

EVALUATION OF SINGLE DOSE SODIUM POLYSTYRENE SULFONATE FOR MANAGEMENT OF HYPERKALEMIA AND ITS EFFECT ON OTHER SERUM ELECTROLYTES

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ABSTRACT

Objective: To assess the effectiveness of sodium polystyrene sulphonate in treating hyperkalemia and its effect on different serum electrolytes level.

Study Design: Quasi-experimental study.

Place and Duration of Study: Lyari general hospital, 500 bedded tertiary care public sector hospital at Karachi, from Jan 2017 to Mar 2017.

Material and Methods: Hyperkalemic patients were included in study who fulfilled inclusion criteria and were administered with single STAT 30 grams dose of Sodium Polystyrene Sulfonate. Serum electrolytes such as sodium, chloride, magnesium, phosphate and calcium were measured before and after 2 hours of administration of Sodium Polystyrene Sulfonate. Paired t-test was used as tool for statistical analysis.

Results: Significant ($p < 0.05$) decrease in serum potassium level with mean decrease of 0.61 mmol/L was observed in hyperkalemic patients ($n=83$) after single dose of Sodium Polystyrene Sulfonate. Among 83 studied patient, 67 (81%) recovered from hyperkalemia. Besides, there was significant ($p < 0.05$) increase in sodium level with a mean increase of 2.26 mmol/L. Serum magnesium and calcium levels were significantly decreased ($p < 0.05$) with mean difference of 0.02mmol/L and 0.13mmol/L respectively. No significant difference was found in serum chloride and phosphate levels ($p > 0.05$).

Conclusion: Sodium polystyrene sulphonate found to be effective in treating hyperkalemia and considerable changes in serum sodium level have been observed with minimal changes in serum magnesium and calcium levels.

Keywords: Electrolytes level, Hyperkalemia, Sodium polystyrene sulphonate.

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INTRODUCTION

High serum potassium level is an emergency condition that can lead to multiple therapeutic challenges like weakening of muscles, cardiac arrhythmias and paralysis. It is also a cause of increased death rates¹. More than 5mEq/L of serum potassium is called as Hyperkalemia. Hyperkalemia rarely appears among healthy individuals as potassium is well regulated by kidneys². When function of kidneys get disturbed then it might leads to increased potassium levels by various means such as increased potassium level due to decreased excretion by kidneys, movement of potassium outside the cell due to

metabolic acidosis and retention of dietary potassium¹. Therefore, to counter hyperkalemia Sodium polystyrene sulfonate (SPS) is frequently used either as a single agent or in combination with other drugs. SPS was approved in 1958 by FDA for the treatment of hyperkalemia. It is a cation exchange resin which acts by exchanging its sodium with potassium, but may also bind magnesium, calcium and ammonium³. Previously, SPS was used with cathartic agent for treating acute hyperkalemia especially in patients with end stage renal disease. However, the use was very limited because of unfavorable side effects and inconsistent effectiveness. Newer agents for treating hyperkalemia include sodium zirconium cyclosilicate and patiromer. They indicated promising outcomes in controlled

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Received: 18 Aug 2017; revised received: 22 Nov 2017; accepted: 11 Dec 2017

trials but are not easily available in many countries⁴.

In adults with chronic kidney disease, a fixed dose of 30 g of sodium polystyrene sulfonate orally once daily for 7 days significantly lowered mean potassium levels from baseline compared with placebo in a randomized trial⁵. SPS replaces its sodium ion with the potassium in the large bowel and causes increased potassium loss in stool. There are 1500 mg of sodium in 15 gram of SPS¹. Previously, SPS was also being used in combination with sorbitol but FDA in Sep 2009 released a black box warning against this combination for causing intestinal necrosis⁵. The use of sodium polystyrene sulfonate is also linked to certain side effects such as those related with gastro-intestinal tract like diarrhea and constipation. SPS use is also associated with systemic toxicities like sodium loading, hypocalcemia, hypomagnesemia, and colonic necrosis⁶.

Cation-exchange resins interact with negatively charged structural components. And this process of cationic exchange occurs all over the gastrointestinal tract with liberation of a cation from the resin and combining of other cations available. Following oral administration of SPS, a cation i.e. sodium ion is released from the resin in exchange for hydrogen ions in the stomach. As it moves down to small and large intestines where hydrogen ions are exchanged with those cations which are abundant in colon, such as potassium ions⁷. The liberation of extra sodium ions from SPS may progress to hypernatremia, edema, hypertension and even congestive heart failure in patients with acute or chronic renal failure^{8,9}.

This study aimed to evaluate the effectiveness of single 30 gram dose of SPS for treating hyperkalemia in patients who are secondarily diagnosed with high serum potassium. Moreover, the effect of single dose of SPS has also been evaluated on other serum electrolytes.

MATERIAL AND METHODS

The study was undertaken with informed patient consent in medical ward of Lyari General

hospital, a public sector tertiary care hospital. The hospital is a 500-bedded general hospital providing health care facilitates to eastern region of Karachi, Pakistan.

The study was carried during a study period of three months from Jan 2017 to Mar 2017.

This prospective quasi-experimental study includes those admitted patients in medical ward of hospital who were secondarily diagnosed with symptomatic or asymptomatic acute hyperkalemia through serum electrolyte level test which was done on daily basis in the morning for all the patients who require monitoring of serum electrolytes. Hyperkalemic state is defined as potassium serum blood levels above 5.1 mmol/L. Sample size was based on change in pre- and post-serum electrolyte level with $p=0.05$, study power=80%, effect size=0.3. Total 256 patients were selected by non-probability convenience sampling. The selected hyperkalemic patients included those patients who were given a single STAT dose of 30 grams of SPS prescribed by on-duty staff physician or consultant. The serum electrolyte level test was again repeated soon after 2 hours of dose to check change in serum potassium level and other serum electrolyte level i.e sodium, magnesium, phosphate, calcium and chloride.

Age above 18 years and less than 60 years, sodium polystyrene dose given via oral route and patients who have not been given any other medication for decreasing potassium serum level such as salbutamol nebulization, dextrose with insulin infusion or bicarbonate infusion before and after 2 hours of sodium polystyrene dose were included in the study.

Burns, trauma or patient with rhabdomyolysis, patients with severe renal impairment i.e creatinine clearance above 2.0 mg/dl or on peritoneal or hemodialysis and patient who been given any sodium, magnesium, chloride or phosphate containing intravenous infusion were excluded in the study.

Statistical Analysis

Data was expressed as mean \pm standard deviation. A paired t-test was used to evaluate the correlation between quantitative variables. A p -value <0.05 reflected significant correlation and p -value <0.001 denotes highly significant correlation.

RESULTS

During the study period of this prospective cohort research, a total of 256 patients were given SPS for treatment of hyperkalemia. Out of these 256 patients, 121 (47%) patients were given single STAT dose of 30gm sodium polystyrene while other 135 (53%) patients were given routine daily dosing of SPS. Of these 121 patients, 83 patients fulfilled the above defined inclusion criteria for

of 5.6-6 mmol/L, 19 (60%) patients serum potassium level found to be in normal range i.e below 5.1 mmol/L two hours after the single dose.

In contrast to lowering effect of SPS on serum potassium level, post dose analysis of serum sodium level found to be increased by a mean 2.26 mmol/L ($p>0.05$; 0.08) with a maximum and minimum increase of 4.2 mmol/L and 0.58 mmol/L in one patient respectively. None of the patients move towards hyper-natremia. a similar trend of slight increase in serum chloride level with mean increase of 0.37 mmol/L ($p>0.05$; 0.82).

For serum phosphate level, almost no

Table: Serum Electrolyte Level 30 minutes before dose (Pre- SPS Dose Level) and 2 hours after dose (Post-SPS Dose Level).

Electrolyte (mmol/L)	Normal level	Pre- SPS Dose Level	Post- SPS dose Level	p -value
Serum sodium	136-145	137 \pm 4.2	139.6 \pm 2.2	0.004
Serum Potassium	3.5-5.1	5.32 \pm 0.36	4.71 \pm 0.58	0.08
Serum Chloride	98-107	100.7 \pm 4.9	101.1 \pm 4.8	0.82
Serum Magnesium	0.66-1.07	0.78 \pm 0.2	0.76 \pm 0.1	0.68
Serum Calcium	2.20-2.50	2.35 \pm 0.1	2.25 \pm 0.2	0.61
Serum Phosphate	0.74-1.52	1.29 \pm 0.3	1.29 \pm 0.4	0.91

study.

Among these 83 studied patients, 52 (63%) were male and 31 (37%) were female patients. The mean age of patients was 47 \pm 8 (24-60) years with a mean body mass index of 27 \pm 1.3 (16-29) kg/m².

The study aims to find out the effect of single dose of SPS on level of other serum electrolytes apart from well-established fact on lowering serum potassium level. For serum potassium level, a single dose of SPS lowers mean serum potassium level by 0.61 mmol/L ($p<0.05$; 0.004) with a maximum lowering of 1.3 mmol/L and minimum of 0.1 mmol/L in one patient. for 51 (61%) patients of hyperkalemic state with serum potassium levels between 5.1-5.5 mmol/L, 48 (94%) patients serum potassium became normokalemic after single dose of SPS. For 32 (39%) hyperkalemic patients with pre-dose level

change i.e 0.03mmol/L ($p>0.05$; 0.91) was observed suggesting that SPS has no interaction whatsoever with phosphate ions. For serum magnesium and calcium levels, a similar trend appears with decrease in both electrolytes level was observed. For serum magnesium level, a mean difference of 0.02 mmol/L ($p>0.05$; 0.68) was observed in post-dose analysis with no patient reported to suffer from hypomagnesemia. Post-dose analysis of serum calcium levels reveals a mean difference of 0.13 mmol/L ($p>0.05$;0.61) with a maximum reduction of 0.24 mmol/L in one patient. Out of 83 studied patients, around 7 (8%) reported to suffer from hypocalcemia with their calcium levels falls below 2.10 mmol/L. a summary of pre-dose and post dose serum electrolytes level with mean \pm standard error is given in table. Box plot representation of pre- and post-dose serum blood level of different electrolytes is given in figure.

DISCUSSION

The finding of this study revealed that 30 grams STAT dose of SPS is effective for lowering the elevated potassium level in patients who are secondarily diagnosed with hyperkalemia. The difference in the mean values of pre and post administration indicates that this much dose reduces 0.61 mmol/L of serum potassium. Beside this it was also disclosed that single dose of 30 grams SPS slightly reduces the level of other cations like magnesium and calcium while there was increase in mean serum level of sodium after two hours of its administration. To the best of our knowledge, this study is first to demonstrate the

and neuromuscular complications. For this reason, cation exchange resins such as SPS are used clinically⁴. The findings of current study observed that single dose of 30gm of SPS are effective in treating the hyperkalemic state of patient to return back serum potassium level to within the normal range. Chi square analysis showed that single dose significantly ($p < 0.05$) reduced the serum potassium level in 67 (81%) studied hyperkalemic patients.

Nepal *et al*, reported a case of 44 years old woman who developed hyponatremia within few hours of administration of SPS and it was concluded that hyponatremia in this patient was

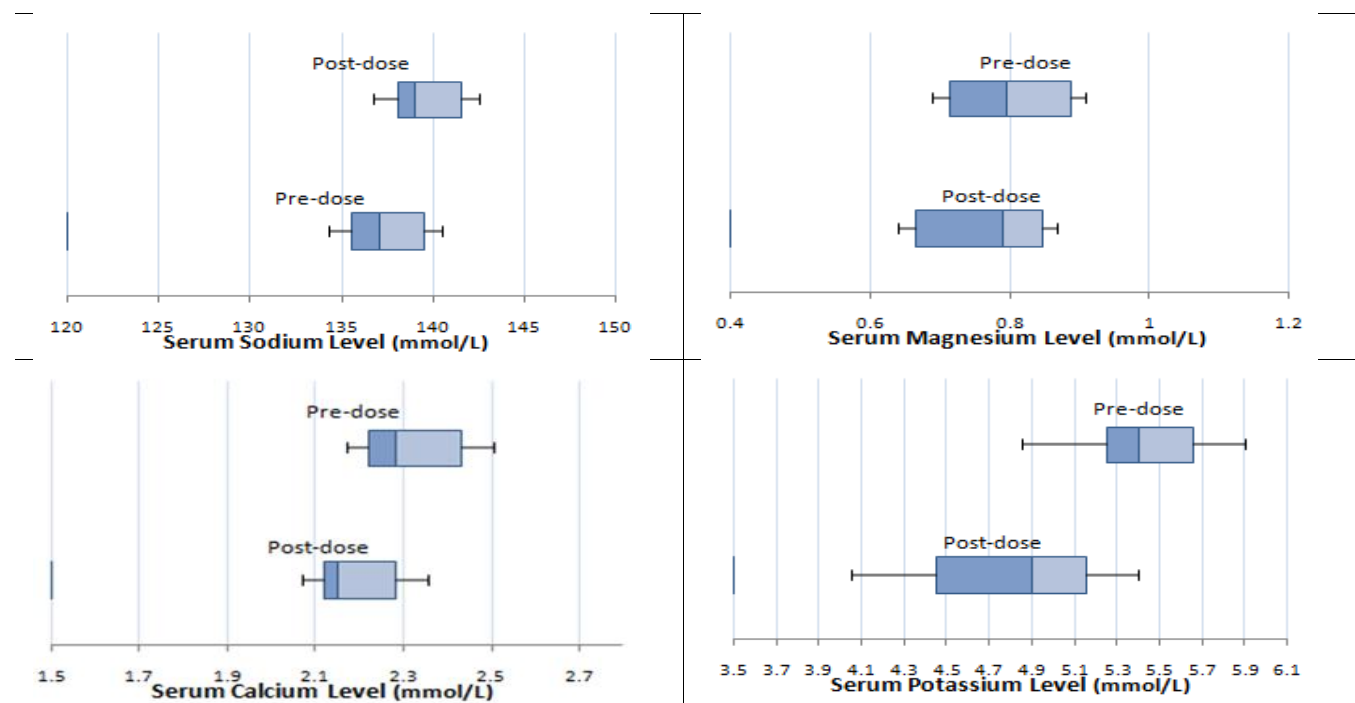


Figure: Box-Plot presentation of Pre-SPS dose and Post-SPS dose electrolyte levels.

effect of single dose i.e. 30 grams on serum electrolyte after two hours of its administration.

SPS is most frequent choice therapy, when serum potassium levels are high. Treatment choices for hyperkalemia are well documented, and urgent therapy is indicated for rapid and substantial elevations in serum potassium. On the other hand, less aggressive therapy could be recommended for patients with moderate elevations in serum potassium without cardiac

because of net intestinal water loss caused by profuse osmotic diarrhea stimulated by SPS therapy. It was ambiguous whether salt loading from the cation exchange mechanism contributed to hyponatremia¹⁰. Our findings of study also reported considerable but statistically non-significant ($p < 0.05$) increase in sodium level after giving single dose of SPS but none of the patient reported to be hyponatremic after 2 hours of ingestion of dose. One of the possible reasons was may be due to the fact that none of the

studied patient has serum sodium level above 143 mmol/L before the ingestion of dose. Filippi *et al*, also reported two other cases reported in extremely low birth weight neonates who developed hypernatremia within few hours of SPS administration. Although, both neonates presented clinical signs of dehydration but further clinical evaluation excluded dehydration as the reason of hypernatremia and suggested strong correlation with SPS¹¹. It is worthy to mention here that although this hypernatremia associated with SPS was in neonates but it was due again due to salt loading from SPS.

SPS is non-selective type of resin which does not specifically interact with potassium only. It may also effect other cationic serum electrolytes e.g. magnesium and calcium, therefore, SPS therapy is associated with hypomagnesaemia and hypocalcemia as clinical side effect. Diet deprived of essential minerals or use of diuretics for edema can intensify loss of these electrolytes along with the use of SPS and it might lead to life-threatening arrhythmias, especially in patients with cardiovascular diseases¹². Serum electrolytes monitoring and assessment of acid-base balance is necessary in such high risk patients⁸. Moreover, concurrent administration oral SPS and non-absorbable antacids/phosphate binders containing magnesium hydroxide, aluminum carbonate or calcium carbonate may produce an unexpected metabolic alkalosis. Hypomagnesaemia and systemic alkalosis are rare adverse events that have been reported with SPS therapy¹³⁻¹⁸. Recently two cases of acute hypocalcaemia and associated metabolic alkalosis have been reported with the use of SPS, warranting attention of clinicians to potential risk of SPS in paediatric population¹³. Newer agents have been studied for the use in management of chronic hyperkalemia in patients with chronic kidney disease like sodium zirconium cyclosilicate which is selective for potassium cation and patiromer which is calcium based therapeutic agent for treatment of hyperkalemia⁶.

The results of our study are consistent with these adverse effects of SPS i.e. hypomagnesaemia

and hypocalcemia⁵. However, the decrease in concentration of calcium and magnesium level were within the normal range, but still they require monitoring especially in patients with multiple cardiac risk and patient with renal impairment. Therefore, it is recommended that serum electrolytes as well as acid-base balance should be monitored closely in high risk patients.

CONCLUSION

SPS alone is found to be effective in treating hyperkalemia to substantial extent especially in patients with hyperkalemia ranging from 5.1-5.5 mmol/L with no cases reported to suffer from hypokalemia. Considerable but statistically non-significant increase in serum sodium and chloride levels with concurrent slight decrease in serum calcium and magnesium levels are reported with no patient leading to hypernatremia, hypocalcemia and hypomagnesaemia. But still precaution must be needed to monitor patient with chronic renal failure and congestive heart failure.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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