# Design of Phosphate Binder Used as Chronic Kidney Disease Therapy at General Hospital Dr. Iskak Tulungagung

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Abstract: Chronic Kidney Disease (CKD) can be defined as impaired kidney function that occurs for > 3 months or more. This was indicated by a decrease in Glomerular Filtration Rate (GFR) (<60 ml/minute/ 1.73m$^2$). CKD stage 3 has frequent hyperphosphatemia, a complication of the disease. The effects of hyperphosphatemia are the bone mineral connection and tissue calcification process. Phosphate binder was one of the therapeutic options that can be used for hyperphosphatemia. This study aims to determine the design therapy of phosphate binders used by CKD patients at hospitalization services of General Hospital Dr. Iskak Tulungagung. Observational research and retrospective. The presentation data has used descriptive of the medical record patients CKD hospitalized in the period Juli to December 2017. Phosphate binder has been used as a single therapy without combination, 130 patients (77%) used calcium carbonate, while 11 patients (7%) used calcium acetate, and of 27 patients (16%) had received switching therapy. The hyperphosphatemia therapy regimen used more calcium carbonate orally (3x500mg) in 121 patients (62%) than calcium acetate orally (1x169mg) in 16 patients (8%).



## 1 INTRODUCTION

Chronic kidney disease (CKD) can be defined as abnormalities in the structure or function kidney that occurred for three months or more (joseph T. DiPiro, Barbara G. Wells, 2015). Patients with GFR values > 60ml/min can't be said to suffer from CKD unless accompanied by a matter which shows the damage in the kidneys like disorders in urine composition, kidney structure, genetic diseases, and disorders that are detected by histological examination (Leung and Taal, 2007). The prevalence of CKD in Asia based on epidemiology in 2011, Indonesia ranks 10th out of 12 countries in Asia. CKD prevalence was higher in Central Sulawesi. The etiology of CKD that has occurred hypertension 44%, diabetic nephropathy 22%, and primary glomerulopathy / GNC 8% (Indonesian renal Registry, 2012).

The development of clinical manifestations in CKD patients one of which is impaired mineral homeostasis and bone nutrition (hyperphosphatemia and hypocalcemia) (Munoz *et al.*, 2014)(goleman, daniel; boyatzis, Richard; Mckee, 2019). Hyperphosphatemia causes complications including osteomalacia, fibrous cystic osteitis, and soft tissue calcification. This condition requires non-pharmacological therapy such as phosphorus diet, hemodialysis, and parathyroidectomy. Pharmacological therapies used are phosphate binder, vitamin D and calcimimetics. Effective therapy to overcome hyperphosphatemia has reduced phosphate absorption in the GI tract using phosphate binders (joseph T. DiPiro, Barbara G. Wells, 2015). If serum phosphorus levels can't be controlled by limiting food intake, the phosphate binder group can be used to bind phosphate to the digestive tract. The use of phosphate binders must be with a meal to bind the phosphate that is in food.

## 2 METHODS

This research was conducted in an observational descriptive manner and retrospective retrieval of data. This descriptive observational study aims not to treat



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the sample. Data were collected retrospectively because used patient's medical records (PMR) in the July-September 2017 period at General Hospital Dr. Iskak Tulungagung. Based on Patient's Medical Record (PMR) data for the period July-September 2017 obtained 218. The population that received inclusion criteria was 168 samples and 50 samples were excluded.

## 3 RESULTS AND DISCUSSION

The study showed 78 male patients (46%) and 90 female patients (54%). History of the disease based on this study included diabetes 53 patients (38%), hypertension 76 patients (55%), heart disease 5 patients (4%), and stroke 4 patients (3%). Disease complications in this study included anemia (39%), hypertension (17%), hyperkalemia (13%), diabetes mellitus (9%), dyspepsia (5%), pneumonia (4%), sepsis (3%), uremic syndrome (3%), CVA (2%), metabolic acidosis (2%), acute myocardial infarction (1%), decompensation Cordis (1%) and acute lung oedema (1%).

The study showed 78 male patients (46%) and 90 female patients (54%). The results of a study conducted by Yu et al., 2015 the women with diabetes had a higher risk of CKD than the men, which can't be explained by biological risk factors, depression or diabetes self-care (Yu, Katon and Young, 2015). Goldberg & Krause, 2016 showed the male has more potential to increase disease progression, but the prevalence CKD in women more often as a result of postmenopausal disease and diabetes (Goldberg and Krause, 2016). In this study, the highest percentage of patients with CKD were aged 51-60 years, namely 67 patients (40%). In a study by Delima, et al., 2017 the highest percentage was at age 52-60 years (28.2%) (Indrayanti *et al.*, 2019). Aging has been a natural biological process and the kidney has decreased function (Berlin, 2013).

History of the disease based on this study included diabetes 53 patients (38%), hypertension 76 patients (55%), heart disease 5 patients (4%), and stroke 4 patients (3%). As IRR data, 2015 etiology of CKD patients undergoing hemodialysis 44% have been caused by hypertension, and 22% caused by diabetes mellitus (Indonesian renal Registry, 2012).

Table 1 a profile of the use of phosphate binders. All patients received single therapy from phosphate binder, none of the patients received combination therapy.

Table 1: Profile of used of Phosphate binder therapy.

| Profile of Therapy | Patients * | % |
|---|---|---|
| Single | 195 | 100 |
| Combination | 0 | 0 |
| Total | 195 | 100 |

***** Each patient can get more than one phosphate binder therapy design

Table 2 shows the type of phosphate binder used in patients while being hospitalized. There was a switch/change in the use of phosphate binder both in changing the dose, frequency, or type of phosphate binder.

Table 2: Type of Phosphate binder used in CKD patients.

| Phosphate binder | Patients * | % |
|---|---|---|
| Calcium carbonate | 130 | 77 |
| Calcium acetate | 11 | 7 |
| Switch | 27 | 16 |
| Total | 168 | 100 |

***** Each patient can get two type phosphate binder therapy

The dosage regimen for the use of phosphate binders can be seen in Table 3.

Table 3: Profile of the use of a single therapeutic Phosphate binder in CKD patients.

| Regimentation dosis | Patients * | % |
|---|---|---|
| CaCO3 (1x500mg) PO | 36 | 18 |
| CaCO3 (2x500mg) PO | 16 | 8 |
| CaCO3 (3x500mg) PO | 121 | 62 |
| Subtotal | 173 | 89 |
| Ca-Asetat (1x169mg) PO | 16 | 8 |
| Ca-Asetat (2x169mg) PO | 3 | 2 |
| Ca-Asetat (3x169mg) PO | 3 | 3 |
| Subtotal | 22 | 11 |
| Total | 195 | 100 |

***** Each patient can get more than one phosphate binder therapy with difference regiment

Table 4 switch designs the use of phosphate binders. This study has been dominated by hypertension and diabetes mellitus. Disease complications in this study included anemia (39%), hypertension (17%), hyperkalemia (13%), diabetes mellitus (9%), dyspepsia (5%), pneumonia (4%), sepsis (3%), uremic syndrome (3%), CVA (2%), metabolic acidosis (2%), acute myocardial infarction (1%), decompensation Cordis (1%) and acute lung oedema (1%). Data from this study came as the results of a study by Wetmore, et al., 2016, comorbid conditions in CKD patients that often occur, namely anemia, and hypertension (Cozzolino *et al.*, 2018).

Table 4: Design of Substitution of Phosphate Binders in CKD Patients.

| Phosphate Binder | | | Patients | % |
|---|---|---|---|---|
| Design 1 | | Design 2 | | |
| CaCO3 (1x500mg) PO | → | CaCO3 (3x500mg) PO | 10 | 37 |
| CaCO3 (1x500mg) PO | → | CaCO3 (2x500mg) PO | 1 | 4 |
| CaCO3 (2x500mg) PO | → | CaCO3 (3x500mg) PO | 1 | 4 |
| CaCO3 (2x500mg) PO | → | CaCO3 (1x500mg) PO | 1 | 4 |
| CaCO3 (3x500mg) PO | → | CaCO3 (2x500mg) PO | 2 | 7 |
| CaCO3 (3x500mg) PO | → | CaCO3 (1x500mg) PO | 1 | 4 |
| CaCO3 (1x500mg) PO | → | Ca-Asetat (1x169mg) PO | 1 | 4 |
| CaCO3 (3x500mg) PO | → | Ca-Asetat (1x169mg) PO | 3 | 11 |
| CaCO3 (3x500mg) PO | → | Ca-Asetat (3x169mg) PO | 2 | 7 |
| Ca-Asetat (1x169mg) PO | → | CaCO3 (3x500mg) PO | 3 | 11 |
| Ca-Asetat (2x169mg) PO | → | CaCO3 (3x500mg) PO | 1 | 4 |
| Ca-Asetat (1x169mg) PO | → | CaCO3 (2x500mg) PO | 1 | 4 |
| Total | | | 27 | 100 |

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All patients received single therapy from phosphate binder, none of the patients received combination therapy. Table 2 a type of phosphate binder used. There are two types of phosphate binders used, namely calcium carbonate and calcium acetate. Research by Wang, et al., 2015 explains that calcium-based phosphate binders can increase serum calcium, there was no significant difference in calcium concentration between therapy using calcium carbonate and calcium acetate (Wang *et al.*, 2015). Based on research by Mai, et al., 1989 in the in vivo test.

This research showed the effectiveness of calcium-based phosphate binder in phosphate binding, the dose of calcium acetate and calcium carbonate which was equivalent to 50 mEq of calcium showed that calcium acetate was twice as much in phosphate binding (Mai *et al.*, 1989). Calcium acetate is more effective in binding phosphate because calcium acetate has more rapid solubility than acidic or basic conditions. Unlike calcium carbonate, it must be acidic to dissolve, and phosphate binding takes longer. Calcium carbonate has a fairly slow solubility compared to calcium acetate, so when consumed it need to chew, while calcium acetate doesn't. Based on the explanation, calcium acetate was more beneficial as a phosphate binder than calcium acetate.

Calcium carbonate (CaCO3) in acidic pH in the stomach would be broken down to form $Ca^{2+}$ and $HCO3^-$ or to form $Ca(HCO_3)_2$, both of these forms can be absorbed in the body (Engineering, 2006). When using calcium carbonate with food, the free calcium ions would bind to the phosphate ion to form a complex that cannot be absorbed. $HCO_3^-$ ions can be absorbed in the body so that they reduced metabolic acidosis. Study by Akatsuka, et al., 2008 administration of calcium carbonate in metabolic acidosis can increase $HCO3^-$ from 17.7 ± 0.5 mmol / L to 20.6 ± 0.7 mmol / L (Akatsuka, Mochizuki and Koike, 2008). Calcium-based phosphate binders such as calcium carbonate and calcium acetate were alkaline so that they have an effect on the correction of metabolic acidosis (Chávez Valencia *et al.*, 2018).

Table 2 shows the type of phosphate binder used in patients while being hospitalized. There was a switch/change in the use of phosphate binder both in changing the dose, frequency, or type of phosphate binder. The dosage regimen for the use of phosphate binders can be seen in Table 3. The dosage and type of phosphate binder that is often used is calcium carbonate (3x500mg) by mouth. Phosphate binders are most effective when taken with food (Setiani Agus, Effendi and Abdillah, 2014). It aims to bind the phosphate contained in food so that most of its use with a frequency of 3x1 with meals. The difference in the frequency of the used of phosphate binders in General Hospital Dr. Iskak based on the condition of the patient, especially the patient's food intake and laboratory data.

Table 4 switch designs the use of phosphate binders. The design changes in the type, daily dose, or frequency in the use of phosphate binders. The substitution of the phosphate binder is the same as the difference in the frequency of the used of phosphate binder. This change was also due to the patient's food intake and the patient's calcium laboratory data. Side effects of calcium-based phosphate binder are hypercalcemia, besides this in a state of hyperphosphatemia, CKD patients usually experience hypocalcemia due to reduced calcium absorption from food.

The maximum length of the phosphate binder has been used 1-3 days as many as 91 patients (54)%. The results from the duration use of phosphate binder in CKD patients only refer to the length of use during hospitalization, whereas to maintain phosphate

homeostasis this therapy not only used during hospitalization but also used as outpatient care. Goal therapy was to help reduce the amount of phosphate absorbed from food. Therefore the duration of use of phosphate binders doesn't indicate the actual duration of therapy. Duration hospitalization was 40% of patients treated for ≤ 4 days, 87% treated 5-10 days, 9% treated for 11-15 days and 4% treated for> 15 days. The length of patient care depends on the development of the patient's condition. Patients were discharged from the hospital with 166 patients (99%) and 2 patients (1%) forcibly discharged. None of the patients recovered fully due to hemodialysis.

## 4 CONCLUSIONS

Only one phosphate binder was used, 130 patients (77%) used calcium carbonate, 11 patients (7%) used calcium acetate, and 27 patients (16%) had a switch. Regimentation of the highest dose of calcium carbonate (3x500mg) PO in 121 patients (62%), while calcium acetate was the most (1x169mg) PO in 16 patients (8%).

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