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ORIGINAL RESEARCH

STUDY OF *PHOSPHATE BINDER DRUG USE PATTERNS* IN CHRONIC KIDNEY DISEASE PATIENTS AT PRIVATE HOSPITAL SEMARANG

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Abstract

Introduction: Chronic kidney disease (CKD) is a progressive and irreversible end-stage renal disease or impairment of kidney function. Hyperphosphatemia is an independent predictor of cardiovascular disease and death in patients with advanced chronic kidney disease (stages 4 and 5) and is caused by impaired renal excretion of phosphate. Serum phosphate is usually managed with oral phosphate binders along with dietary phosphate restriction. **Method:** Descriptive with retrospective data collection using patient medical record data from July 2020 to December 2022 in the medical record room at Private Hospital X Semarang **Results:** The results of data analysis showed that 30 patients met the inclusion criteria. The results showed the accuracy of the use of phosphate binder drugs in chronic kidney failure patients, namely 100% correct patient, 100% correct indication, 100% correct drug, 100% correct dose in accordance with the literature. **Conclusion:** The pattern of phosphate binder use at Private Hospital X Semarang is in accordance with the literature

Background

Chronic kidney disease (CKD) is a progressive and irreversible end-stage renal disease or impairment of kidney function. According to the 2020 US Renal Data System, more than 14.9% of the adult population in America has chronic kidney disease (CKD) of varying severity (Johansen et al., 2021) . In Indonesia, the incidence of CKD increased from 0.2% in 2013 to 0.38% in 2018. Meanwhile, the incidence of chronic kidney disease in Central Java was 17.3% of 34 provinces, ranking 18th in the world. Hyperphosphatemia is an independent predictor of cardiovascular disease and death in patients with advanced chronic kidney disease (stages 4 and 5) and is due to impaired renal excretion of phosphate. This is usually managed with oral phosphate binders along with dietary phosphate restriction. These medications aim to lower serum phosphate. by reducing the absorption of dietary phosphate in the intestine (Chan et al., 2017) Management of hyperphosphatemia is necessary to reduce the absorption of phosphate levels in the blood (Sholihah, 2022) . In patients with CKD (Chronic Kidney Disease) on hemodialysis, calcium carbonate administration is very necessary to ensure adequate calcium and phosphorus intake to prevent hyperphosphatemia because phosphate levels in the body are higher in patients on hemodialysis. Based on the 2020 KDOQI (Kidney Disease Outcome Quality Initiative) guidelines, the recommended calcium intake is no more than 2000 mg (500

mg from diet/food and 1500 mg of calcium-based phosphorus binders) (Prasetya et al., 2022) .To achieve maximum therapeutic results, *phosphate binders* should be taken with food (which also limits calcium absorption), which is the most effective way to take the drug. Patient compliance with the medication also plays a role in achieving controlled serum phosphate levels (Chan *et al*., 2017) .

Method

Design This study uses a descriptive method with retrospective data collection using medical records of chronic kidney failure patients. Data collection This study was conducted at Private Hospital X Semarang in June 2023. The number of data samples obtained was 30 patients who met the inclusion criteria, namely inpatients diagnosed with chronic kidney failure with the use of phosphate binder drugs in the period July 2020-December 2022, patients aged ≥ 18 years, patients with complete Medical Record data. The instrument in the study used was a Data Collection Sheet and this study has been reviewed for ethical code, with *Ethical Clearance number* NO. 081/VI/KE/STIKES/2023.

Results

The study was conducted by taking patient medical record data. The initial sample obtained was 88 patients, of which 30 patients met the inclusion criteria and then 58 patients met the exclusion criteria. The final sample results obtained were 30 patients diagnosed with chronic kidney failure using phosphate binder drugs.

Table 1. Patient Characteristics

No	Information	Frequency (n=30)	Percentage (%)
	Patient characteristics		
1.	Gender		
	Man	17	56.7
	Woman	13	43.3
2.	Age		
	33-43	8	26.7
	44-56	10	3.3
	57-74	12	40.0
	Mean ± SD	2.1333± 8.1931	
3.	Severity of the disease		
	Stage 3	18	60.0
	Stage 4	2	6.7
	Stage 5	10	33.3

Based on Table.1 above, Characteristics of inpatients with a diagnosis of CKD at Private Hospital X Semarang for the period July 2020 – December 2022 based on gender, it was found that the patients were mostly male (56.7%) and female (43.3%). Based on age, the majority of patients were aged 57 – 74 years with a percentage (40.0%) and the highest disease severity was at stage 3 (60.0%).

Treatment Profile of Phosphate Binder Use

Table 2. Treatment Profile of Phosphate Binder Use

No	Information	Frequency (n=30)	Percentage (%)
Treatment Profile			
1.	Types of Drugs		
	$CaCO_3$ (Calcium Carbonate)	30	100
2.	Dose		
	CaCO3 (Calcium Carbonate) 500 mg	30	100
3.	Drug Frequency		
	24 hours	2	6.7
	12 hours	12	40.0
	8 hours	16	53.3
4.	Duration of treatment		
	1 day	8	26.7
	2 days	18	60.0
	3 days	3	10.0
	4 days	1	3.3
	Mean ± SD	1.90 ± 712	
5.	Dosage Form		
	Capsule	30	100.0

Based on data in Table 2 As shown above , the phosphate binder used is 100% calcium carbonate. The dosage form used for phosphate binder therapy is a capsule with a dosage strength of 500 mg. The maximum frequency of use is every 8 hours (53.3%). The duration of use of the phosphate binder itself ranges from 1-4 days and the maximum duration of administration is 2 days as much as 60%.

a. Right indication

According to Tuloli (2017), the appropriateness of indications for drug use is seen from the accuracy of deciding to administer drugs that are entirely based on medical reasons . Evaluation of the appropriateness of indications can be seen from whether or not the patient needs to be given medication based on complaints and diagnoses. Based on the results of the study obtained on the use of phosphate binders according to indications, namely a total of 30 patients with a diagnosis of CKD stage 3, stage 4 and stage 5 showed that all patients received appropriate indications for prescribing and using phosphate drugs. binder as indicated

b. Right Patient

Selecting medication based on the patient's condition can increase the therapeutic effect and prevent side effects that can worsen the patient's illness. Evaluation of the patient's appropriateness in using medication is carried out by comparing the contraindications of the medication given with the patient's condition according to the doctor's diagnosis **.** Based on the research results**,** it shows that the accuracy of selecting CKD stage 3, stage 4, and stage 5

patients is 100%. According to Inayatush (2022), phosphate binders are used by hemodialysis patients who experience high phosphate levels or hyperphosphatemia.

c. Right Medicine

The accuracy of this drug selection is seen from the use of phosphate binders, which are indicated according to the KDOQI literature. The accuracy of medication in patients with CKD in the inpatient ward is 100% appropriate. Drug selection is made after a correct diagnosis is made to achieve the desired therapy. Therefore, the selected treatment is appropriate for the disease's severity (Ministry of Health, 2011).

d. Right Dose

The administration of drug dosage can affect the desired therapeutic effect of the drug (Ministry of Health, 2011). The intended dose of phosphate binder is determined by the National Formulary and other supporting literature such as KDOQI and PERNEFRI. The results of this study are 100% accurate for chronic kidney disease patients in the inpatient installation of Private Hospital X Semarang.

Table 3. Evaluation data for the use of phosphate binder

Drug name	Number of Patients	Drug frequency	The dose given	Literature dose	Results
Calcium Carbonate	30	Every 24 hours Every 12 hours Every 8 hours	500 mg 500 mg 500 mg	500 – 1500 mg (KDOQI, 2020)	Appropriate

Based on the results in Table 3**,** it shows that 30 patients were given phosphate binder according to the dose or 100% at the correct dose.

Discussion

Based on the results of the evaluation of patient characteristics based on gender, it shows that the incidence of chronic kidney failure based on male gender (56.7%) is higher than female gender (43.3%). Everyone is certainly at risk of developing chronic kidney failure, but based on gender, the highest prevalence falls in men who are more susceptible to kidney disorders than women (Pernefri, 2016) . This is in line with research by Al Kamaliah (2021) which showed the highest results in men (51.76 %) and women (48.24%). Men are more susceptible to kidney disorders than women. This is influenced by the content of urinary compounds (natural compounds containing calcium, such as oxalate or phosphate, and other compounds such as the amino acid cysteine), hormonal influences, physical condition, and the patient's routine activities. Furthermore , men's urinary tracts are smaller, putting them at risk for kidney stones. Another contributing factor is a male lifestyle, particularly smoking. Male smokers are at higher risk of developing chronic kidney disease because smoking puts pressure on the kidneys, requiring them to work harder. Men's kidneys are twice as large as women's, and men are more likely to experience systemic diseases and have a family history of inherited diseases. Men are more susceptible to kidney disorders than women, such as kidney stones. Men's

lifestyles increase the risk of developing CKD due to smoking and alcohol consumption, which can put strain on the kidneys, forcing them to work harder. Alcoholic carcinogens, filtered from the body through the kidneys, alter DNA and damage kidney cells, thus affecting kidney function (Hartini, 2016).

Age characteristics , the results of the study showed that patients with chronic kidney failure were mostly aged 57-74 years (40.2%). This shows that patients aged 57-74 years are more numerous than those aged under that. The results of this study are in accordance with previous research, according to the results of Pranandari's (2015) research, clinically, patients aged > 60 years have a 2.2 times greater risk of experiencing chronic kidney disease compared to patients aged < 60 years. This is because with increasing age , what happens is a decrease in kidney function, a decrease in the rate of glomerular excretion and worsening tubular function. At the age of 40 years, the number of functional nephrons decreases by about 10% every 10 years, and at the age of 80 years, only 40% of nephrons are functioning. The Baltimore Longitudinal Study of Aging (BLSA) found that creatinine clearance decreased by an average of 0.75 mL/minute/year with age in respondents without kidney disease or other comorbidities, resulting in a decrease in filtration rate of 1 mL/minute after age 30. /1.73m. (Nasution *et al* ., 2020). Based on the results of the evaluation characteristics of the severity level (Stage), the results of the study showed that most patients with chronic kidney failure experienced stage 3 (60.0%). Phosphate binders are used by patients starting hemodialysis. This is in accordance with the KDOQI (2020) guidelines, which state that phosphate binders can be administered starting with a diagnosis of stage 3 and 4 CKD to maintain normal phosphate levels. They are also used in patients with stage 5 CKD or hemodialysis to maintain serum phosphate levels within the range of 3.5–5.5 mg/dl (Sholihah, 2022). Based on the results of the evaluation characteristics of the calcium-based phosphate binder dose used in inpatient installations, namely Calcium carbonate ($CaCO_3$) 500 mg. the evaluation characteristics, the dosage form used for calcium carbonate is in the form of capsules. Based on the results of the evaluation of the frequency of calcium-based phosphate binder use, the frequency of calcium carbonate administration was 6.7% at 24 hours, 40.0% at 12 hours, and 53.3% at 8 hours. This is in line with research by Al Kamaliah (2021), which stated that the highest frequency of calcium carbonate administration was 3x1 (99.36 %). This is in accordance with the KDOQI (2020) guidelines, which recommend the use of elemental calcium is no more than 2000 mg (500 mg from diet/food and 1500 mg of calcium-based phosphate binder). Based on the results of the evaluation characteristics, the most commonly used treatment durations were 2 days (60.0%), 3 days (10.0%), and 4 days (3.3%). This indicates that the duration of calcium carbonate therapy varies depending on the condition of each patient. (Al Kamaliah et al., 2021)

The appropriateness of drug use in this study refers to the rational use of drugs. A rational drug use pattern occurs when patients receive treatment according to their clinical needs, in appropriate doses, within an appropriate time period, and at an affordable cost. The appropriateness of drug use analyzed in this study includes the right patient, right indication, right drug, right dose, and alertness to side effects according to KDOQI (2020) obtained from medical records of chronic kidney failure patients at Private Hospital X Semarang from January

2020 to December 2022. Patient appropriateness is the accuracy of drug selection based on individual patient conditions to avoid contraindications (Sumawa et al., 2015) . Patient appropriateness needs to be considered to avoid errors in administering drugs to patients who are not suitable for the drug or whose conditions may increase the risk of side effects. The results of a study on patient appropriateness at Private Hospital X Semarang from January 2020 to December 2022 showed that 30 samples obtained a value of 100% for the accuracy of phosphate binder drug selection based on patient appropriateness. Phosphate binder drugs given to patients with chronic kidney failure include calcium carbonate. This study was conducted by reviewing patient medical records and found no history of allergies to calcium carbonate drugs. This is in line with Tuloli's research (2017). In this study, the value of drug use based on the right patient was 100% because all drugs prescribed to chronic kidney failure patients undergoing hemodialysis at the hemodialysis installation of Toto Kabila Regional Hospital in the period January 2017 - October 2018 were in accordance with the pathological and physiological conditions of the patients and did not cause contraindications for the patients. Indication accuracy refers to the correspondence between the indication and the doctor's diagnosis. Drug selection is considered appropriate if the drug is given based on the established diagnosis, namely chronic kidney failure with serum phosphate levels exceeding the range of 2.5-4.5 mg/dl according to the KDOQI or experiencing hyperphosphatemia.

The results of a patient accuracy study at Private Hospital X Semarang from January 2020 to December 2022 showed that 30 samples obtained were in accordance with the indication accuracy, reaching 100%. According to the Ministry of Health (2011), signs and symptoms of chronic kidney failure include high blood pressure, changes in urine volume, blood in the urine, shortness of breath, and swelling, especially in the feet and ankles. According to James (2022), common causes of hyperphosphatemia include decreased renal excretion of phosphate, diabetic ketoacidosis, and systemic infections. Signs and symptoms of hyperphosphatemia in most patients do not show immediate symptoms. However, hyperphosphatemia can remove calcium from the bones and blood which can lead to hypocalcemia. Drug appropriateness means that the drug used must have a therapeutic effect that is appropriate to the spectrum of the disease. Based on the results obtained, the accuracy of the drug was 100% for 30 patients. Phosphate binder drug therapy given to patients with chronic kidney failure can be in the form of calcium-based phosphate binder therapy or non-calcium phosphate binder therapy. In this study, the phosphate binder used was entirely calcium carbonate ($CaCO_3$) 500 mg. According to research by Al Kamaliah (2021), the most commonly used phosphate binder was calcium carbonate (99.68 %). This is in line with research by Sholihah (2022), where the most commonly used phosphate binders were calcium carbonate (62.03%), calcium acetate (10.13%), sevelamer carbonate (25.32%), and lanthanum carbonate (2.53%). The results showed that calcium carbonate was the most popular. Calcium carbonate is the most widely used phosphate binder because it has been proven to be effective and inexpensive (Sholihah, 2022).

Table **4** shows the results of a comparison showing the advantages and disadvantages of calcium and non-calcium based phosphate binders (Hutchison, 2008).

Phosphate Binder	Profit	Lack
Calcium carbonate	Aluminum-free, Moderately effective, Moderate pill load, Inexpensive	Efficiency is influenced by pH, Unpalatable, Hypercalcemia, GI side effects, Possible ectopic calcification
Calcium acetate	Aluminum free, Efficacy some pH dependent, Reasonably priced	Large tablets need to be swallowed, Hypercalcemia, GI side effects, Possible ectopic calcification
Sevelamer	Calcium and aluminum, No GI tract absorption, Moderate efficiency Lowers total and LDL cholesterol	Expensive, Efficiency affected by pH, High pill load, GI side effects, Binds fat-soluble vitamins
Lanthanum carbonate	Calcium and aluminum, Chewed not swallowed whole, High efficiency regardless of, pH, Low pill load	Expensive, GI side effects, Minimal GI absorption

According to Niko's research (2020), Calcium carbonate 500mg capsules were the most commonly used drug by CKD patients undergoing hemodialysis at Hospital X Bekasi in the period January - March 2020 (59.07%). Calcium carbonate is a type of multivitamin or supplement, which is used as an additional calcium for the body. Calcium carbonate is freely available and can also be used to treat stomach acid and for hyperphosphatemia (high blood phosphorus levels) in CKD patients.

Hyperphosphatemia in CKD patients occurs due to the release of phosphate from cells due to the frequent conditions of acidosis (very high acid levels in the body) and uremia (very high urea levels in the body). Calcium carbonate works by binding phosphate (phosphate binder) in the digestive tract, thereby reducing phosphate absorption. (Mahdiana, 2011) CKD patients undergoing hemodialysis have insufficient calcium and phosphorus intake because during dialysis the body cannot regulate phosphorus and calcium intake.

Dosage accuracy is analyzed by comparing the dose of medication received by the patient with the stated dose. Medication administration must be tailored to the patient's condition to achieve optimal results. A study conducted on dosage accuracy at Private Hospital X Semarang from July 2020 to December 2022 showed that 100% of 30 samples obtained a phosphate binder drug selection accuracy based on the correct dosage. This is consistent with Niko's (2022) study, which used 500 mg of calcium carbonate as the phosphate binder. Inayatush's (2020) study also used 500 mg of calcium carbonate. KDOQI guidelines (2020) recommend that calcium from elements

containing calcium binders should not exceed 1500 mg/day, which is in accordance with the dosage given to patients with chronic kidney failure at Private Hospital X Semarang. This is also in accordance with the dosage for patients with HD ≤2000 mg/day (Pernefri, 2016). Be aware of side effects. In this study, no side effects were found in inpatients at Semarang's X Private Hospital. According to research (Al Kamaliah *et al.* , 2021), a side effect of calcium supplements is constipation. Based on research at Ulin Regional Hospital in Banjarmasin, information on side effects from calcium use was obtained from patient medical records and complaints experienced by patients. A total of 18 out of 313 patients who used calcium supplements experienced side effects of constipation . This is in accordance with literature that states that calcium carbonate can have an impact on the digestive tract, for example, causing gas in the stomach (flatulence) and constipation (Ashley & Morlidge, 2008)..

Conclusion

The pattern of phosphate binder use at Private Hospital X Semarang is in accordance with the literature that is adjusted to the treatment standards, with results of 100% correct indications, 100% correct patients, 100% correct doses, and 100% correct drugs.

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