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Evolving Role of Potassium Binders: Evidence, Clinical Use, and Future Directions

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Background: The Clinical Dilemma Hyperkalemia is a major barrier to maintaining life-saving renin-angiotensin-aldosterone system inhibitors (RAASi) and mineralocorticoid receptor antagonists (MRA) in patients with CKD and heart failure (HF). Traditional binders like SPS are limited by slow onset and severe gastrointestinal toxicities (e.g., constipation, colonic necrosis), restricting their use to reactive crisis management. The Evolving Role & Novel Potassium Binders The clinical paradigm has shifted from reactive HK treatment to proactive prevention. Novel binders are now positioned as "enablers" of optimal RAASi/MRA therapy. Patiromer (Veltassa): A non-absorbed, sodium-free polymer that exchanges calcium for potassium, primarily in the distal colon. With an onset of action of ~7 hours, trials like OPAL-HK and PEARL-HF demonstrated its long-term efficacy in sustaining normokalemia and enabling spironolactone use in high-risk cardiorenal patients. Sodium Zirconium Cyclosilicate (SZC, Lokelma): A highly selective, non-swelling inorganic crystal that traps potassium across the entire GI tract. It provides a rapid onset (<1 hour). Trials like HARMONIZE and REALIZE-K showed it rapidly corrects HK and maximizes MRA optimization without the risk of GI swelling. Clinical Impact & Future Directions Real-world evidence, such as the ZORA study, demonstrates that novel binders more than double the odds of maintaining RAASi therapy, significantly reducing the risk of end-stage kidney disease progression. As their role continues to evolve, these potassium binders are transforming from simple electrolyte-lowering drugs into essential adjunctive therapies that secure long-term cardiorenal protection and improve patient survival.

Keywords: hyperkalemia , potassium binders, renin angiotensin system