J Nepal Health Res Counc 2011 April;9(18):67-70

Role of CaCO3 alone and CaCO3 plus Vitamin D3 in terms of Calcium Phosphorus Product in Chronic Kidney Diseases

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ABSTRACT

Background: CaCO3 alone and CaCO3 plus vitamin D3 metabolites are commonly prescribed in CKD patients. The objective of this study is to analyze the changes in Ca x P product, calcium level and phosphorus level in CKD patients receiving calcium carbonate alone and calcium carbonate with vitamin D3 in combination.

Methods: A prospective, cross sectionalstudy among CKD patients under maintenance hemodialysis two times a week were studied over a period of one year. The patients were divided into two groups receiving oral CaCO3 alone and CaCO3 plus vitamin D3 once a day. The patients were followed for 1 month and result of Ca x P product was analyzed accordingly.

Results: Mean decrease of Ca x P product in CaCO3 group is (50.42+/-8.85 to 47 +/-6.63) in one month, p value =0.001(0.6-5) and CI- 95%. There is also significant reduction of phosphorus level in CaCO3 group than CaCO3 plus vitamin D3 group. Mean decrease in phosphorus in CaCO3 group is (5.51+/-0.76 to 5.17+/- 0.05) in one month. P value =0.01(0.14-0.53) and CI 95%.

Conclusions: There is a significant decrease in Ca x P product and phosphorus level was observed in CKD patients taking CaCO3 alone.

Keywords: calcium carbonate, calcium phosphorus product, chronic kidney disease, vitamin.

INTRODUCTION

Calcium-phosphorus product (Ca x P),intact parathyroid hormone(iPTH) and vitamin D are the known regulatory factors regarding bone mineral disease and extra skeletal calcification in chronic kidney disease (CKD) patients. Metabolicparameter such as calcium, phosphorus, calcium phosphorus product (Ca x P), iPTH and vitamin D (calcitriol) must be maintained within target range to decrease cardiac risk and maintain homeostasis of body system.[1] The consequences of hyperphosphatemia includes the development and progression of secondary hyperparathyroidism and a predisposition to metastatic calcification when the Ca x P product is elevated. Both of these conditions may contribute to the substantial morbidity and mortality in CKD patients.Those in the highest quintile of the Ca x Pproduct (>72 mg^2/dL^2) had a relative mortality risk of 1.34 relative to those with products of 42 to 52 mg^2/dL^2 and mortality risk rose sharply when the phosphorus level increased above 6.5 mg/dl.[2] High phosphorus levels are known to inhibit 1, 25dihydroxyvitamin D synthesis in numerous studies.[3,4] Lower levels of 1, 25dihydroxyvitamin D are hypothesized to decrease cardiac contractility and to increase coronary calcification.[5] Stage 5 CKD patients experience 2 to 5 fold more coronary artery calcification than age and gender matched individuals.[6] Adding to it higher phosphorus and calcium phosphorus product have been

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more specifically linked to chronic heart disease (CHD) and sudden cardiac deaths.[7] So therapeutic prescription of calcium containing phosphate binder (CCPB) and vitamin D are crucial for maintaining therapeutic range ofCax P product.

METHODS

A prospective,cross sectional study was done on Kathmandu Medical College Teaching Hospital from April 2010 to April 20ll.The patients aged more than 18years under maintenance hemodialysis in different dialysis center twice a week were included in the study. Sample size of 85 was calculated using WHO sample size formula, taking power of 90%, 5% level of significance,and assuming standard deviation of 10 from previous studies. After the approval from ethical clearance committee of Kathmandu Medical College, patients were divided into two groups, one group taking oral calcium carbonate in specified doses while the other group taking calcium carbonate and vitamin D3(oral CaCO3 500mg thrice a day alone and calcium CaCO3 500 mg thrice a day andcalcitriol 0.25 mcg once a day) along with their previous antihypertensive medication except thiazide diuretic. At first patient taking CaCO3 was included in study then waited till patient taking Caco3 and D3 was admitted then both groups are included alternately. The patients were followed for successive 1 month and result of Ca x P product wasanalyzed accordingly. Increase in serum creatinine level due to acute renal failure (ARF), septicemia, acute tubular necrosis (ATN)and patients lost in follow up were excluded from the study.

Analysis was done usingcalcium level, phosporus level and ca x p product. The sample was analyzed before and after 1 month at KMC pathology lab.Comparable parameters in both groups were analyzed by using paired t test in stastistical package for social sciences (SPSS) software version 16 for windows.

Table 1.Base line characteristic of patients.

Variables	CaCO3 only (means + SD/ %) N=53	CaCO3 + D3 (means + SD/ %) N=41	P value at 95 %CI
Age	40.36+9.015	39.22+8.005	0.518
Sex- male	50.94%	51.21%	0.979
Hemoglobin	9.334+1.18	9.527+1.6	0.632
Calcium level	9.1208+.75278	9.2585+.66407	0.605
Phosphorus level	5.5151+.76996	5.5463+.95893	0.147
Ca x P product	50.4234+8.85084	51.4688+10.28251	0.180

RESULTS

Significant decrease in Ca x P product was observed in CKD patients taking CaCO3 alone than with CaCO3 and D3. Meandecrease of Ca x P product in CaCO3 group is (50.42+/-8.85 to 47 +/-6.63) in one month, p value =0.001(0.6-5) and CI 95%. There is also significant reduction of phosphorus level in CaCO3 group than CaCO3 plus vitamin D3 group.Meandecrease in phosphorus in CaCO3 group is (5.51+/-0.76 to 5.17+/- 0.05) in one month. P value =0.01(0.14-0.53) and CI 95%. However our study hasn't shown significant increase in calcium level in calcium carbonate plus D3 group.Significant different in comparable data is said when P value is less than 0.05 at 95% CI.

Table 2. Result of change in Ca x P product in two groups.

Groups	Ca x P product before 1 month mean + SD	Ca x P product after 1 month mean + SD	P value at 95% CI
CaCO3 (N=53)	50.42+8.85	47.52+6.63	0.001(0.6-5)
CaCO3 plus D3 (N=41)	51.4688+10.28	50.6937+8.44	0.000 (-1.9-3.48)

Table 3.Result of change in calcium and phosphorus level in calcium carbonate group.

Variable	Caco3befor	Caco3after	P value at 95% CI
Calcium	9.12 +0.75	9.166+0.56	0.71(-0.3-0.2)
Phosphorus	5.51+0.76	5.17+0.59	0.01(0.14-0.53)

Table 4.Result of change in calcium and phosphorus level in calcium carbonate plus D3 group.

Variable	Caco3 +D3before	Caco3+D3 after	P value at 95% CI
Calcium	9.25+0.66	9.46+0.61	0.09(-0.45-0.4)
Phosphorus	5.54+0.95	5.35+0.81	0.18(-0.96-0.48)

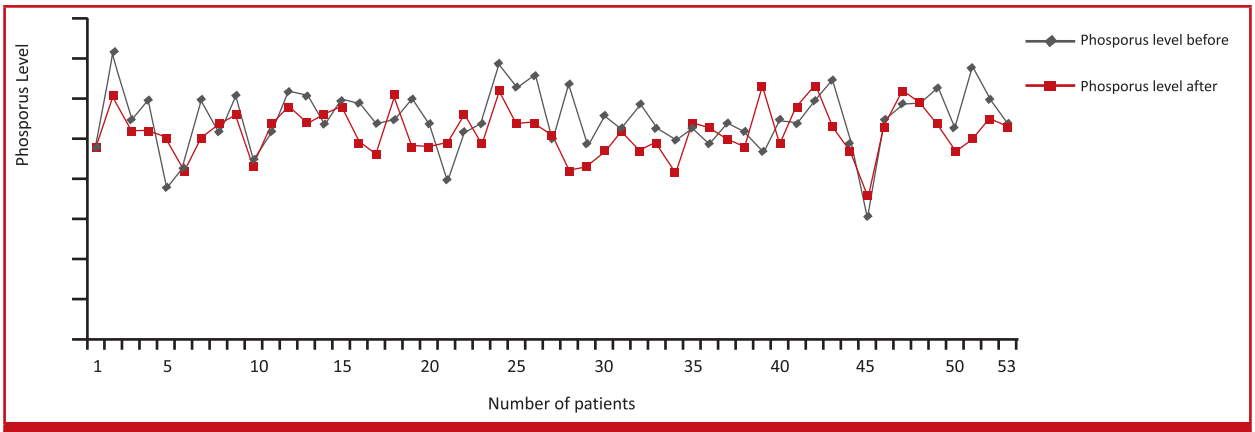

Figure 1.Decrease in phosphorous level after one month in calcium carbonate group.

DISCUSSION

The study was carried out to compare decrease in Ca x P product in patients taking CaCO3 alone (group a) and CaCO3 plus D3 (group b) in CKD patients. CKD patients are known to have mineral and bone disorder due to alteration in their calcium and phosphorus homeostasis.[8] This causes loss of normal regulatory mechanism of calcium and phosphorus in CKD patients due to renal dysfunction. Controlling serum phosphorus level in End Stage Renal Disease(ESRD) usually requires dietary phosphorus restriction, adequate dialysis, and the use of phosphate binders. CCPB, such as calcium carbonate and calcium acetate, are adequate in controlling the serum phosphorus levels but due to the high calcium load that they provide (especially with calcium carbonate) increase the calcium phosphorus product and stimulate vascular calcification.[9] Data suggest that high dose calcium administration in the absence of vitamin D therapy can suppress plasma PTH level while leading to optimal calcium and phosphate product in patients with mild hyperparathyroidism.[10] A strategy that relies upon calcium-containing phosphate binders increases the risk of positive calcium balance particularly in setting of concomitant vitamin D therapy. This may increase the risk of vascular calcification and arterial disease.[11]As vitamin D promote concentration dependent plaque calcification and atherosclerosis.[12] According to K/DOQI guideline serum level of phosphate should be maintain between 3.5-5.5 mg/dl,serum level of corrected total calcium should be maintain between 8.4-9.5 mg/dl and serum Ca x P should be maintain at less than 55 mg^2/dl^2.[13]

Our study showed a cleared reduction in Ca x P product with $CaCO_3$ alone. Adding D3 metabolite had minimal effect regarding reducing of Ca x P product. D3 metabolite is used to prevent secondary hyperparathyroidism in CKD patients and its limitations include hypercalcemia, hyperphosphatemia and suppression of bone turnover with risk of adynamic bone disease.[14]Our study did not look for iPTH level, so before starting D3 therapy iPTH level should be consider strongly. Due to cost and unavailability of the testingmany centers it is difficult to test iPTH level in each patient in our population. Since D3 as a phosphate binder is not well known phenomenon, however it increases the Calcium and phosphorus level.[15] In this study duration of dialysis in one session and duration of treatment of calcium carbonate or D3 or both before the study were not considered.

Our result was of shorter duration, so results might change if studies of longer duration and with more patients are included. A detail study in this issue is awaited in future.

CONCLUSIONS

Calcium carbonate alone can decrease the Ca x P product and phosphorus level significantly in CKD patients. In our country where most of people lives in poverty, before prescribing drugs and investigation compliance of its adherence should be consider. Prescribing a single drug along with its good advantage will be promising to our population.

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