Original Article

Comparison Between the Effect of Calcium Carbonate versus Calcium Acetate on Hyperphosphatemia in Patients with End Stage Kidney Disease

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ABSTRACT

Objective: To compare phosphate binding power and hypercalcemic effect of calcium acetate and calcium carbonate in patients of end stage renal disease on maintenance hemodialysis.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Nephrology Department, Sahiwal Teaching Hospital, Sahiwal from March 2022 to February 2023.

Materials and Methods: Seventy patients on hemodialysis were enrolled and divided into two groups by simple random numbering technique. Patients were given calcium acetate and calcium carbonate for period of two months after washout period of two weeks. Serum phosphate, calcium and albumin were noted. SPSS version 24 was used for data analysis.

Results: The average Ca (CaAc) and Ca ($CaCO_3$) of the patients was 2.31±0.17 and 2.82±0.11, respectively. The difference was statistically significant, ($p<0.001$). The average Po4 (CaAc) and Po4 ($CaCO_3$) of the patients was 1.28±0.19 and 1.71±0.10, respectively. The difference was statistically significant, ($p<0.001$). Whereas, the average albumin (phase-II) and albumin (phase-IV) of the patients was 38.59±3.42 and 34.72±4.49, respectively. The difference was statistically significant, ($p<0.001$).

Conclusion: Calcium acetate and calcium carbonate have a similar effect on serum phosphate levels and tolerance is also same. Calcium acetate results in a lesser frequency of hypercalcemia compared to calcium carbonate.

Key Words: Calcium carbonate, Calcium Acetate, Phosphate binding, Hemodialysis, end stage renal disease.

Citation of article: Khan SU, Jabbar MN, Nawaz A, Saif A, Waqas A. Comparison Between the Effect of Calcium Carbonate versus Calcium Acetate on Hyperphosphatemia in Patients with End Stage Kidney Disease. Med Forum 2023;34(8):98-101.doi:10.60110/medforum.340823.

INTRODUCTION

Serum phosphate (PO4) concentration is an essential parameter in the body, as phosphate plays a important role in various physiological processes, including bone formation, energy production, and cellular signaling[1]. The balance of serum phosphate levels is tightly regulated to ensure normal cellular function. In normal subjects, the kidneys are highly efficient in reabsorbing or excreting phosphate as needed, depending on the body's requirements[2].

This allows the body to maintain a relatively stable serum phosphate concentration even when the intake of dietary phosphate is increased significantly, up to 4000 mg/day, which is quite high[3].

In ESRD, the kidneys are unable to adequately filter and excrete waste products, including phosphorus, from the body[4]. Hyperphosphatemia refers to a condition where there is an abnormally high level of phosphorus in the blood. In ESRD patients, the impaired kidney function leads to an accumulation of phosphorus in the blood because the kidneys cannot effectively eliminate it[5].

Calcium salts, particularly calcium carbonate (CaCO3) and calcium acetate (CaAc), are being widely used in Pakistan as oral phosphorus binders for patients undergoing maintenance hemodialysis to control hyperphosphatemia[6]. Both calcium carbonate and calcium acetate serve the purpose of binding excess phosphorus from the diet, preventing its absorption and subsequently reducing its levels in the blood[7]. However, as mentioned, calcium carbonate has a hypercalcemic effect, meaning it can raise the levels of calcium in the blood[8].

On the other hand, calcium acetate has been reported to have similar phosphorus binding efficiency but with a less pronounced hypercalcemic effect[9]. This makes

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Received: April, 2023
Accepted: June, 2023
Printed: August, 2023

calcium acetate a preferable option compared to calcium carbonate for patients on maintenance hemodialysis, as it helps control hyperphosphatemia without causing excessive calcium levels in the blood[10]. Since there were no local published studies available for the ESRD population under consideration, this new study was designed to fill this gap in knowledge and provide insights into the comparative efficacy of the two calcium salts.

MATERIALS AND METHODS

Study conducted at Nephrology Department, Sahiwal Teaching Hospital, Sahiwal from March 2022 to February 2023 in one year. The study recruited seventy consecutive patients with end-stage renal disease (ESRD) who were already undergoing maintenance haemodialysis for at least 3 months. The study included both male and female participants aged 12 years and above.

Phosphate binding power refers to the ability of certain drugs to effectively bind and reduce the levels of phosphate in the blood serum. This is particularly important in patients with End-Stage Renal Disease (ESRD) because they often have impaired kidney function and are unable to excrete phosphate efficiently. Maintaining serum phosphate levels within the normal range (less than 1.61 mmol/l) is a desired effect as elevated phosphate levels can lead to various complications, including bone and cardiovascular problems. Hypercalcemia is characterized by elevated levels of calcium in the blood serum, typically defined as serum calcium levels greater than 2.54 mmol/l.

Patients who underwent parathyroidectomy and had advanced malignancy/metastasis excluded such patients and involved hemodialysis being performed two or three times a week. Additionally, the patients' other medications and usual diet were maintained without any changes during the study. The randomized controlled trial (RCT) investigating the effects of calcium acetate (CaAc) and calcium carbonate (CaCO3) on some parameters or conditions.

Both groups (participants receiving calcium acetate and calcium carbonate) stopped taking their respective medications (CaAc and CaCO3) for a period of 2 weeks. This is known as the washout period. The purpose of the washout period is to allow any residual effects of the previous treatments to wear off, ensuring a clean slate for the subsequent phases. After the 2-week washout period, baseline tests were conducted for all participants. Baseline tests are measurements or assessments of the relevant parameters or conditions before the participants begin any treatment. These baseline measurements serve as a reference point for comparison with the results obtained after the intervention phases.

Study involving two groups, A and B, where they were given different doses of calcium-containing substances for a period of 4 weeks (phase 2) and then underwent a 2-week washout period (phase 3). In phase 2 group A was given 4.002 g/day of CaAc, which contains 1.014 g of elemental calcium, and group B was given 5.625 g/day of CaCO3, which contains 2.25 g of elemental calcium. After the initial treatment period (phase 2) was completed, a "crossover" was implemented. In this phase, patients from group A switched to CaAc, and patients from group B switched to CaCO3. The crossover design allows each patient to serve as their control, as they receive both medications at different points in the study.

SPSS version 24 was used for data analysis. Numerical values presented as mean ± SD and categorical values were presented as frequency (percentages). Test of significance was applied. P value less than or equal to 0.05 was taken as significant.

RESULTS

Overall, 70 patients were included in this study, both genders in which41 (58.6%) males and 29 (41.4%) females. The mean age of the patients was 45.21±6.68 years. The mean duration of dialysis of the patients were 29.58±6.15 months. (Table. 1).

The average Ca (CaAc) and Ca ($CaCO_3$) of the patients was 2.31±0.17 and 2.82±0.11, respectively. The difference was statistically significant, ($p<0.001$). The average Po4 (CaAc) and Po4 ($CaCO_3$) of the patients was 1.28±0.19 and 1.71±0.10, respectively. The difference was statistically significant, ($p<0.001$). Whereas, the average albumin (phase-II) and albumin (phase-IV) of the patients was 38.59±3.42 and 34.72±4.49, respectively. The difference was statistically significant, ($p<0.001$). (Table. 2).

Table No. 1: Demographic and baseline characteristics of the study patients

Variable	Frequ-ency	%	Mean±S.D
Sex			
Male	41	58.6	
Female	29	41.4	
Age (years)			45.21±6.68
Duration of dialysis (months)			29.58±6.15

Table No. 2: Comparison of outcome variables of the study patients

Variable	Mean±S.D	p-value
Ca (CaAc)	2.31±0.17	<0.001
Ca ($CaCO_3$)	2.82±0.11	
Po4 (CaAc)	1.28±0.19	<0.001
Po4 ($CaCO_3$)	1.71±0.10	
Albumin (phase-II)	38.59±3.42	<0.001
Albumin (phase-IV)	34.72±4.49	

DISCUSSION

Choice of phosphate binder should be based on individual patient factors, such as their level of kidney function, the severity of hyperphosphatemia, and any other medical conditions they may have. Additionally, the dose and frequency of administration will be tailored to the patient's needs. In a study suggested that CaAc is better tolerated, binds phosphate more effectively, or causes less hypercalcemia compared to CaCO3 (calcium carbonate) in all situations. In another similar study by Saif et al[11] concluded that both calcium carbonate and calcium acetate have same effect in serum phosphate level but calcium carbonate has a higher propensity to cause hypercalcemia compared to calcium acetate.

Study conducted by Naghibi et al[12] on Iranian population reported more episodes of muscle cramps with use of CaAc but CaCo3 have no complaints of muscle cramps. Some international studies have claimed that a specific phosphate binder like CaAc is better than calcium carbonate (CaCO3) at binding phosphate. However, our study did not find calcium acetate (CaAc) to be superior to calcium carbonate in its phosphate-binding capabilities.

In a study conducted by Phelps et al[13] reported that serum phosphate level was lower after treatment with acetate compared to carbonate. Additionally, the Ca × P product and PTH (parathyroid hormone) levels were also significantly lower after the acetate treatment. Study conducted by Wang et al[14] suggested that calcium acetate is more effective in controlling hyperphosphatemia compared to calcium carbonate. This means that when patients take calcium acetate, it results in a more significant reduction of phosphate levels in the blood, which is a desirable outcome for managing hyperphosphatemia.

About forty to eighty percent of phosphate contents of our food absorbed in the bowel especially in patients of renal failure. By using phosphate binders, the amount of phosphate absorbed can be further reduced, thereby aiding in the management of hyperphosphatemia[15]. In a study on pediatric population, reported that both calcium acetate and calcium carbonate are effective in controlling hyperphosphatemia in pediatric hemodialysis patients. This is because they both bind to phosphorus in the gastrointestinal tract, preventing its absorption and reducing the amount of phosphorus entering the bloodstream.

Calcium acetate is more soluble property in both alkaline and acidic pH that make it more effective binder of phosphate[16]. One more advantage is that calcium acetate contains around 25% elemental calcium, while calcium carbonate only contains about 40% elemental calcium. This difference means that one gram of calcium acetate provides more elemental calcium than one gram of calcium carbonate[17].

CONCLUSION

Calcium acetate and calcium carbonate have a similar effect on serum phosphate levels. This means that both drugs are equally effective in lowering phosphate levels when taken as prescribed. Calcium acetate results in a lesser frequency of hypercalcemia compared to calcium carbonate. So, if a patient is prone to developing hypercalcemia, calcium acetate might be a more suitable choice.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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