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Efficacy of Sevelamer Hydrochloride in Attenuating Serum Phosphorus Levels in Elderly Patients with Dialytic CKD

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ABSTRACT

Background: *CKD related hyperphosphatemia is associated with CKD mineral and bone disorder (CKD-MBD), which has a high rate of disability among patients especially in the elderly, abnormal rise of serum phosphorus eventually leads to cardiovascular disabilities, left ventricular hypertrophy in patients who are on hemodialysis. Non-calcium, non-metal based phosphate adhering agent that can retard absorption of phosphate from alimentary canal thereby reducing serum phosphate level can prove to be more useful, one such agent is sevelamer hydrochloride.* ***Objective:*** *To study the serum concentration of phosphorus in patients who were known case of chronic kidney disease from stages 3rd to 5th and their clinical profile and therapeutic outcomes with the drug sevelamer hydrochloride. This study also aims to highlight the role of sevelamer hydrochloride in CKD (3-5) and reduce the burden of hypertension (HTN), and chronic kidney disease (CKD).* ***Methodology:*** *Single centered, prospective observational study was conducted in a tertiary care hospital. It was conducted over a period of 6 months. A total of 64 patients were involved in the study, and data were collected through patient data collection form, treatment chart or case sheet and interaction with the patient.* ***Results:*** *Among recruited patients 46.03% were male and 53.96% were female, the majority was between 35-65 years of age. The 4th and 5th stage of CKD was seen in the majority of the subjects.* ***Conclusion:*** *Sevelamer hydrochloride is effective even in an elderly patient; diabetic sluggish retardation may be boon with sevelamer hydrochloride but may hinder the effect of other drugs that reduce serum creatinine levels and improves GFR.*

Keywords: Hyperphosphatemia, Coronary artery calcification, Cardiovascular mortality, Hemodialysis, Sevelamer hydrochloride

INTRODUCTION

Hyperphosphatemia is associated with CKD mineral and bone disorder (CKD-MBD), previous studies concluded that poor control of serum phosphorus is the reason behind the rise in mortality and morbidity among patients especially the elders. Elevated serum phosphorus levels among patients who are hemodialysis poses the risk of increased calcification of vascular tissue as it also affects the calcium metabolism, coronary artery calcification, and cardiovascular mortality has also been reported [1].

Kidney Disease Outcomes Quality Initiative (KDOQI) has given a set of instructions for different levels of severity of chronic kidney disease at an Estimated glomerular filtration rate (EGFR) between 15-59 ml/min/1.73m^2 (stage 3 and stage 4 CKD), the serum phosphate should be between 2.7 mg/dl and 4.6 mg/dl (0.87 mmol/l and 1.49 mmol/l). At an EGFR ≤ 15 ml/min/1.73m^2 (stage 5 CKD), the serum phosphate should be between 3.5 mg/dl and 5.5 mg/dl (1.13 mmol/l and 1.78 mmol/l) [2-4].

Sevelamer hydrochloride is non-calcium and metal-based phosphate adherent, which forms a non-absorbable complex when it comes in contact with dietary phosphate, which helps in further increase in serum phosphate level. Hemodialysis clears the remaining serum phosphorus thereby maintaining balance, this also helps in keeping calcium level in check, if not that may lead to overexpression of parathyroid hormone thereby playing a role in the reduction of the cardiovascular calcification [5,6].

PATIENTS AND METHODS

Data and Study Design

It is a single centered, prospective observational study. The study was undertaken after the approval of the Institutional Ethics Committee (IEC). It has been conducted in the Nephrology Department of Princess Esra Hospital, over a period of 6-months. A total of 64 patients data was collected through, patient data collection form, treatment chart or case sheet, and interaction with the patients.

Criteria

- The patient who were willing to participate with consent, either gender more than 18 years of age, patient who were undergoing hemodialysis, abnormal serum phosphate levels i.e >1.76 mmol/L (5.50 mg/dL) after 2 weeks before any phosphate adherent, willing to avoid intentional changes in diet such as fasting or dieting were enrolled in the study
- Patients with a history of peritonitis, dysphagia, swallowing disorder, bowel obstruction, or severe gastrointestinal motility disorder, patient with under controlled diabetes mellitus, hypertension, active vasculitis, Human Immunodeficiency Virus (HIV) infection, or any clinically significant, unstable medical condition, patients who were taking antiarrhythmic medication, seizure medications, patients who are heavy drinkers and tobacco users, if females are pregnant, planning on becoming pregnant in the next 6 months or breastfeeding, patients with a known hypersensitivity to sevelamer were excluded from the study

Statistical Analysis

Statistical analysis was split into the descriptive and inferential analysis. Excel was used to generate tables and graphs; students paired t-test was used for the comparison of before and after the administration of sevelamer hydrochloride.

RESULTS

Descriptive Analysis

Among recruited patients 46.03% were males and 53.96% were females (Table 1 and Figure1), the majority were between 35-65 years of age (Table 2 and Figure 2). The 4th and 5th stage of CKD were seen in the majority of the subjects (Table 3 and Figure 3). Hypertension and diabetes were present among all patients some of them were suffering from more than 2 years, some of them for more than 5 years.

Table 1 Distribution of patients based on sex

Gender	Number of patients	Percentage
Male	29	46.03%
Female	34	53.96%
Total	63	100.00%

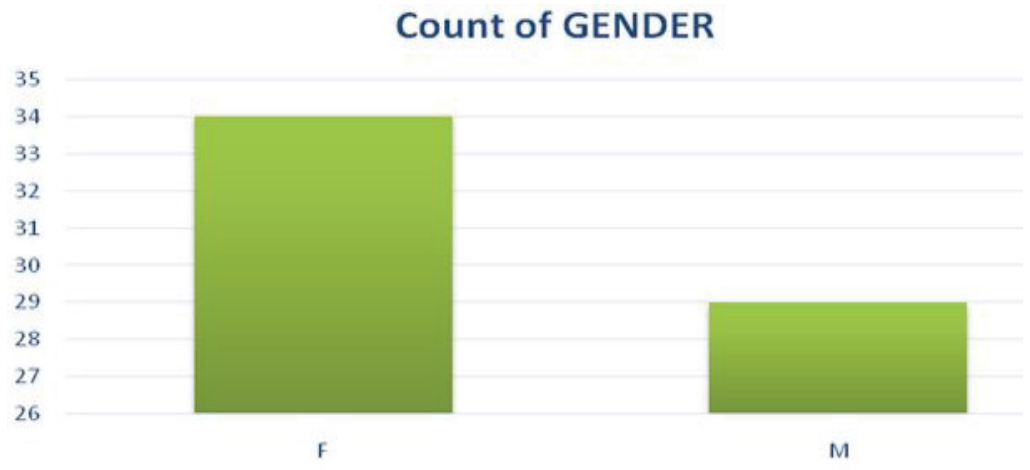

Figure 1 Distribution of patients based on sex

Table 2 Distribution of the patients based on age

Lower bound	Upper bound	Frequency	Relative frequency	Density
20.0	25.7	1	0.016	0.003
25.7	31.4	2	0.032	0.006
31.4	37.1	3	0.048	0.008
37.1	42.8	11	0.175	0.031
42.8	48.5	6	0.095	0.017
48.5	54.2	13	0.206	0.036
54.2	59.9	12	0.190	0.033
59.9	65.6	11	0.175	0.031
65.6	71.3	3	0.048	0.008

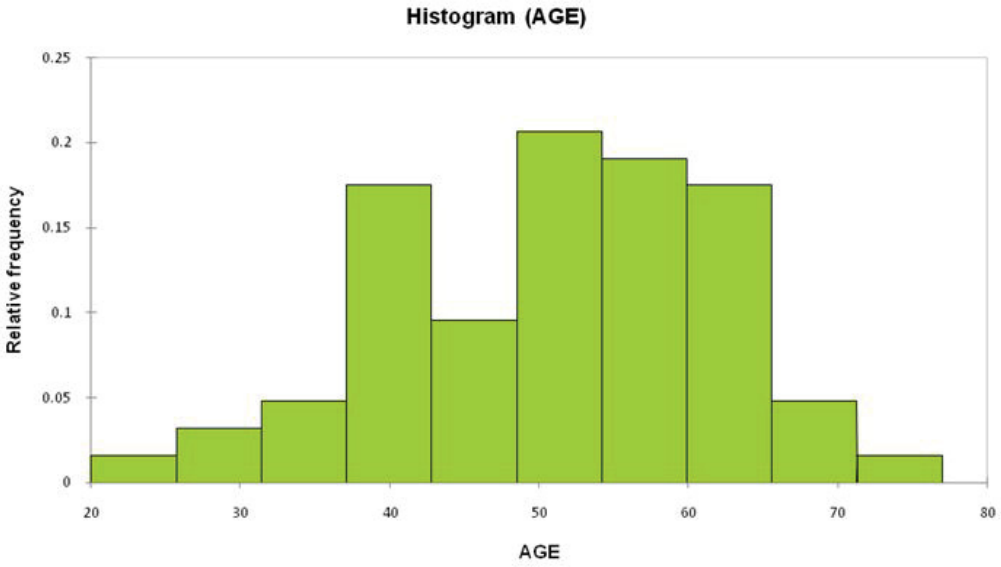

Figure 2 Distribution of the patients based on age

Table 3 Distribution of patient based on the stages of CKD

Lower bound	Upper bound	Frequency	Relative frequency	Density
3.00	3.21	6	0.095	0.454
3.21	3.42	0	0.000	0.000
3.42	3.63	0	0.000	0.000
3.63	3.84	0	0.000	0.000
3.84	4.05	17	0.270	1.285
4.05	4.26	0	0.000	0.000
4.26	4.47	0	0.000	0.000
4.47	4.68	0	0.000	0.000
4.68	4.89	0	0.000	0.000

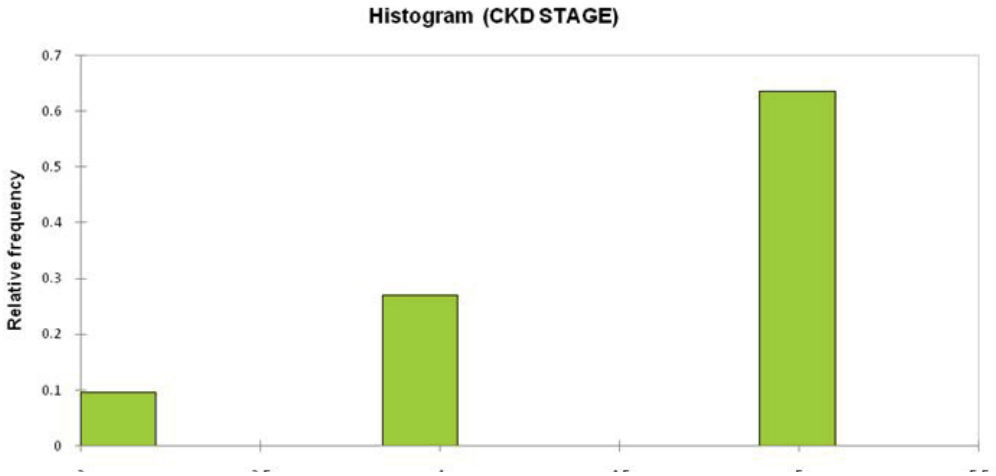

Figure 3 Distribution of patient based on the stages of CKD

Inferential Analysis

Serum phosphate levels after the administration of sevelamer hydrochloride would be less than before the administration of sevelamer hydrochloride, to test this hypothesis one-tailed student paired t-test was performed at a 95% confidence interval, i.e. at a probability of 0.05 (Figures 4 and 5).

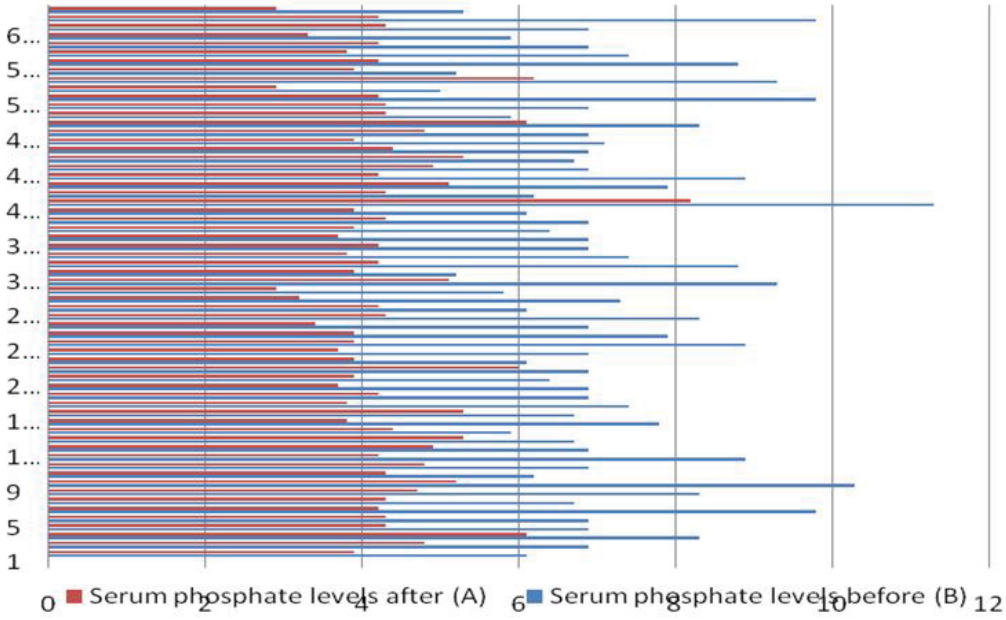

Figure 4 Serum phosphate levels before and after the administration of sevelamer hydrochloride, Blue: After the administration of sevelamer hydrochloride; Red: Before the administration of sevelamer hydrochloride

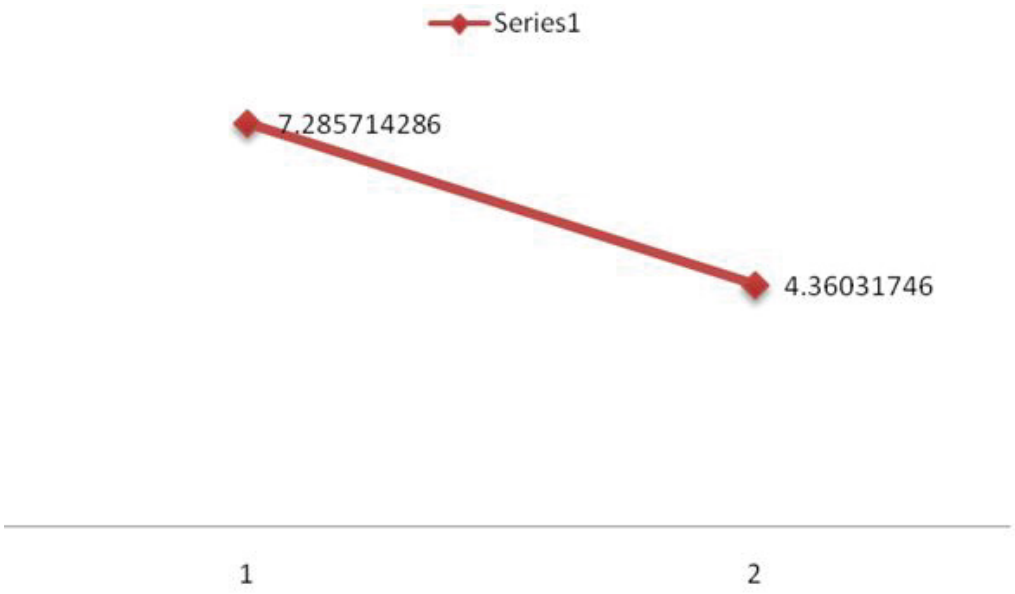

Figure 5 Difference in the mean of serum phosphate levels; 1: Before administration of sevelamer hydrochloride; 2: After administration of sevelamer hydrochloride

Logic of the Analysis

The analysis was done to know that the difference in the sample mean was small enough for us to confirm our hypothesis.

The difference in the mean was found to be 2.925396825 produced a T-statistic of 5.08356E-29. The T-distribution calculator was used to find p ($t<5.08356E-29$)=1.000 (Figure 5).

Interpretation of Results

The null hypothesis cannot be rejected, as p-value was found to be greater than 0.05 so we concluded that there is enough statistical evidence to support the original belief that serum phosphate level after the administration of sevelamer hydrochloride would decrease drastically.

DISCUSSION AND CONCLUSION

The study was carried out in the patients who had elevated serum phosphate levels. After initiation of the sevelamer hydrochloride the serum phosphate levels declined [7]. Elevated serum phosphate levels were associated with serious clinical implications such as mineral bone disease, secondary hyperparathyroidism, cardiovascular calcification, etc., which has raised disabilities among hemodialysis patients, the cornerstone of treating these ailments is a dietary restriction of phosphate along with phosphate adherents [8,9].

Gastropathy in diabetes is common, because of this malabsorption can occur which causes sluggish retardation of the drug in CKD, due to which patient suffers from hyperphosphatemia in which serum phosphorus balance cannot be maintained properly, which worsens with age-related sluggish retardation of the gastrointestinal tract, even with proper phosphate restriction in patients diet [10-12].

In this study majority of patients were diabetic and elderly, sevelamer hydrochloride binds with the dietary phosphate and retards its absorption into the serum but phosphate which is already present in the stomach can only be cleared through dialysis, in this study sluggish retardation and slow absorbing stomach increases the effect of sevelamer and thus serum phosphate levels, but this could backfire with other medicine that act after entering serum, thus we need more effective strategy in lowering phosphate [13-18]. This study showed that sevelamer hydrochloride is effective even in elderly patients; diabetic sluggish retardation may be boon with sevelamer but may hinder the effectiveness of other drugs that reduce creatinine level and improve GFR [19,20].

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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