ORIGINAL ARTICLE

TREATMENT OF HYPERKALEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A COMPARISON OF CALCIUM POLYSTYRENE SULPHONATE AND SODIUM POLYSTYRENE SULPHONATE

Kiran Nasir, Aasim Ahmad

Department of Nephrology, Kidney Centre, Post Graduate Training Institute, Karachi, Pakistan

Background: Hyperkalemia is one of the most dreadful complications of chronic kidney disease (CKD). Medical management includes use of cation exchange resins to reduce the amount of excessive potassium from the body. Sodium polystyrene sulphonate (SPS) and calcium polystyrene sulphonate (CPS) are currently used for hyperklemia of CKD all over the world. The objective was to compare the efficacy and safety of two different cation exchange resins (CPS and SPS) in patients of CKD with hyperkalemia. **Methods:** This randomized control trial was done at the Kidney Centre, Post Graduate Training Institute (PGTi), Karachi, Pakistan between 15th January 2010 till 31st December 2010 to compare the efficacy and safety of, CPS and SPS in 97 CKD patients with hyperkalemia. The subjects were divided in two groups. Group-A received CPS while group-B received SPS. The data included symptoms, food recall, physical signs of volume overload and electrolytes. After receiving potassium binding resin for 3 days patients were evaluated for symptoms, weight gain, worsening of blood pressure and effect on electrolytes. Adverse events were recorded in an event reporting form. **Results:** Average potassium level pre resin was 5.8±0.26 in group-A and 5.8±0.6 in group-B, which reduced to 4.8±0.5 in group-A and 4.3±0.53 in group-B suggesting the efficacy of both drugs for treatment of hyperkalemia in CKD patients. Systolic blood pressure remains stable in both the groups while an increase in diastolic blood pressure was noticed in group-B patients (*p*-value 0.004). No major adverse effect occurred in both the groups. **Conclusion**: Both CPS and SPS can be used effectively for reducing hyperkalemia of CKD. CPS showed fewer side effects as compared to SPS.

Keywords: Hyperkalemia, Chronic Kidney Disease, Cation exchange resin

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INTRODUCTION

Hyperkalemia is a known complication of chronic kidney disease (CKD). Reasons are multiple, including decreased urinary excretion secondary to poor kidney function, dietary intake, potassium-sparing diuretics, ACE inhibitors, ACE receptor blockers, urinary tract obstruction, sickle cell disease, Addison disease and systemic lupus erythromatosis (SLE).[1]

Potassium is a major ion of the body. Nearly 98% of potassium is intracellular. The ratio of intracellular to extra cellular potassium is important in determining the cellular membrane potential. Small changes in the extra cellular potassium level can have profound effects on the function of the cardiovascular and neuromuscular systems.[2] Total body potassium stores are approximately 50 mEq/kg (3500 mEq in a 70 kg person). Hyperkalemia is defined as a potassium level greater than 5.2 mEq/L and ranges are as follows:. 2–6.0 mEq/L, Mild 6.1–7.0 mEq/L-Moderate 7.0 mEq/L and greater-Severe[3] Kidneys adapt to acute and chronic alterations in potassium intake. When potassium intake is chronically high, potassium excretion also is increased. Renal adaptive mechanisms allow the kidneys to maintain potassium homeostasis until the glomerular filtration rate drops to less than 15–20 mL/min. In the presence of renal failure, the proportion of potassium excreted through the gut increases. The colon is the major site of gut regulation of potassium excretion. Therefore, potassium levels can remain relatively normal under stable conditions, even with advanced renal insufficiency. However, as renal function worsens, the kidneys may not be capable of handling an acute potassium load.[4]

Different medications are used for decreasing serum potassium concentration and thus preventing the life threatening complications. These include administration of calcium, insulin, glucose, adrenergic blockers, diuretics and cation exchange resins. The cation exchange resins exchange an ion for the potassium in the gut. They may contain calcium, sodium or aluminium and exchange these ions for potassium in the gut, thus removing the excessive potassium from the body.

Sodium polystyrene sulphonate removes 0.5–1.0 mg of potassium in exchange for 2–3 mg of sodium. A single daily dose of sodium polystyrene sulphonate (15 grams) contains approximately 60 mg of sodium. Therefore it use is associated with significant sodium load and can result in volume overload in patients with CKD.[5] Calcium polystyrene sulphonate contains 7–9% calcium, 1 gram of which is exchanged for 53–71 mg (1.39–1.82 mEq/g) of potassium in vitro.[6–8] Because of the absence of sodium, calcium containing exchange resins can be

used safely in patients with volume overload, cardiac failure, oedema, hypertension and CKD.[9–12]

MATERIAL AND METHODS

This single blind randomized control trial was done from 15th January 2010 till 31st December 2010. All CKD patients who came to emergency department during the study periods were checked for hyperkalemia. Ninety-seven adult patients (age more than 18 years) at various stages of CKD on conservative management were found to be hyperkalemic and were included in the study. The objective was to compare the efficacy and safety of two different cation exchange resins (CPS and SPS) in patients of CKD with hyperkalemia, As SPS got high content of sodium which can lead to worsening of volume overload in patients with CKD while CPS being free of sodium, did not lead to volume overload, so we hypothesize that CPS is better than SPS for patients with CKD.

The patients of either gender above 18 years of age with CKD on conservative management and with serum potassium level of >5.2 mg/dl were included in the study. Patients on medication like ACE inhibitors, ACE receptor blockers, Beta Blockers, Digitalis, Potassium sparing diuretics, NSAIDS, Cyclosporin, Tacrolimus, which can alter the potassium levels were excluded from the study. Patients with hemodynamic compromise, arrhythmias or heart block, patients on maintenance hemodialysis and those with renal transplants were also excluded.

Chronic Kidney Disease (CKD) was defined as a Serum creatinine more than 1.5 mg/dl for at least three months before induction in the study. Hyperkalemia was defined as a serum potassium level of more than 5.2 mg/dl. The patients who were willing to participate in the study signed a written informed consent. The study was done according to the recommendations of Good Clinical Practice and the Declaration of Helsinki.

After signing the informed consent all patients underwent evaluation by research officer or symptoms and food recall. Physical signs of volume overload and electrolytes were noted. Patients were randomly allocated to one of the two groups. Patients were given potassium binding resins in a dose of 5 grams three times per day PO for three days. In group-A Fifty patients were given Calcium polystyrene sulphonate (CPS) while in group-B 47 patients were treated with Sodium polystyrene sulphonate (SPS) .After three days of resin administration, patients were evaluated for symptoms, weight gain, worsening of blood pressure and effect on electrolytes. (Figure-1) Adverse events were recorded in an event reporting form.

The data was collected and analyzed with the help of SPSS-17. Quantitative data mean with standard deviation was also calculated and non-parametric X2 test and K independent sample mean test was applied for significance.

RESULTS

Among the 97 patients, 36 were males and 61 were females with a mean age of 53.08±12.86. All patients had CKD stage 1–4. Ninety-three patients had hypertension while 63 had diabetes mellitus as a co morbid condition. All patients were on anti hypertensive medications and majority were taking diuretics either loop diuretic or thiaziade diuretic. In group-A 50 patients were included which were given CPS while 47 patients in group-B were given SPS. Average potassium level pre resin was 5.8±0.26 in group-A and 5.8±0.6 in group-B, which reduced to 4.8±0.5 in Group-A and 4.3±0.53 in group-B suggesting that both drugs are equally effective for treatment of hyperkalemia in CKD patients. No significant effect of both resins was seen on other electrolytes (Calcium, Phosphorus, and Sodium). Systolic blood pressure remains stable in both the groups while a significant increase in diastolic blood pressure was noticed in group-B patients (*p*-value 0.004). No statically significant difference in weight was seen. Most significant side effect encountered was nausea in patients in group-B who received sodium polystyrene sulphonate as compared to patients in Group-A receiving calcium polystyrene sulphonate (*p*-value 0.005), anorexia (*p*-value 0.013), abdominal distension (*p*-value 0.092) and abdominal pain (*p*-value 0.062). Worsening of oedema was noticed more in Group-B but the results were not statistically significant (*p*-value 0.573).table-1. Table-2 showed the comparative analysis of effect of Calcium and sodium polystyrene on various electrolytes, weight and blood pressure of the patient.

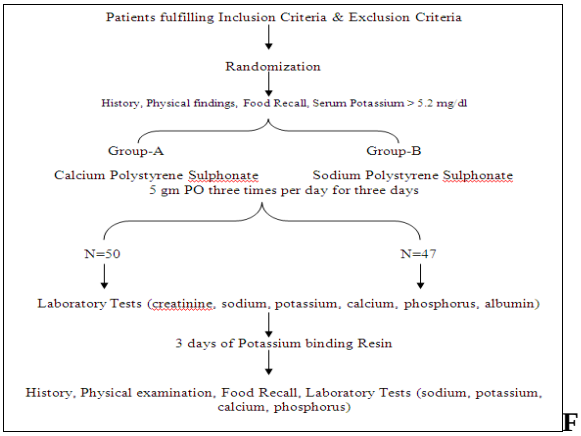

Figure-1: Study design, outpatients of chronic kidney disease clinic of the kidney centre

Table-1: Adverse events recorded during the study period.

Adverse Events	Calcium Polystyrene Sulphonate (n=50)	Sodium Polystyrene Sulphonate (n=47)	*p*-Value
Constipation	6	8	0.407
Abdominal Pain	1	3	0.062
Nausea	9	20	0.005
Vomiting	0	2	0.535
Diarrhea	1	0	0.348
Anorexia	7	16	0.013
Edema	3	4	0.573
Cough	1	0	0.348
Sputum	0	0	1.00
Abdominal distention	1	6	0.092

Table-2: Comparison of effect of Calcium Polystyrene sulphonate (CPS) and Sodium Polystyrene sulphonate (SPS) on serum electrolytes, weight and blood pressure

Variables	Calcium Polystyrene Sulphonate		Sodium Polystyrene Sulphonate	
	(n=50) Before Treatment Mean±S.D	After Treatment Mean±S.D	(n=47) Before Treatment Mean±S.D	After Treatment Mean±S.D
Sodium	139.6±18.6	135.3±24.6	140.3±6.4	139.05±6.6
Potassium	5.8±0.26	4.8±0.5	5.8±0.6	4.3±0.53
Calcium	8.7±0.74	8.72±0.6	8.6±0.97	8.4±0.74
Phosphorus	4.3±1.05	4.6±1.2	11.23±43.6	4.5±1.15
Systolic Blood Pressure	136±24.4	139.25±18	134.2±18.9	136.6±19.3
Diastolic Blood Pressure	80.23±16	77.9±13.5	76.67±9.3	82.2±11.7
Weight	64.1±13.6	63.3±13.2	65.54±14.75	65.61±14.6

DISCUSSION

In the past decade, a number of cation exchange resins become available in clinical use for treatment of hyperkalemia of CKD. Sodium polystyrene sulphonate was the first available compound which becomes available to the market in early 1950's.[13] Later it was found out that administration of sodium polystyrene sulphonate to renal failure patients leads to worsening of oedema, poor blood pressure control, and excessive weight gain, owning to the release and absorption of sodium from the resin in the gut.[14] After this came to notice major emphases was placed on the use of calcium and aluminium containing exchange resins (not available in Pakistan, but used all over the world). Aluminium containing binders got the disadvantage of causing oral ulcerations and risk of aluminium toxicity in CKD patients. In comparison, the calcium containing resin leads to re-absorption of calcium from the gut, which might be beneficial for the CKD patients with hypocalcaemia secondary to vitamin D deficiency. In a study published it was reported that calcium resins might lead to hypercalcemia and worsening of calcifications in patients with renal failure if used for long time.[15] Majority of other studies did not show hypercalcemia as a side effect of calcium polystyrene sulphonate.[9,10,14] Till date no study has compared the two commonly used cation resins in regards to efficacy, safety and on their effect on serum electrolytes, blood pressure and weight in CKD patients. In our study we found both the resins are equally effective for treatment of hyperkalemia. We did not encounter any change in levels of other electrolytes (sodium, calcium and phosphorus) with the use of both resins, which could be because of usage for a shorter duration. It is known that with the sodium containing resin there is simultaneous binding with other cations like calcium which can lead to decrease in serum calcium levels. In renal failure patients serum calcium is already low because of deficiency of active vitamin D and this loss of calcium can have detrimental effects. Increased intestinal absorption of non-neutralized bicarbonate due to binding of magnesium and calcium by sodium polystyrene sulfonate is one of the fearsome side effect in patients with CKD.[16,17] We did not encounter this in our study. Because of the high content of sodium, sodium polystyrene sulphonate can leads to worsening of blood pressure control, a highly undesired side effect in CKD patients as this is known to cause rapid detoriation of residual renal function.[14,18,19] Though the systolic blood pressure remains same pre and post resin administration in both groups, a significant increase in diastolic blood pressure was noticed in patients given sodium polystyrene sulphonate in our study. Our study showed that calcium containing resins are as effective as sodium containing resins without causing hypercalcemia in patients with hyperkalemia and pre dialysis CKD. None of our patient develops weight gain or worsening of oedema, as seen in other studies with sodium polystyrene sulphonate.[13–15] This could be because of use of diuretics in majority of our study patients. Other undesirable side effect including nausea, loss of appetite, abdominal distension and abdominal pain were encountered in patients who received sodium polystyrene sulphonate as compared to patients who received calcium polystyrene sulphonate. CKD patients already have these problems due to the uremic state and so any drug precipitating or worsening these symptoms become undesirable in these patients. Intestinal necrosis is one of the known adverse effect with sodium polystyrene sulphonate[20–22] is not encountered in our study with both of the drugs. Our study has proven the comparative efficacy of two cation exchange resins in patients with CKD and hyperkalemia and highlighted side effects important in CKD patients

namely worsening of blood pressure and gastro intestinal adverse effects with sodium polystyrene sulphonate. More studies are needed in this regards.

CONCLUSION

The study showed equal efficacy of both drugs. Calcium polystyrene showed low side effect profile as compared to Sodium polystyrene in this study, suggesting it a better choice in patients with CKD.

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Address for Correspondence:

Dr Kiran Nasir, Assistant Professor & Consultant Nephrologist, The Kidney Centre Post Graduate Training Institute 197/9 Rafiqui Shaheed Road. Karachi, Pakistan
Cell: +92-334-3015711
Email: neph.kiran@yahoo.com