JMS 2024;Vol 7(1):136-141
UDC:616.152.32-085.31:616.61-008.64
https://doi.org/10.55302/JMS2471136s

SHORT TERM TREATMENT OF CHRONIC HYPERKALEMIA WITH ORAL POTASSIUM BINDER IN CHRONIC KIDNEY DISEASE PATIENTS

Sabir Sulejman, Angela Kranfilovikj, Ana Stojanoska, Mimoza Milenkova, Julijana Usprcov, Bleron Kolonja, Izet Salkoski, Hristina Minovska, Adrian Memeti, Adrijana Spasovska, Oliver Ristovski.
Clinic of Nephrology, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, North Macedonia

Abstract

The aim of our study was to analyse the efficacy of short-term administration of oral calcium polystyrene sulfonate (CPS) to treat hyperkalemia in non-dialysis CKD patients.

A prospective interventional study was conducted in 65 CKD patients with chronic hyperkalemia with a month of therapy.

Patients were stratified into groups in respect of potassium level (mild <5.9; moderate 6-6.5; severe ≥6.5 mmol/l). Regression analysis was applied to investigate associations of hyperkalemia with different variables. Paired T-Test was used for comparative analysis of potassium levels before and after therapy.

Patients mean age was 67 years, eGFR ranged between 8 to 52ml/min. More than half of patients presented with moderate or severe hyperkalemia. None of the demographic, clinical or pharmacological variables predicted potassium level.

The comparative analysis with paired samples T-Test showed significantly lower potassium levels after one month of therapy ($p<0.001$). The portion of patients that were encountered for mild hyperkalemia significantly increased (21% vs. 59%, $p<0.001$) and conversely, the portions of those with moderate and severe hyperkalemia significantly decreased (29% vs. 3%, $p<0.001$; 15% vs, 3%, $p<0.001$), respectively.

Short term treatment of hyperkalemia with oral potassium binder is effective in non-dialysis CKD patients.

***Key words*:** hyperkalemia, potassium binder, CKD, GFR, RAAS therapy.

Introduction

In chronic kidney disease (CKD) one of the most common metabolic complications is hyperkalemia, since the kidney is the major route of potassium excretion, and the gastrointestinal tract being the second (with less than 10% excretion of potassium). As CKD advances, the excretion of potassium declines. This leads to chronic hyperkalemia which is associated with significantly higher all-cause and cardiovascular mortality, and with higher risk of end-stage renal disease.It is mostly associated with cardiovascular events [1].

Bradycardia,as an early sign of acute severe hyperkalemia, it is uncommon in chronic hyperkalemia because of adaptive mechanisms. Severe hyperkalemia can also trigger fatal arrhythmias. Hyperkalemia also plays and indirect role in the progression of CKD to dialysis by dictating the withdrawal of nephroprotective anti-RAAS agents.

The incidence of hyperkalemia is also higher in diabetic patients. The most common causal factor of chronic hyperkalemia in diabetics is the reduced tubular secretion of K+ due to the hyporeninemic hypoaldosteronism syndrome. Additional factor that can lead to hyperkalemia is CKD associated with heart failure (HF).

HF can lead to low GFR. Also, patients with HF and CKD are extensively treated with RAAS inhibitors [2].

They are the most frequently used pharmacological agents for treatment of CKD associated with diabetes mellitus and heart failure.Sometimes this can lead to down-titration or withdrawal of RAAS inhibitors for safety reasons, but it prevents these high-risk patients from receiving the best available therapy in CKD.

In these cases, the patients are either receiving a low dose or the drugs are withdrawn, losing their cardioprotective effect which is not to be underestimated. CKD patients usually are on a low potassium diet, depriving them of the benefits of a plant-based diet [3].

In the end, all this is associated with increased incidence of adverse events and mortality. To overcome these contradictory treatment strategies,first a proper dietary counseling is mandatory for the patient, to restrict dietary potassium intake. Secondly, in the case of kidney disease the gastrointestinal tracts excretion of potassium can go up to 50 % which makes the colon a target organ for potential therapies.

Potassium binders have emerged as new options to increase fecal potassium excretion[4]. Sodium polystyrene sulfonate (SPS) is a potassium binding resin, which exchanges sodium for calcium, ammonium, and magnesium in addition to potassium.

Calcium polystyrene sulfonate (CPS) is another potassium binding resin, which exchanges calcium for potassium.They both act in the distal colon. CPS is superior to SPS because it avoids sodium retention.

Also, two new potassium-binding agents sodium zirconium cyclosilicate (ZS-9) and Patiromer (a non-absorbable polymer) areapproved by the FDA, they are more potent and highly effective [5,6].

This study aimedto investigate the short-term efficacy of potassium binding resin in CKD patients with chronic hyperkalemia.

Material and methods

This was a prospective interventional study on a cohort of 65 CKD ambulatory patients diagnosed with chronic hyperkalemia in the period from January until end of December 2023. Demographics as age and gender, clinical, laboratory and pharmacologic data were obtained from the patients' medical files. GFR was calculated by CKD EPI formula.

Chronic hyperkalemia was defined as potassium serum level above 5.5mmol/l in at least three previous measurements. Patients were prescribed CPS for a 1 month, with a daily dose at discretion of the ordinating physician.Signed informed consent was mandatory as inclusion criteria. All patients were advised for a medical check and blood sampling for potassium level after a month.

Statistical analysis: Continuous data is presented as mean/standard deviation and nominal as percentage.Patients were stratified into groups in respect of potassium level (mild <5.9; moderate 6-6.5 and severe ≥6.5 mmol/l).Regression analysis was applied to investigate associations of hyperkalemia with different variables. Paired T-Test was used for comparative analysis of potassium levels before and after therapy. $P<0.05$ was considered significant.

Results

Baseline demographic, biochemical and clinical characteristics of the study group are shown in Table 1. Patients were adults ranging from 27-88 years of age, more than half were male (65%).The diagnosis of diabetes was more frequently present than cardiomyopathy (31 (47.6%); 18 (27.6%)), respectively.

The eGFR showed wide range between 8 to 52ml/min, with nearly half of patients in the fifth stage of CKD. More than half of patients presented with moderate or severe hyperkalemia and 32% with mild. The mean serum potassium before initiation of therapy was 6.15 and after therapy 5.13 mmol/l.

Table 1. Demographics, biochemical and clinical characteristics of the study group

N=65	Mean± SD N (%)	Rang (Min – max)
Age (years)	67.24 ± 11.85	27 - 88
Male gender	42 (65%)	
Diabetes	31 (47.6%)	
Cardiomyopathy	18 (27.6%)	
Creatinine (μmol/l)	293.76 ± 121.14	122 - 602
eGFR (ml/min)	20.61 ± 11.68	8 - 52
eGFR < 15(ml/min)	29 (45%)	
Potassium (pre-therapy) mmol/l	6.15 ±0.43	5.2 – 7.5
Hyperkalemia (mmol/l)		
mild	21 (32%)	
moderate	29(45%)	
severe	15 (23%)	
Potassium (post-therapy) mmol/l	5.13 ± 0.75	3.40 - 7

eGFR – estimated glomerular filtration rate

Based on prescription records, we identified that almost half of the patients (49%) were under RAAS inhibition therapy, two thirds were treated with thiazide diuretic and smaller part of patients needed potassium sparing diuretic (9%) or combination with RAAS inhibitor (5%) (Table 2). In 6(9%) of the patients the ACE/ARB therapy was discontinued after one month of treatment.

Table 2. Concomitant therapy

N=65	N (%)
Therapy	
RAAS inhibitor	32 (49%)
Potassium sparing diuretic	6 (9%)
Thiazide diuretic	43 (66%)
RAAS inhibitor + potassium sparing diuretic	3 (5%)

None of the demographic, clinical or pharmacological variables predicted potassium level in the univariate regression analysis (Table 3).

Table 3. Correlations of potassium level with therapy before introducing potassium binder

N=65	r	p
age	0.152	0.227
Male gender	-0.002	0.998
Thiazide diuretic	-0.216	0.083
Potassium sparing diuretic	0.086	0.498
RAAS inhibitor	0.162	0.196
RAAS inhibitor + potassium sparing diuretic	0.183	0.145
eGFR	0.114	0.369

The comparative analysis with paired samples T-Test showed significantly lower potassium levels after one month therapy with the oral potassium binder ($p<0.001$) as shown in Figure 1.

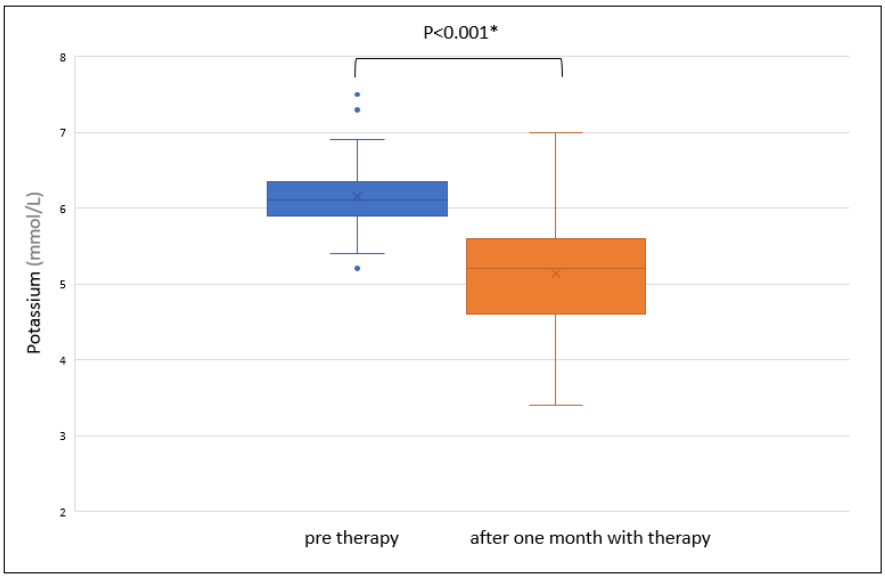

Figure 1. Potassium serum levels pre and post therapy with potassium binder

The distrubution of patients in respect of the blood potassium level before and after therapy is shown in Figure 2. The portion of patients that were encountered for mild hyperkalemia significantly increased after therapy (21% vs. 59%, $p<0.001$) and conversely, the portions of those with moderate and severe hyperkalemia significantly decreased (29% vs. 3%, $p<0.001$; 15% vs, 3%, $p<0.001$), respectively.

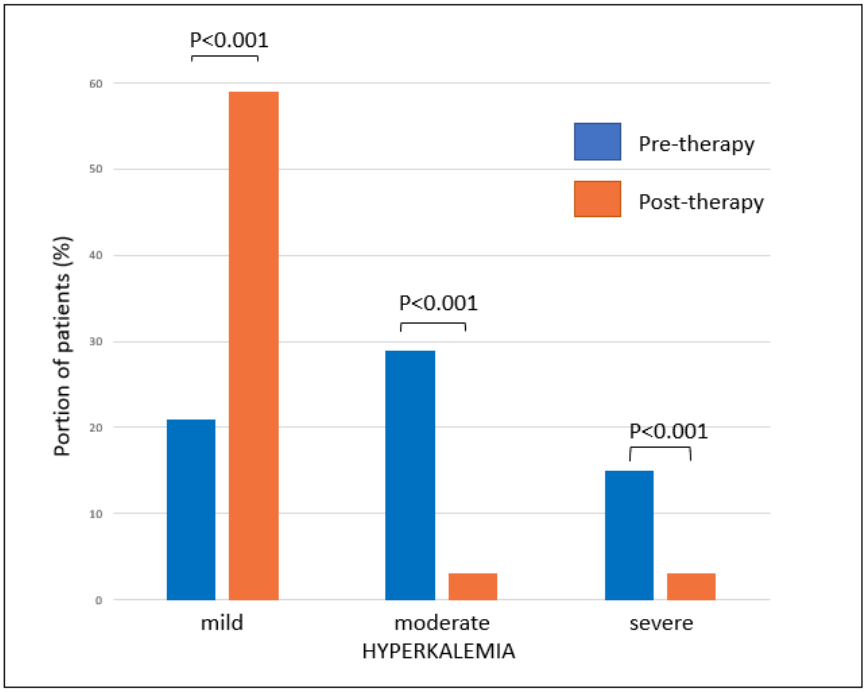

Figure 2. Distrubution of patients in respect of the blood potassium level before and after therapy

Discussion

Since hyperkalemia can cause serious cardiovascular events and can lead to higher risk of end-stage renal disease, management of chronic hyperkalemia is one of the primary focuses in CKD patients.

One of the most optimal treatments of chronic hyperkalemia are potassium binders, they have been used for a long time for this sole purpose. Our study investigated the short-term treatment with CPS. The vast majority of our patients had eGFR below 60ml/min, high proportion of them presented with diabetes (47%) and cardiomyopathy (28%), which is in line with the recent review of De Nikola [1].

In a study done by Jose M. Valdivielso et al. serum potassium levels were higher and hyperkalemia and severe hyperkalemia more prevalent in men than in women in non-dialysis CKD[7].

These findings were comparable to our results where men were dominant in respect of hyperkalemia. In our study, after the therapy with CPS, the potassium levels dropped significantly for each patient as self-control and a significant shift of patients from severe and moderate hyperkalemia to the group with mild hyperkalemia occurred. There are other studies that prove the effectiveness of potassium binders [8-10].

The study of Mi-Yeon Yu et al. enrolled a larger group of patients and were given small doses of CPS for a longer period (3 to 12 months treatment). The short- and long-term CPS treatment significantly decreased the serum potassium levels and the serum potassium effect was dose dependent [8].

Our study is limited in respect of analysing the doses of CPS that were prescribed and actually taken by the patients. Also, we did not take into consideration of the impact of the diet. Almost half of our patients were treated by RAAS inhibitors.

The basal potassium level was not correlated to eGFRin Mi-Yeon Yu's study as we also found in our study, but the positive association with the therapy with RAAS we did not confirm. This also might be explained with the lack of information on our patient's diet. Most of them were advised to a low potassium diet but under RAAS inhibitor therapy, although it has been proposed that potassium binders may be useful in enabling the patients a freer and more diverse diet [11,12].

In spite of the generally good results we obtained with this therapy, in 6 patients (9%) the ACE/ARB therapy was discontinued after one month of treatment. The limitations of our study consist of having a rather small number of participants and short follow up period. This study elucidated the need of better education of patients with hyperkalemia in respect of dietetic regime.

Conclusion

In general, oral CPS was effective in short-term controlling serum potassium levels in CKD pre-dialysis patients with almost all of them continuing their RAAS inhibitor therapy.

References

1. De Nicola L, Di Lullo L, Paoletti E, Cupisti A, Bianchi S. Chronic hyperkalemia in non-dialysis CKD: controversial issues in nephrology practice. J Nephrol. 2018 Oct;31(5):653-664. doi: 10.1007/s40620-018-0502-6. Epub 2018 Jun 7. PMID: 29882199; PMCID: PMC6182350.
2. Muneer K, Nair A. Angiotensin-converting enzyme inhibitors and receptor blockers in heart failure and chronic kidney disease - Demystifying controversies. Indian Heart J. 2017 May-Jun;69(3):371-374. doi: 10.1016/j.ihj.2016.08.007. Epub 2016 Sep 8. PMID: 28648436; PMCID: PMC5485404.
3. Clegg DJ, Headley SA, Germain MJ. Impact of Dietary Potassium Restrictions in CKD on Clinical Outcomes: Benefits of a Plant-Based Diet. Kidney Med. 2020 Jun 15;2(4):476-487. doi: 10.1016/j.xkme.2020.04.007. PMID: 32775988; PMCID: PMC7406842.
4. Kim GH. Pharmacologic Treatment of Chronic Hyperkalemia in Patients with Chronic Kidney Disease. Electrolyte Blood Press. 2019 Jun;17(1):1-6. doi: 10.5049/EBP.2019.17.1.1. Epub 2019 Jun 30. PMID: 31338108; PMCID: PMC6629599.
5. Morales E, Cravedi P, Manrique J. Management of Chronic Hyperkalemia in Patients With Chronic Kidney Disease: An Old Problem With News Options. Front Med (Lausanne). 2021 Jun 4;8:653634. doi: 10.3389/fmed.2021.653634. PMID: 34150795; PMCID: PMC8213200.

6. St-Jules DE, Clegg DJ, Palmer BF, Carrero JJ. Can Novel Potassium Binders Liberate People with Chronic Kidney Disease from the Low-Potassium Diet? A Cautionary Tale. Clin J Am Soc Nephrol. 2022 Mar;17(3):467-472. doi: 10.2215/CJN.09660721. Epub 2021 Oct 20. PMID: 34670798; PMCID: PMC8975039.
7. Valdivielso JM, Carriazo S, Martin M, Fernandez-Fernandez B, Bermudez-López M, Ortiz A; NEFRONA investigators. Gender-specific risk factors and outcomes of hyperkalemia in CKD patients: smoking as a driver of hyperkalemia in men. Clin Kidney J. 2023 Oct 9;17(1):sfad212. doi: 10.1093/ckj/sfad212. PMID: 38186899; PMCID: PMC10768768.
8. Yu MY, Yeo JH, Park JS, Lee CH, Kim GH. Long-term efficacy of oral calcium polystyrene sulfonate for hyperkalemia in CKD patients. PLoS One. 2017 Mar 22;12(3):e0173542. doi: 10.1371/journal.pone.0173542. PMID: 28328954; PMCID: PMC5362098.
9. Wang X, Chen D, Song X, Wang J, Zhang H. Efficacy and safety of calcium polystyrene sulfonate in patients with hyperkalemia and stage 3-5 non-dialysis chronic kidney disease: a single-center randomized controlled trial. J Int Med Res. 2023 Apr;51(4):3000605231167516. doi: 10.1177/03000605231167516. PMID: 37063062; PMCID: PMC10119845.
10. Georgianos PI, Liampas I, Kyriakou A, Vaios V, Raptis V, Savvidis N et al. Evaluation of the tolerability and efficacy of sodium polystyrene sulfonate for long-term management of hyperkalemia in patients with chronic kidney disease. Int Urol Nephrol. 2017 Dec;49(12):2217-2221. doi: 10.1007/s11255-017-1717-5. Epub 2017 Oct 11. PMID: 29027620.
11. Packham DK, Rasmussen HS, Lavin PT, El-Shahawy MA, Roger SD, Block G et al. Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med. 2015 Jan 15;372(3):222-31. doi: 10.1056/NEJMoa1411487. Epub 2014 Nov 21. PMID: 25415807.
12. Clegg DJ, Headley SA, Germain MJ. Impact of Dietary Potassium Restrictions in CKD on Clinical Outcomes: Benefits of a Plant-Based Diet. Kidney Med. 2020 Jun 15;2(4):476-487. doi: 10.1016/j.xkme.2020.04.007. PMID: 32775988; PMCID: PMC7406842.