



EFFICACY OF SEVELAMER CARBONATE IN CKD PATIENTS: A SINGLE CENTRE STUDY

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ABSTRACT

Hyperphosphatemia is a common complication in chronic kidney disease (CKD) and is associated with increased cardiovascular morbidity and mortality. Sevelamer Carbonate, a non-calcium phosphate binder, is used to manage elevated phosphate levels. This study aimed to evaluate the clinical efficacy of Sevelamer Carbonate in reducing serum phosphorus levels in CKD patients. A single-centre observational study was conducted, involving 30 CKD patients, most of whom (86.37%) were in stage 5 CKD and received Sevelamer Carbonate (400 mg), primarily twice daily. The average age was 50.6 ± 13.58 years, with 66.6% being male. Sevelamer Carbonate significantly reduced serum phosphorus levels from 6.73 to 5.69 mg/dL ($p < 0.0001$) and the calcium-phosphorus product from 132.97 to 111.27 mg^2/dL^2 ($p < 0.0001$). Significant reductions were also observed in potassium and sodium levels ($p < 0.01$ and $p < 0.05$, respectively). However, no significant changes were observed in calcium levels, creatinine, PTH, albumin, hemoglobin, and venous bicarbonate levels. By the final follow-up, 65.38% of stage 5 patients and 25% of stage 4 patients achieved target phosphorus levels. The study confirms the efficacy of Sevelamer Carbonate in lowering serum phosphorus and calcium-phosphorus product levels in CKD patients, supporting its role in managing hyperphosphatemia and improving clinical outcomes.

KEYWORDS: Chronic Kidney Disease (CKD), Hyperphosphatemia, Sevelamer Carbonate, Phosphate Binder, Serum Phosphorus, Calcium-Phosphorus Product.

I. INTRODUCTION

Chronic kidney disease (CKD) is a progressive, irreversible condition characterized by long-term structural and/or functional abnormalities of the kidneys, typically defined by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m² for three or more months.^[1,2] CKD is classified into five stages based on GFR and into three categories based on albuminuria levels, which together help predict the risk of progression and adverse outcomes.^[1,3] In its advanced form, CKD progresses to end-stage renal disease (ESRD), defined by a GFR of less than 15 mL/min/1.73 m².^[2]

CKD is a growing global health concern. In 2017, more than 700 million people were affected worldwide, with a significant burden in China and India, accounting for over 250 million cases combined.^[4] In India, CKD prevalence is estimated at 800 per million population, with 150–200 per million progressing to ESRD.^[4,5] Alarming, the annual CKD-related deaths in India have doubled from 3.78 million in 1990 to 7.63 million in 2020, constituting 66.7% of total deaths.^[6] As the aging population and incidence of risk factors such as diabetes,

hypertension, and obesity increase, the global number of patients requiring renal replacement therapy is projected to exceed 5 million by 2030.^[4]

The pathophysiology of CKD is complex and multifactorial, involving glomerular, tubular, and vascular injury. Common initiating factors include glomerular hypertension, oxidative stress, immune complex deposition, and pro-inflammatory cytokines like TGF- β 1, which contribute to fibrosis and nephron loss.^[7] CKD progression is also influenced by modifiable risk factors such as smoking, poor diet, and uncontrolled hypertension or diabetes.^[8,9,10] Several studies have highlighted the strong association between CKD and cardiovascular disease, with complications like hyperphosphatemia playing a key role.^[11]

Hyperphosphatemia, a hallmark complication in CKD stages 4 and 5, arises due to impaired renal phosphate excretion. Elevated phosphate levels (>6.5 mg/dL) are associated with an 18–39% increase in mortality.^[11] Chronic phosphate retention contributes to secondary hyperparathyroidism, arterial calcification, and renal

osteodystrophy.^[12,13] Therefore, maintaining serum phosphate levels within the reference range (2.5–4.5 mg/dL) is crucial for improving outcomes in CKD patients.

Management of hyperphosphatemia typically includes dietary phosphate restriction, phosphate removal via dialysis, and the use of oral phosphate binders.^[14] Among these, Sevelamer Carbonate is a non-calcium, non-metal-based anion exchange resin that binds dietary phosphate in the gastrointestinal tract, reducing serum phosphate levels. It avoids complications associated with calcium-based binders, such as hypercalcemia and vascular calcification.^[15] Unlike Sevelamer Hydrochloride, Sevelamer Carbonate does not contribute to metabolic acidosis, making it preferable for long-term use in CKD patients.^[15]

While most data on the efficacy of phosphate binders come from studies involving dialysis patients, fewer studies have explored their impact in non-dialysis CKD populations. Nonetheless, phosphate control remains crucial across all CKD stages due to the independent risk posed by hyperphosphatemia, regardless of dialysis status.^[14]

In light of the high burden of CKD and the established risks of hyperphosphatemia, the current study aims to evaluate the efficacy of Sevelamer Carbonate in controlling serum phosphorus and associated biochemical parameters in CKD patients at Upasna Kidney Hospital, Mehsana.

II. METHODOLOGY

A single-centre observational study was conducted at Upasana Kidney Hospital, Mehsana, Gujarat, to evaluate the efficacy of Sevelamer Carbonate in patients diagnosed with chronic kidney disease (CKD). The study was carried out over a period of approximately three and a half months, from 28th December 2024 to 12th April 2025. All patients diagnosed with CKD and meeting the inclusion and exclusion criteria during this period were enrolled using a convenient sampling method.

Eligible participants included men and women aged 18 to 60 years, diagnosed with CKD stages 3 to 5 based on the Cockcroft-Gault estimated glomerular filtration rate (eGFR) between 15–45 mL/min/1.73 m², and presenting with hyperphosphatemia. Participants were required to provide informed consent and may or may not have been undergoing haemodialysis. Patients were excluded if they had poorly controlled diabetes or hypertension, malignant tumors, significant unstable medical conditions, severe gastrointestinal issues, hypersensitivity to Sevelamer, or if they were pregnant, lactating, below 18 or above 60 years of age, terminally ill, or unable to comply with the study protocol. Additional exclusions included enrollment in other interventional studies or use of sevelamer, other

adsorbents, or broad-spectrum antibiotics within the month prior to screening.

The study began with screening and identification of potential patients, followed by counselling and obtaining informed consent. Baseline data were collected, including demographic information (age, gender, height, weight, BMI), haemoglobin, renal and liver function tests, serum electrolytes, parathyroid hormone levels, CKD stage, and any concomitant illnesses. Patients were then treated with Sevelamer Carbonate for a period of 2 to 3 months. Follow-up assessments were conducted at the end of the treatment duration, during which all baseline parameters were re-evaluated.

The primary endpoint of the study was the response rate, defined by a reduction in serum phosphorus levels by at least 1 mg/dL in stage 3 patients, a level between 2.7 and 4.6 mg/dL in stage 4 patients, and below 5.5 mg/dL in stage 5 patients. Secondary endpoints included reductions in serum calcium levels and calcium-phosphorus product. Continuous variables were presented as mean $\pm$ standard deviation, and categorical variables as percentages. The Wilcoxon signed-rank test was used for statistical comparisons from baseline to end of the study, with a p-value of less than 0.05 considered statistically significant. Graphs were prepared using Microsoft Excel, and analysis was conducted using Statistical Kingdom (2017) and GraphPad Prism software.

The study protocol, along with the case report form and informed consent documents, was submitted to the Sarvajanic Clinical Research Ethics Committee (SCREC) and received approval prior to the initiation of the study. The research was carried out in accordance with the ICH-GCP guidelines and the New Drugs and Clinical Trial Rules, 2019. All participant information was treated with strict confidentiality.

III. RESULTS

A total of 30 patients meeting the inclusion and exclusion criteria were enrolled in the study. The baseline demographic and clinical characteristics are detailed in **Table 1**. The mean age of the participants was 50.6 ± 13.58 years, with a higher proportion of males (66.6%) than females (33.3%). The average Body Mass Index (BMI) was 24.47 ± 2.38 for males and 24.03 ± 7.93 for females.

Table 1: Demographic Data of Patients

Sr. No.	Characteristics	Sevelamer Carbonate (n=30)
1.	Age(year; mean $\pm$ SD)	50.6 $\pm$ 136.58
2.	Gender[n (%)]	
	Male	20(66.6)
	Female	10(33.3)
3.	BMI(mean $\pm$ SD)	
	Male	24.47 $\pm$ 2.38
	Female	24.03 $\pm$ 7.93
4.	Primary cause of CKD[n (%)]	
	Diabetes mellitus& Diabetic nephropathy	9(30)
	Chronic glomerulonephritis	4(13.3)
	Pyelonephritis	2(6.6)
	Polycystic kidney disease	3(10)
	Genetic	3(10)
	Unknown	17(56.6)
5.	Estimated GFR(mean $\pm$ SD)	
	Baseline	10.03 $\pm$ 3.72
	Follow up	10.1 $\pm$ 3.62
6.	CKD stage [n (%)]	
	4 (GFR 15-20 ml/min/1.73m ²)	4 (13.33)
	5(GFR <15 ml/min/1.73m ²)	26 (86.67)
7.	Symptomatology	
	Ache & pain	20(66.6)
	Anorexia	7(23.3)
	Nausea	16(53.3)
	Vomiting	12(40)
	Fatigue	24(80)
	Itching	9(30)
	H/O fracture	1(3.3)
	Swelling	3(10)
	Bony deformity	1(3.3)
8.	Dose [n (%)]	
	400mg	29(96.6)
	800mg	1(3.3)
9.	Frequency [n (%)]	
	BD	27(90)
	TDS	3(10)

The leading causes of CKD among the patients were diabetes mellitus and diabetic nephropathy (30%), followed by chronic glomerulonephritis (13.3%), polycystic kidney disease (10%), pyelonephritis (6.6%), and genetic causes (10%). However, in 56.6% of patients, the cause of CKD remained unidentified. According to the Cockcroft-Gault equation, the mean estimated glomerular filtration rate (eGFR) was 10.03 $\pm$ 3.72 mL/min/1.73m² at baseline and 10.1 $\pm$ 3.62 mL/min/1.73m² at follow-up. A large majority (86.67%) of the participants were in Stage 5 CKD.

Common symptoms reported included fatigue (80%), generalized aches and pains (66.6%), nausea (53.3%), vomiting (40%), anorexia (23.3%), and itching (30%). Swelling, bony deformities, and fractures were less frequently observed. Most patients (96.6%) were prescribed Sevelamer Carbonate at a dose of 400 mg, and 90% of them were on a twice-daily (BD) dosage regimen, while the remaining 10% were on thrice-daily (TDS) dosing.

3.1 Biochemical Parameters and Efficacy Outcomes

The primary endpoint of the study was to evaluate the response rate based on serum phosphorus levels. Responders were defined as those achieving the following targets:

- For stage 3 patients: a reduction of at least 1 mg/dL
- For stage 4 patients: phosphorus levels between 2.7–4.6 mg/dL
- For stage 5 patients: phosphorus levels less than 5.5 mg/dL

As depicted in **Fig. 1**, 25% of Stage 4 CKD patients and 65.38% of Stage 5 CKD patients met their respective target phosphorus levels. In total, 60% of all enrolled patients achieved the desired phosphorus control.

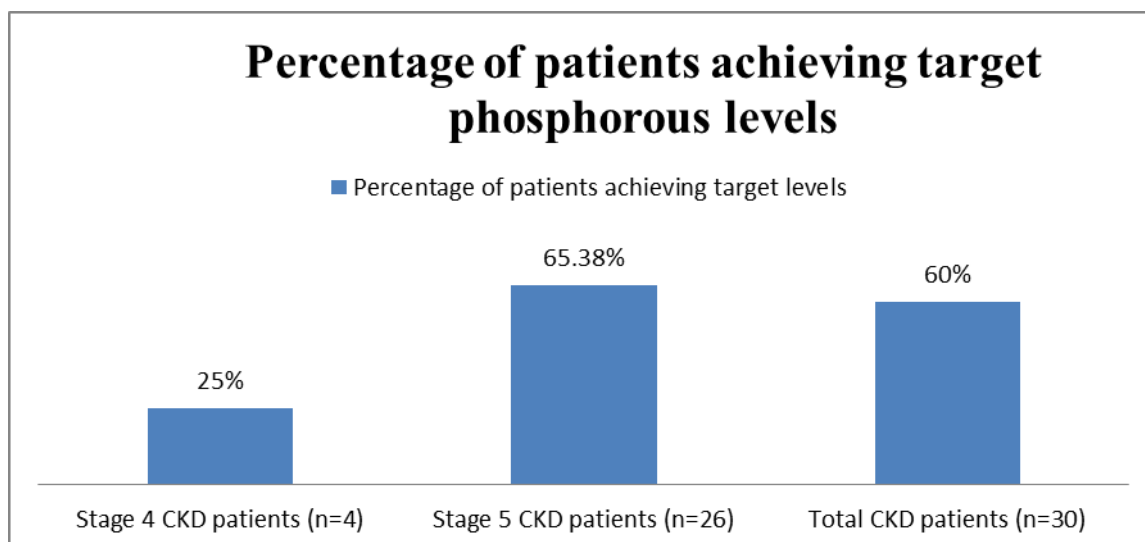


Fig. 1: Percentage of Patients achieving target Phosphorous levels.

Table 2 outlines the changes in biochemical parameters from baseline to the end of the study.

Phosphorus levels significantly decreased from 6.73 ± 1.86 mg/dL to 5.69 ± 1.57 mg/dL ($p < 0.0001$).

The **calcium-phosphorus product** also showed a statistically significant reduction, from 132.97 ± 46.60 mg²/dL² to 111.27 ± 40.51 mg²/dL² ($p < 0.0001$).

Calcium levels declined slightly from 20.24 ± 4.28 mg/dL to 19.93 ± 4.06 mg/dL, but the change was not statistically significant ($p = 0.67$).

Potassium levels dropped significantly from 5.132 ± 0.68 mmol/L to 4.75 ± 0.62 mmol/L ($p = 0.004$).

Sodium levels also showed a significant reduction from 142.94 ± 14.67 mmol/L to 138.55 ± 3.75 mmol/L ($p = 0.039$).

No significant differences were observed in **serum creatinine** ($p = 0.598$), **PTH** ($p = 0.784$), **albumin** ($p = 0.108$), **hemoglobin** ($p = 0.91$), or **venous bicarbonate** ($p = 0.367$).

Table 2: Biochemical Parameters of Patients.

Sr. No.	Parameters	Baseline (Mean $\pm$ SD)	Follow up (Mean $\pm$ SD)	p-value (Wilcoxon Signed Rank Test)
1.	Creatinine (mg/dL)	7.81 $\pm$ 2.55	7.79 $\pm$ 2.87	0.598
2.	Sodium (mmol/L)	142.94 $\pm$ 14.67	138.55 $\pm$ 3.75	0.039
3.	Potassium (mmol/L)	5.132 $\pm$ 0.68	4.75 $\pm$ 0.62	0.004
4.	Calcium (mg/dL)	20.24 $\pm$ 4.28	19.93 $\pm$ 4.06	0.67
5.	Phosphorus (mg/dL)	6.73 $\pm$ 1.86	5.69 $\pm$ 1.57	< 0.0001
6.	Calcium-Phosphorus product (mg ² /dL ²)	132.97 $\pm$ 46.60	111.27 $\pm$ 40.51	< 0.0001
7.	PTH (pg/mL)	255.39 $\pm$ 261.54	256.95 $\pm$ 256.77	0.784
8.	Albumin (g/dL)	4.28 $\pm$ 1.09	3.99 $\pm$ 0.90	0.108
9.	Hb (g/dL)	9.99 $\pm$ 2.41	9.85 $\pm$ 1.59	0.91
10.	Venous Bicarbonate (mmol/L)	19.16 $\pm$ 4.63	19.84 $\pm$ 3.49	0.367

IV. DISCUSSION

Hyperphosphatemia remains a frequent and clinically significant complication in individuals with chronic kidney disease (CKD), particularly in those with end-stage renal failure. Elevated serum phosphorus levels have been identified as a contributing factor to increased mortality, morbidity, and hospitalization rates in this population.^[16] This condition plays a central role in the development of CKD-related complications, including secondary hyperparathyroidism, mineral and bone disorders (MBD), and cardiovascular disease.^[16]

While dietary phosphate restriction is commonly advised, it is often insufficient to achieve effective control of serum phosphorus, especially in advanced CKD. Dialysis is also limited in its effectiveness at phosphate removal, due to phosphate's primary storage within the intracellular compartment. Consequently, the use of oral phosphate binders, such as Sevelamer Carbonate, becomes essential in reducing gastrointestinal phosphate absorption.^[16]

According to the KDOQI 2003 clinical practice guidelines, recommended serum phosphorus levels

should be maintained within 2.7–4.6 mg/dL for CKD stages 3 and 4, and between 3.5–5.5 mg/dL for stage 5 CKD. In our study, Sevelamer Carbonate therapy led to a statistically significant reduction in serum phosphorus levels. Specifically, 25% of patients with stage 4 CKD and 65.38% of those with stage 5 CKD achieved target phosphorus levels. Overall, 60% of the study participants were able to attain phosphorus levels within the guideline-recommended range.

These findings are comparable to those reported by Ketteler *et al.* (2008), who demonstrated a significant decline in mean phosphorus levels in hyperphosphatemic CKD patients not on dialysis following an 8-week Sevelamer Carbonate regimen. Their results showed target phosphorus levels were achieved in 75% of stage 4 and 70% of stage 5 CKD patients.^[17] Similarly, Bommer *et al.* (2004) documented a 50% response rate with Sevelamer therapy.^[18]

In the present study, a significant reduction was also observed in the calcium-phosphorus product—a finding consistent with previous literature.^[17,19] Although earlier studies have reported increases in serum calcium levels following Sevelamer Carbonate treatment^[17,19,20], our data showed a non-significant change in calcium concentration.

Parathyroid hormone (PTH) levels remained largely unchanged in our cohort, in contrast to other studies that noted a decrease in PTH following Sevelamer treatment. Since phosphorus levels influence PTH secretion, its reduction often leads to suppressed PTH levels, as previously reported.^[17,19,20]

A slight increase in bicarbonate levels was also noted post-treatment, suggesting a mild improvement in metabolic acidosis, a common condition among CKD patients.^[17]

Compared to traditional phosphate binders such as aluminium hydroxide and calcium-based agents, Sevelamer Carbonate offers several advantages. It does not contribute to systemic toxicity or calcium overload—an important consideration given recent evidence linking calcium-based phosphate binders with accelerated vascular calcification.^[21]

V. CONCLUSION

Phosphate retention and hyperphosphatemia is associated with poor outcomes and can affect the prognosis of CKD patients. Our study demonstrates that Sevelamer Carbonate is effective in significantly reducing serum phosphorus levels and calcium-phosphorus product in CKD patients, consistent with the existing literature. Its favourable safety profile and non-calcium-based mechanism make it a valuable option for managing hyperphosphatemia in advanced CKD.

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