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SAFETY ASSESSMENT OF PHOSPHATE BINDERS IN RENAL FAILURE PATIENTS UNDERGOING HEMODIALYSIS: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Hyperphosphatemia is a common complication among patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis. Oral phosphate binders are the cornerstone of therapy for controlling serum phosphate levels; however, their use is associated with adverse drug reactions (ADRs) that may affect treatment tolerability and patient outcomes. Careful safety evaluation is therefore essential to optimize therapy and minimize treatment-related complications. **Objective:** To evaluate the safety profile of phosphate binders in renal failure patients undergoing maintenance hemodialysis by assessing the incidence and pattern of adverse drug reactions associated with calcium acetate and sevelamer. **Methods:** A prospective observational study was conducted over a period of six months in the Hemodialysis Department of a tertiary care hospital in Kottayam, Kerala. Fifty adult patients receiving maintenance hemodialysis and prescribed phosphate binders were enrolled. Demographic details, clinical characteristics, phosphate binder therapy, and adverse drug reactions were documented using a structured data collection form. ADRs were evaluated throughout the study period, and descriptive statistical analysis was performed using IBM SPSS version 22.0. **Results:** Among the 50 study participants, 15 patients received calcium acetate and 35 received sevelamer. Gastrointestinal adverse effects were the most frequently observed reactions. Hypercalcemia was reported only among patients receiving calcium acetate (n = 2). Diarrhea occurred in two patients receiving calcium acetate and two receiving sevelamer. Constipation was observed only with sevelamer (n = 2), whereas colicky abdominal pain (n = 1) and gastritis (n = 1) were reported only with calcium acetate. Overall, calcium acetate demonstrated a higher frequency of adverse drug reactions than sevelamer. **Conclusion:** Phosphate binders were generally well tolerated in patients undergoing maintenance hemodialysis. Most adverse drug reactions were mild and predominantly gastrointestinal in nature. Calcium acetate was associated with a greater incidence of adverse reactions, particularly hypercalcemia, whereas sevelamer demonstrated a comparatively favorable safety profile. Regular monitoring of adverse drug reactions and individualized selection of phosphate binders are essential to ensure safe and effective long-term management of hyperphosphatemia in hemodialysis patients.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive disorder characterized by irreversible deterioration of renal function, resulting in impaired regulation of electrolyte and mineral homeostasis. As kidney function declines, phosphate excretion becomes inadequate, leading to hyperphosphatemia, a common complication among patients with advanced CKD and those receiving maintenance hemodialysis. Persistent elevation of serum phosphate contributes to chronic kidney disease–mineral and bone disorder (CKD–MBD), vascular calcification, secondary hyperparathyroidism, cardiovascular disease, and increased mortality. Consequently, effective control of serum phosphate is an important therapeutic objective

in the management of patients with end-stage renal disease (ESRD).

The management of hyperphosphatemia involves dietary phosphate restriction, adequate dialysis, and the administration of oral phosphate binders. Since dietary restriction alone is often insufficient and conventional hemodialysis removes only a limited amount of phosphate, phosphate binders remain the cornerstone of long-term treatment. Available phosphate binders include calcium-based agents such as calcium acetate and calcium carbonate, as well as non-calcium-based agents including sevelamer and lanthanum carbonate. These medications reduce intestinal phosphate absorption by binding dietary phosphate within the gastrointestinal tract, thereby lowering serum phosphate concentrations. Selection of an appropriate phosphate binder is influenced by efficacy, tolerability, safety profile, pill burden, and treatment cost.

Despite their therapeutic benefits, phosphate binders are associated with several adverse drug reactions that may compromise patient safety and adherence. Gastrointestinal adverse effects, including nausea, vomiting, diarrhea, constipation, abdominal pain, and gastritis, are among the most frequently reported reactions. Calcium-based phosphate binders may induce hypercalcemia and increase the risk of vascular calcification, adynamic bone disease, and secondary hyperparathyroidism with prolonged use. Aluminium-containing phosphate binders are associated with aluminium toxicity, osteomalacia, anemia, and neurological complications, whereas sevelamer has been linked to gastrointestinal intolerance and metabolic acidosis. Iron-based phosphate binders may result in iron overload, and lanthanum-containing formulations have been associated with tissue accumulation following prolonged exposure. These safety concerns necessitate careful selection of therapy and regular clinical monitoring during treatment.

Several studies have demonstrated that adverse drug reactions and high pill burden adversely affect medication adherence among patients undergoing maintenance hemodialysis. Poor adherence may result in persistent hyperphosphatemia, increasing the risk of cardiovascular complications, hospitalization, and mortality. Therefore, evaluating the safety profile of phosphate binders is essential not only to identify treatment-related adverse effects but also to optimize therapeutic outcomes and improve patients' quality of life. Continuous pharmacovigilance and individualized therapy can assist healthcare professionals in selecting safer treatment options while minimizing medication-related harm.

Considering the limited prospective safety data available in the local population, the present study was undertaken to evaluate the safety profile of phosphate binders in renal failure patients undergoing maintenance hemodialysis. The study primarily focused on identifying the incidence and pattern of adverse drug reactions associated with commonly prescribed phosphate binders and assessing their overall tolerability in routine clinical practice.

MATERIALS AND METHODS

Study Design

A prospective observational study was conducted to evaluate the safety profile of phosphate binders in renal failure patients undergoing maintenance hemodialysis. The study was carried out over a period of six months in the Hemodialysis Department of a tertiary care hospital in Kottayam, Kerala.

Sample Size Determination

- Hemodialysis patients in nephrology department.
- Sample size for a given means is

$$N= \frac{(Z_{1-\frac{\alpha}{2}})^2 \, p \, q}{E^2}$$

p is the estimated proportion of an attribute that is present in the population.

- q = 1-p.
- E is the acceptable margin of error.
  Based on a previous study the prevalence was 20.5%.
- Here p= 0.21
- q= 1-p= 1-0.21= 0.79
- z= 1.96 (assuming 95% confidence level)
- If we take at least 12 % precision, then E= 0.12.

$$N= \frac{z^2 \, p \, q}{E^2}$$

$$N= \frac{1.96^2 \text{ X } 0.21 \text{ X } 0.79}{0.1^2}$$

$$= 44.3$$

Anticipating loss to follow up and missing of data, the minimum sample size is rounded to be **50.**

Study Population

The study included adult patients diagnosed with chronic kidney disease and hyperphosphatemia who were receiving maintenance hemodialysis and prescribed oral phosphate binders. A total of 50 patients who fulfilled the study criteria were enrolled after obtaining written informed consent. Among the enrolled participants, 15 patients received calcium acetate and 35 patients received sevelamer according to the treating physician's clinical judgment.

Inclusion Criteria

- Adult patients (≥18 years) undergoing maintenance hemodialysis.
- Patients diagnosed with hyperphosphatemia receiving oral phosphate binders.
- Patients willing to participate and providing written informed consent.

Exclusion Criteria

- Patients unwilling to participate in the study.
- Patients with incomplete medical records.
- Patients not receiving phosphate binder therapy.

Data Collection

Relevant information was collected prospectively from patient medical records, laboratory investigations, treatment charts, and direct patient interviews using a structured data collection form. The following variables were documented

- Demographic characteristics (age and gender)
- Medical and medication history
- Dialysis frequency
- Type of phosphate binder prescribed
- Dose and frequency of administration
- Laboratory investigations relevant to patient monitoring
- Adverse drug reactions associated with phosphate binders

Safety Assessment

The primary outcome of the study was the assessment of adverse drug reactions associated with phosphate binder therapy. Patients were monitored throughout the study period for the occurrence of adverse events. Particular attention was given to gastrointestinal adverse effects and calcium-related complications. The recorded adverse drug reactions included.

- Hypercalcemia
- Diarrhea
- Constipation
- Colicky abdominal pain
- Gastritis

The frequency and distribution of these adverse drug reactions were documented separately for calcium acetate and sevelamer to compare their safety profiles.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 22.0. Descriptive statistics were used to summarize demographic variables and adverse drug reactions. Continuous variables were expressed as mean ± standard deviation where appropriate, while categorical variables were presented as frequencies and percentages. Student's t-test was used for statistical analysis where applicable, and a p value of less than 0.05 was considered statistically significant.

RESULT AND DISCUSSION

A total of 50 patients met with the inclusion criteria were included in the study.

Table 1: Frequency and percentage distribution according to age in years.

N=50

AGE	FREQUENCY (n)	PERCENTAGE (%)
31-50	13	26
51-70	25	50
71-90	12	24

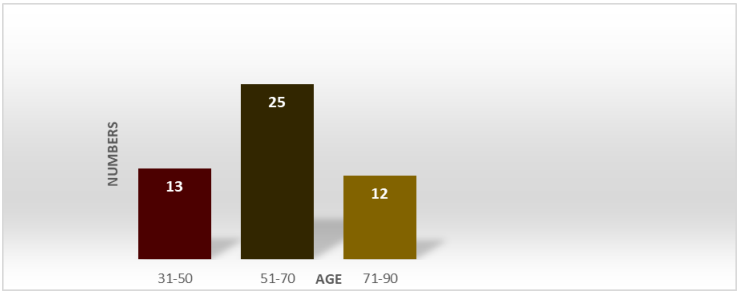

Fig. 1: Age wise distribution of study population.

INFERENCE: The above chart shows higher prevalence of patients with hyperphosphatemia in the age group of 51-70 years. This is potentially due to a combination of physiological, pathological, and lifestyle related factors.

Table 2: Frequency and percentage distribution according to gender.

N=50

GENDER	FREQUENCY (n)	PERCENTAGE (%)
MALE	32	64

FEMALE	18	36

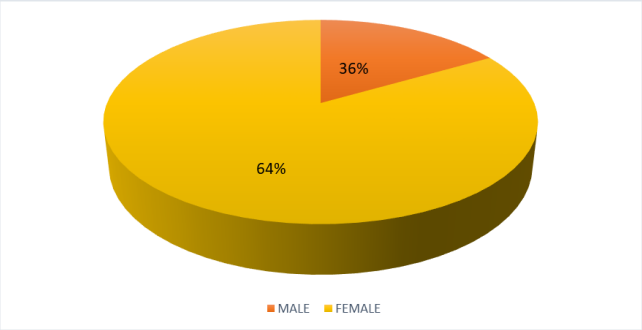

Fig. 2: Gender wise distribution of study population.

INFERENCE: This data highlights the prevalence of hyperphosphatemia with a higher percentage observed in males (64%). This is due to the increased muscle mass and protein rich diet in males.

Table 3: Percentage distribution based on the frequency of hemodialysis.

N=50

DIALYSIS/ WEEK	FREQUENCY (n)	PERCENTAGE (%)
1 DIALYSIS/ WEEK	13	26
2 DIALYSIS/ WEEK	26	52
3 DIALYSIS/ WEEK	11	22

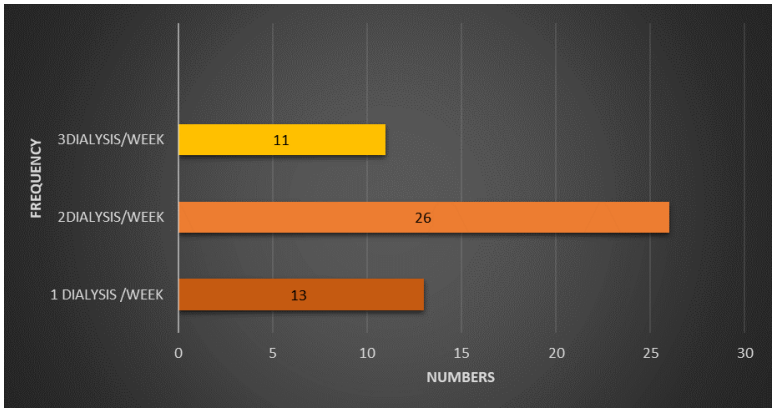

Fig 3: Percentage distribution based on the frequency of hemodialysis.

INFERENCE: This data shows that majority of patients with hyperphosphatemia (52%) undergoes hemodialysis twice weekly. Compared to twice weekly dialysis, once weekly dialysis was insufficient to remove body's phosphate burden. Better tolerability of patients were observed with twice weekly dialysis than thrice weekly dialysis**.**

Table 4: Distribution of adverse effects of phosphate binders.

N=50

ADVERSE DRUG REACTIONS	FREQUENCY	
	CALCIUM ACETATE	SEVELAMER
Hypercalcemia	2	0
Diarrhea	2	2
Constipation	0	2
Colicky pain	1	0
Gastritis	1	0

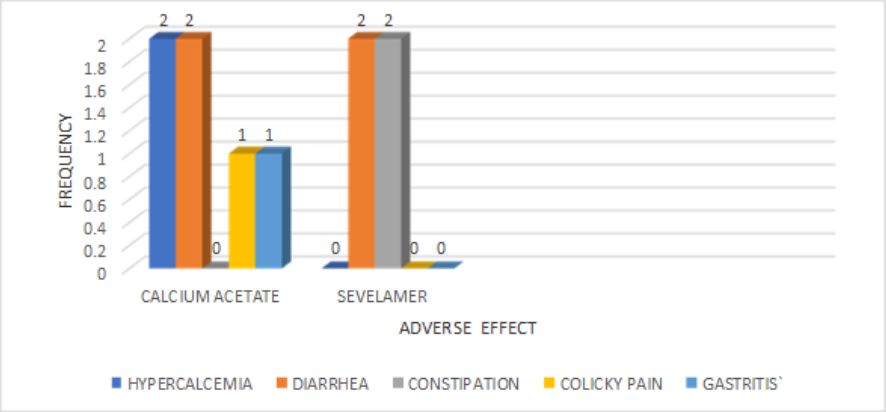

Fig. 4: Adverse drug reaction observed in the study population.

INFERENCE: The above chart shows the frequency of samples according to adverse effect. Hypercalcemia was reported only with calcium acetate, not sevelamer. Diarrhea was common with both drugs. 2 samples were reported constipation with sevelamer. Colicky pain and gastritis were reported with calcium acetate. More frequent adverse effect was reported in calcium acetate.

DISCUSSION

The present prospective observational study evaluated the safety profile of phosphate binders among patients with chronic kidney disease undergoing maintenance hemodialysis. The findings indicate that both calcium acetate and sevelamer were generally well tolerated, with most reported adverse drug reactions (ADRs) being mild and predominantly gastrointestinal. However, calcium acetate demonstrated a higher frequency and broader spectrum of adverse reactions compared with sevelamer.

In the present study, gastrointestinal adverse effects constituted the majority of reported ADRs. Diarrhea was observed in patients receiving both calcium acetate and sevelamer, while constipation occurred only among patients treated with sevelamer. In addition, colicky abdominal pain and gastritis were reported exclusively in the calcium acetate group. These findings are consistent with the known tolerability profile of phosphate binders described in the literature, where gastrointestinal symptoms are recognized as the most common treatment-related adverse effects.

Hypercalcemia was observed only among patients receiving calcium acetate and was not reported in those treated with sevelamer. This finding is clinically important because calcium-based phosphate binders increase intestinal calcium absorption, predisposing susceptible patients to hypercalcemia. Persistent hypercalcemia may contribute to vascular calcification, cardiovascular complications, and abnormalities in bone metabolism among patients with chronic kidney disease. Consequently, regular monitoring of serum calcium concentrations is recommended, particularly in patients receiving long-term calcium-based phosphate binders.

Sevelamer demonstrated a comparatively favorable safety profile in the present study. Although mild gastrointestinal adverse effects such as diarrhea and constipation were observed, no cases of hypercalcemia were reported among patients receiving sevelamer. These observations support the clinical preference for non-calcium phosphate binders in patients who are at increased risk of calcium overload or vascular calcification.

The results of this study highlight the importance of routine pharmacovigilance during phosphate binder therapy. Early identification and appropriate management of adverse drug reactions may improve treatment tolerability, promote medication adherence, and support long-term control of hyperphosphatemia. Clinical pharmacists can contribute significantly by educating patients, monitoring for medication-related adverse effects, and collaborating with nephrologists to optimize phosphate binder therapy according to individual patient characteristics.

The present study has certain limitations. It was conducted at a single center with a relatively small sample size of 50 patients, which may limit the generalizability of the findings. In addition, the follow-up period was relatively short, and long-term safety outcomes could not be evaluated. Larger multicenter studies with longer follow-up periods are warranted to further characterize the comparative safety of phosphate binders in patients undergoing maintenance hemodialysis.

Overall, the findings of this study demonstrate that phosphate binders are generally safe for use in maintenance hemodialysis patients. Nevertheless, careful selection of therapy, regular biochemical monitoring, and continuous assessment of adverse drug reactions remain essential to minimize treatment-related complications and improve patient outcomes.

CONCLUSION

The present study evaluated the safety profile of phosphate binders among patients with chronic kidney

disease undergoing maintenance hemodialysis. Overall, phosphate binders were well tolerated, and most adverse drug reactions were mild and predominantly gastrointestinal in nature. Calcium acetate was associated with a higher incidence of adverse drug reactions, including hypercalcemia, colicky abdominal pain, and gastritis, whereas sevelamer demonstrated a comparatively favorable safety profile, with only mild gastrointestinal adverse effects observed.

The findings emphasize the importance of individualized selection of phosphate binders based on patient characteristics and risk factors. Regular monitoring of serum calcium levels and adverse drug reactions is essential to ensure the safe use of phosphate binders and to prevent treatment-related complications in patients undergoing maintenance hemodialysis.

Further multicenter studies with larger sample sizes and longer follow-up periods are recommended to strengthen the evidence regarding the comparative safety of phosphate binders and to support evidence-based clinical decision-making in the management of hyperphosphatemia among patients with chronic kidney disease.

Declaration

Ethics Approval and Consent to Participate

The study protocol was approved by the Institutional Ethics Committee before commencement of the study. Written informed consent was obtained from all participants prior to enrollment.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Jaseela S: Conceptualization, data collection, data analysis, manuscript preparation.
Nandana Dayi: Data collection and literature review.
Neeraja Raj: Data collection and manuscript editing.
Chitra C. Nair: Study supervision, methodology, critical revision of the manuscript.
Beena P: Administrative support and final approval of the manuscript.

(Modify the author contributions to accurately reflect each author's role before submission.)

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