures

ADVERSE REACTIONS: The most common adverse reaction in non-dialysis patients with LOKELMA was mild to moderate edema. In placebo-controlled trials up to 28 days, edema was reported in 4.4%, 5.9%, 16.1% of non-dialysis patients treated with 5 g, 10 g, and 15 g of LOKELMA once daily, respectively vs 2.4% of non-dialysis patients receiving placebo.

DRUG INTERACTIONS: LOKELMA can transiently increase gastric pH. In general, oral medications with pH-dependent solubility should be administered at least 2 hours before or 2 hours after LOKELMA. Spacing is not needed if it has been determined the concomitant medication does not exhibit pH-dependent solubility.

PLEASE READ FULL PRESCRIBING INFORMATION FOR LOKELMA AT WWW. LOKELMA.COM.

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REFERENCES:

1. Betts KA, Woolley JM, Mu F, Xiang C, Tang W, Wu EQ. The cost of hyperkalemia in the United States. *Kidney Int Rep*. 2018;3(2):385-393.
2. Epstein M, et al. Evaluation of the treatment gap between clinical guidelines and the utilization of renin-angiotensin-aldosterone system inhibitors. *Am J Manag Care*. 2015;21(11 suppl):S212-S220.
3. Palmer BF. Potassium binders for hyperkalemia in chronic kidney disease—diet, renin-angiotensin-aldosterone system inhibitor therapy, and hemodialysis. *Mayo Clin Proc*. 2020;95(2):339-354.
4. National Kidney Fund. Clinical Update on Hyperkalemia: A Chronic Risk for CKD Patients and a Potential Barrier to Recommended CKD Treatment. https://www.kidney.org/sites/default/files/02-10-6785_HBE_Hyperkalemia_Bulletin.pdf
5. Data on File. REF-34835. AZPLP
6. Clegg DJ, et al. Challenges in treating cardiovascular disease: restricting sodium and managing hyperkalemia. *Mayo Clin Proc*. 2017;92(8):1248-1260.
7. Rastogi A, et al. New agents in treatment of hyperkalemia: an opportunity to optimize use of RAAS inhibitors for blood pressure control and organ protection in patients with chronic kidney disease. *Curr Hypertens Rep*. 2016;7:(55). 1-14. doi 10.1007/s11906-016-0663-4
8. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2020;98(4S):S1-S115.
9. LOKELMA®(sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2021.
10. Stavros F, Yang A, Leon A, Nuttall M, Rasmussen HS. Characterization of structure and function of ZS-9, a K^+ selective ion trap. *PLoS One*. 2014;9(12):e114686.
11. Kosiborod M, et al. Effect of sodium zirconium cyclosilicate on potassium lowering for 28 days among outpatients with hyperkalemia: the HARMONIZE randomized clinical trial. *JAMA*. 2014;312(21):2223-2233.
12. Packham DK, et al. Sodium zirconium cyclosilicate in hyperkalemia. *N Engl J Med*. 2015;372(3):222-231.
13. Roger SD, et al. Efficacy and safety of sodium zirconium cyclosilicate for treatment of hyperkalemia: an 11-month open-label extension of HARMONIZE. *Am J Nephrol*. 2019;50(6):473-480.
14. Spinowitz BS, et al; ZS-005 Study Investigators. Sodium zirconium cyclosilicate among individuals with hyperkalemia: a 12-month phase 3 study. *Clin J Am Soc Nephrol*. 2019;14(6):798-809.

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