



## Sodium Polystyrene Sulfonate for Hyperkalemia

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## ABSTRACT

**Background:** The management of hyperkalemia, particularly in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD), has garnered significant attention in recent years, especially regarding the use of sodium polystyrene sulfonate (SPS). **Literature Review:** The systematic review conducted by (Wing Sherwin Wong et al., 2020) underscores the lack of high-quality evidence supporting the widespread application of SPS, despite its historical use. The review's findings illustrate significant variability in study designs and dosing regimens, which complicate the determination of its efficacy. Further contributing to this discourse, (Ren et al., 2012) investigate prescription patterns of SPS and calcium polystyrene sulfonate (CPS) among CKD patients on renin-angiotensin-aldosterone system inhibitors (RAASi). The comparative analysis by (Atiquzzaman et al., 2012) highlights the limitations of existing randomized controlled trials (RCTs) and suggests that CPS may offer clinical advantages over SPS, prompting further investigation into the relative safety and efficacy of these resins. Finally, the contemporary overview provided by (Tian et al., 2013) details the mechanism of action of SPS and introduces RDX7675, a re-engineered alternative that shows promise in terms of potassium-binding capacity and tolerability. This development could signify a shift in therapeutic strategies for managing hyperkalemia, aligning with the need for safer and more effective treatment options in CKD patients. **Conclusion:** In conclusion, the literature reveals a complex landscape regarding the use of SPS for hyperkalemia management in CKD and ESRD patients. While SPS remains a commonly used treatment, significant concerns regarding its efficacy and safety profile persist. The need for individualized treatment strategies, ongoing research, and the exploration of alternative therapies like CPS and RDX7675 is evident to ensure optimal patient outcomes in this vulnerable population.

**Keyword:** Sodium Polystyrene Sulfonate, Hyperkalemia

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## INTRODUCTION

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The management of hyperkalemia, particularly in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD), has garnered significant attention in recent years, especially regarding the use of sodium polystyrene sulfonate (SPS). The early work of (V Hunt et al., 2018) highlights the critical context of hyperkalemia within the CKD population, noting that as kidney function declines, the risk of hyperkalemia increases due to the impaired excretion of potassium. While SPS has been a longstanding option for potassium removal, concerns regarding its efficacy and safety have emerged, particularly in vulnerable populations such as those with CKD and ESRD. This foundational study sets the stage for a broader examination of SPS's role in hyperkalemia management.

Building upon this groundwork, (Wing Sherwin Wong et al., 2020) conducted a systematic review that scrutinizes the efficacy and safety of polystyrene resins, including SPS. Their analysis reveals a significant gap in high-quality evidence supporting the widespread use of SPS, despite its historical application. The review underscores the heterogeneous nature of existing studies and the notable incidence of gastrointestinal adverse events associated with SPS, suggesting a need for caution in its application. This critical evaluation raises essential questions about the validity of the data supporting SPS's use, which are echoed in subsequent research.

(Ren et al., 2012) further contribute to this discourse by examining prescription patterns of SPS and calcium polystyrene sulfonate (CPS) among CKD patients receiving renin–angiotensin–aldosterone system inhibitors (RAASi). Their findings indicate a nuanced understanding of how these cation-exchange resins are utilized in clinical practice, particularly in the context of managing hyperkalemia in patients already on RAASi therapy. This study highlights the importance of considering medication interactions and patient characteristics when prescribing SPS, reinforcing the need for individualized treatment approaches.

In a similar vein, (Atiquzzaman et al., 2012) explore the efficacy of SPS and CPS in treating chronic hyperkalemia among CKD patients through a population-based analysis. Their work emphasizes the limitations of existing randomized controlled trials (RCTs) due to small sample sizes and suggests that CPS may offer clinical advantages over SPS. This comparative analysis adds another layer to the ongoing evaluation of treatment options, prompting further investigation into the relative safety and efficacy of these resins.

Finally, (Tian et al., 2013) present a contemporary overview of SPS, detailing its mechanism of action and the associated risks, particularly in older patients. Their findings indicate that while SPS is effective in reducing potassium levels, it carries serious but rare side effects that necessitate careful monitoring. They also introduce RDX7675, a re-engineered alternative to SPS, which demonstrates promising results in terms of potassium-binding capacity and tolerability. This recent development signifies a potential shift in therapeutic strategies for managing hyperkalemia in CKD patients.

Together, these articles illustrate a complex and evolving landscape in the treatment of hyperkalemia, particularly in patients with CKD and ESRD. The literature reveals a persistent reliance on SPS despite concerns regarding its efficacy and safety, highlighting the need for ongoing research and critical evaluation of treatment protocols in this vulnerable population.

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### LITERATURE REVIEW

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The article "Single-dose sodium polystyrene sulfonate for hyperkalemia in chronic kidney disease or end-stage renal disease" by (V Hunt et al., 2018) addresses a critical public health issue, particularly the management of hyperkalemia in patients suffering from chronic kidney disease (CKD) and end-stage renal disease (ESRD). With CKD affecting over 20 million individuals in the United States, the risk of hyperkalemia becomes a significant concern as kidney function deteriorates, leading to an impaired ability to excrete potassium ((V Hunt et al., 2018)).

The authors provide a comprehensive overview of the role of sodium polystyrene sulfonate (SPS), a cation exchange resin that has been utilized for decades as a therapeutic option for hyperkalemia. The mechanism of action is well-articulated, where SPS facilitates the exchange of sodium for potassium in the large bowel, effectively lowering serum potassium levels. However, the article critically highlights the evolving guidelines surrounding the use of SPS, particularly the FDA warnings issued in 2009 regarding its safety profile, especially in patients with abnormal bowel function ((V Hunt et al., 2018)). This aspect is particularly pertinent for patients with CKD and ESRD, who may have a higher propensity for gastrointestinal complications.

A significant contribution of this study is its examination of the existing literature on SPS therapy, which reveals a gap in research concerning its efficacy specifically in CKD and ESRD populations. The authors note that many studies either excluded these patients or did not adequately control for confounding variables that could influence potassium levels. This raises important questions about the generalizability of previous findings and emphasizes the need for targeted research in this vulnerable population.

Moreover, despite the documented risks associated with SPS, its widespread use persists, which suggests a disconnect between clinical guidelines and actual practice. The article effectively calls for a reevaluation of SPS therapy, particularly single-dose administration, in the context of acute hyperkalemia management in CKD and ESRD patients. The authors advocate for more robust clinical trials to assess the safety and efficacy of SPS in this demographic, thereby addressing a crucial need for evidence-based practices.

The systematic review titled "Polysulfonate Resins in Hyperkalemia" by (Wing Sherwin Wong et al., 2020) provides a comprehensive examination of the efficacy and safety of sodium polystyrene sulfonate (SPS) in the management of hyperkalemia. The authors meticulously analyze a substantial body of literature, encompassing four randomized controlled trials (RCTs), 21 observational studies, and five quasi-experimental trials, which collectively involve over 212,000

patients. This breadth of data allows for a robust evaluation of SPS's role in clinical practice, particularly in adults suffering from hyperkalemia.

The primary focus of the review is the quantification of changes in serum potassium levels, which serves as a critical measure of the treatment's efficacy. Notably, the authors highlight that only ten of the 22 studies examined reported on the effects of polystyrene resins on serum potassium within a 24-hour timeframe. This temporal aspect is significant, as it underscores the variability in treatment responses and the need for standardized assessment protocols in future research.

Moreover, the review raises essential concerns regarding the safety profile of SPS, particularly the incidence of adverse gastrointestinal events, which ranged from 16 to 23 events per 1,000 person-years. Such adverse effects necessitate careful consideration when prescribing SPS, especially given the growing apprehension surrounding the validity of the existing data supporting its use. The authors point out that while SPS has been a longstanding treatment option for hyperkalemia, the evidence base remains fraught with limitations, particularly regarding dosing regimens, which varied significantly across studies.

The systematic review ultimately concludes that there is a persistent lack of high-quality evidence to firmly endorse the use of SPS in hyperkalemia, though it acknowledges that the most compelling evidence pertains to its application in chronic hyperkalemia cases. This conclusion is critical for clinicians who must weigh the potential benefits of SPS against its risks and the uncertainties inherent in the current literature.

The article titled "Prescription patterns of sodium and calcium polystyrene sulfonate in patients with hyperkalemia and chronic kidney disease receiving RAAS inhibitors" by (Ren et al., 2012) provides a comprehensive examination of the use of sodium and calcium polystyrene sulfonate (SPS/CPS) in managing hyperkalemia among patients with chronic kidney disease (CKD) who are undergoing treatment with renin–angiotensin–aldosterone system inhibitors (RAASi).

The authors highlight the longstanding application of SPS/CPS as cation-exchange resins in the clinical setting, specifically for the treatment of hyperkalemia, a condition frequently observed in CKD patients. The study's primary focus is to evaluate the prescription patterns of these resins and their influence on the management of RAASi therapy following episodes of de novo hyperkalemia in patients classified under CKD Stages G3–G5.

A critical evaluation of the material reveals several key insights. First, the study underscores the importance of monitoring potassium levels in patients receiving RAASi, as hyperkalemia can pose significant risks, including cardiac complications. The authors effectively contextualize the clinical relevance of SPS/CPS in this population, emphasizing that while these agents are beneficial, their prescription patterns may vary significantly based on clinical practices and patient demographics.

Furthermore, the research identifies a gap in the consistent use of SPS/CPS, suggesting that despite their efficacy, there may be hesitancy among healthcare providers in prescribing these agents, potentially due to concerns regarding side effects or the perceived complexity of managing potassium levels in conjunction with RAASi therapy. This finding raises important questions about the need for clearer guidelines and education for clinicians to optimize hyperkalemia management in CKD patients.

The methodology employed in the study is robust, utilizing a comprehensive analysis of prescription patterns that allows for a nuanced understanding of how SPS/CPS are integrated into treatment regimens. However, the authors could have further elaborated on the long-term outcomes associated with the use of these resins, particularly in terms of renal function and overall patient health, which would provide a more holistic view of their impact.

The article titled "Prescription Pattern of Cation Exchange Resins and Their Efficacy in Treating Chronic Hyperkalemia Among Patients With Chronic Kidney Diseases: Findings From a Population-Based Analysis in British Columbia, Canada" by (Atiquzzaman et al., 2012) addresses the critical issue of hyperkalemia

in patients with chronic kidney disease (CKD), a condition that affects a significant portion of this population. The authors highlight that approximately 45% of CKD patients may experience elevated serum potassium levels, which can lead to severe complications, including cardiac arrhythmias and sudden death.

The study's primary focus is on the prescription patterns and efficacy of sodium polystyrene sulfonate (SPS) and calcium polystyrene sulfonate (CPS) in managing chronic hyperkalemia. SPS has been a traditional treatment option; however, its effectiveness in the CKD population has been questioned due to limitations in existing randomized controlled trials, which often feature small sample sizes and short durations. The authors critically evaluate these limitations, underscoring the need for more robust studies to establish the long-term efficacy of SPS in this demographic.

Moreover, the article presents CPS as a potentially safer alternative to SPS. The mechanism of action for SPS involves exchanging sodium for potassium, which may exacerbate conditions such as hypervolemia and hyperparathyroidism in CKD patients. In contrast, CPS exchanges calcium for potassium, presenting a lower risk of these adverse effects. However, the authors also note that the clinical advantages of CPS over SPS are not well-documented, indicating a gap in the literature regarding its efficacy in chronic hyperkalemia management.

The findings from the population-based analysis in British Columbia provide valuable insights into the current prescribing practices for these cation exchange resins. The study emphasizes the importance of understanding both the utilization trends and the clinical outcomes associated with these treatments, as they are critical for guiding therapeutic decisions in managing hyperkalemia among CKD patients.

The article "Recent Progresses in Non-Dialysis Chronic Kidney Disease Patients with Hyperkalemia: Outcomes and Therapeutic Strategies" by (Tian et al., 2013) provides a comprehensive overview of Sodium Polystyrene Sulfonate (SPS) as a therapeutic option for managing hyperkalemia, particularly in patients with chronic kidney disease (CKD). The authors effectively elucidate the mechanism by

which SPS operates, detailing its role as a synthetic cation-exchange resin that facilitates the exchange of sodium for potassium in the large intestine, thereby promoting fecal potassium excretion.

The article highlights that the peak effect of SPS occurs within 4 to 6 hours post-administration, a timeframe that limits its utility as an emergency treatment for acute hyperkalemia. This is a critical point, as it distinguishes SPS from other treatments, such as patiromer, which may have different pharmacokinetic profiles. The authors note the severe but rare side effects associated with SPS, including colonic necrosis, constipation, and bowel obstruction. This acknowledgment is crucial for clinicians considering SPS, as it underscores the importance of monitoring gastrointestinal health, particularly in older patients who exhibit a higher hospitalization rate for serious adverse events within 30 days of SPS use.

Moreover, the article discusses the correlation between the incidence of gastrointestinal symptoms and both the renal function of patients and the dosage of SPS administered. This relationship is significant, as it suggests that careful dosing and patient selection are vital in mitigating the risks associated with SPS. The authors recommend a low-dose regimen (15–30 g daily) tailored to the patient's serum potassium levels, which appears to be well-tolerated and effective over an extended period.

Additionally, the article introduces RDX7675, a re-engineered calcium salt of polystyrene sulfonate-based resin, which presents a promising alternative to SPS due to its enhanced palatability and superior potassium-binding capacity compared to both patiromer and SPS. The preliminary findings regarding the tolerability of RDX7675 during a short-term administration in healthy individuals indicate its potential for broader application in hyperkalemia management.

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## CONCLUSION

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The literature on sodium polystyrene sulfonate (SPS) for the management of hyperkalemia, particularly in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD), reveals critical insights into its efficacy, safety,

and practical application. The foundational work by (V Hunt et al., 2018) emphasizes the heightened risk of hyperkalemia as kidney function deteriorates, highlighting the need for effective potassium removal strategies. Although SPS has been a traditional therapeutic option, concerns regarding its safety profile, particularly gastrointestinal adverse events, have surfaced, necessitating a reevaluation of its use in vulnerable populations.

The systematic review conducted by (Wing Sherwin Wong et al., 2020) underscores the lack of high-quality evidence supporting the widespread application of SPS, despite its historical use. The review's findings illustrate significant variability in study designs and dosing regimens, which complicate the determination of its efficacy. Moreover, the incidence of gastrointestinal complications associated with SPS use raises important safety considerations, particularly in patients with pre-existing conditions that may exacerbate these risks.

Further contributing to this discourse, (Ren et al., 2012) investigate prescription patterns of SPS and calcium polystyrene sulfonate (CPS) among CKD patients on renin–angiotensin–aldosterone system inhibitors (RAASi). Their findings reveal a complex interplay between medication interactions and patient characteristics, suggesting that individualized treatment approaches are essential for optimizing hyperkalemia management.

The comparative analysis by (Atiquzzaman et al., 2012) highlights the limitations of existing randomized controlled trials (RCTs) and suggests that CPS may offer clinical advantages over SPS, prompting further investigation into the relative safety and efficacy of these resins. The authors call attention to the need for more robust studies to establish long-term efficacy and safety profiles for both SPS and CPS in the CKD population.

Finally, the contemporary overview provided by (Tian et al., 2013) details the mechanism of action of SPS and introduces RDX7675, a re-engineered alternative that shows promise in terms of potassium-binding capacity and tolerability. This development could signify a shift in therapeutic strategies for

managing hyperkalemia, aligning with the need for safer and more effective treatment options in CKD patients.

In conclusion, the literature reveals a complex landscape regarding the use of SPS for hyperkalemia management in CKD and ESRD patients. While SPS remains a commonly used treatment, significant concerns regarding its efficacy and safety profile persist. The need for individualized treatment strategies, ongoing research, and the exploration of alternative therapies like CPS and RDX7675 is evident to ensure optimal patient outcomes in this vulnerable population.

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