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Original Research Article

An Assessment of the Effect of Sevelamer 800 mg and Calcium Acetate 667 mg with Meals on Biochemical Parameters among the Patients of Non-Diabetic Chronic Kidney Disease: A Non-Randomized Comparative Study

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ABSTRACT

Objective: To assess the effect of sevelamer 800 mg and calcium acetate 667 mg with meals on biochemical parameters among the patients of non-diabetic chronic kidney disease.
Methods: This was a prospective comparative study. The diagnosed cases of stable non-diabetic chronic kidney disease coming to the out/in patient clinic were included in the study. The study group was divided into two equal arms; one arm was continued on sevelamer 800 mg with meals (Group 1) and other calcium acetate 667 mg with meals (Group 2) for nine months. All the three levels were subsequently measured again at 6 and 9 months. Hb, TLC, S. urea, creatinine, S. Sodium, Potassium, Serum intact PTH and TSH were measured through standard method.
Results: There was no significant ($p>0.05$) difference in all the biochemical parameters between the groups at 0 month except for serum intact PTH and TSH. The Hb was significantly decreased in both the groups from 0 month to 9 month. TLC was significantly decreased in Group 1 only from 0 to 6 month ($p=0.03$) and 9 month ($p=0.02$) with higher mean change in Group 1 than Group 2. Similar pattern was observed for serum sodium, however, this was increased. Serum potassium was found to be significantly increased in both the groups from 0 to 9 month.
Conclusion: We found significant effect of both sevelamer and conventional phosphate binder calcium acetate on biochemical parameters.

Key words: Sevelamer, Calcium acetate, Biochemical parameters, chronic kidney disease.

INTRODUCTION

With changing life styles and growing use of modern equipment's CKD burden is growing and is expected to increase on the coming years. There is no specific treatment shown to slow the worsening of CKD. Patients with chronic kidney disease (CKD) stage 5 who receive hemodialysis therapy have a more than 10-fold increased risk for cardiovascular events compared with individuals with normal kidney function. [1] In addition to classic cardiovascular risk factors (e.g., arterial hypertension, smoking, dyslipidemia, family history), disturbances in calcium-phosphate metabolism contribute to vascular calcification and higher cardiovascular mortality in CKD patients. [2, 3]

A number of randomized prospective studies have found that sevelamer compared with calcium-based phosphate binders is associated with lower serum calcium levels and higher phosphate and PTH levels. [4-6] In the prospective "Treat-to-Goal" trial, 200 patients undergoing maintenance hemodialysis were

randomly assigned to sevelamer or calcium-based phosphate binders. [7] At one year, serum phosphate control was similar with both agents. The important issues with respect to the choice of sevelamer versus other agents are their relative effects on mortality, vascular calcification, bone disease, and biochemical effects, particularly hypercalcemia. [8]

Additionally use of sevelamer has been associated with amelioration of hyperuricemia, low fetuin A, decrease of uremic toxins, suggesting an anti-inflammatory action. [9] Although conventional dosing of sevelamer is effective, compliance with the requirement for thrice daily dosing with any phosphate binder can be problematic. A small crossover study found that thrice daily and once daily dosing were equally effective. [10] Although further study is required, once daily dosing may simplify the dosing regimen, thereby resulting in increased compliance and overall efficacy.

The present study was carried out to assess the effect of sevelamer 800 mg and calcium acetate 667 mg with meals on biochemical parameters among the patients of non diabetic chronic kidney disease.

MATERIALS AND METHODS

This was a prospective comparative study conducted in the Department of Medicine of tertiary care hospital in north India. The study was approved from the Ethical Committee of the Institute. The consent was taken from each participant after explaining the purpose of the study. The diagnosed cases of stable non-diabetic chronic kidney disease coming to the out/in patient clinic were included in the study. Cases with diabetes, hypercalcemia of malignancy, primary hyper parathyroidism, treatment with immunosuppressive agents, liver & thyroid disorders, organ transplantation and pregnancy were excluded from the study.

The study group was divided into two equal arms; one arm was continued on sevelamer 800 mg with meals (Group 1) and other calcium acetate 667 mg with meals (Group 2) for nine months. All the three levels were subsequently measured again at 6 and 9 months. Hb, TLC, S. urea, creatinine, S. Sodium, Potassium, Serum intact PTH and TSH were measured through standard method.

Statistical analysis

The results are presented in mean±SD. The variables between the groups are compared by using unpaired t-test. The changes in the variables were compared by using Paired t-test. The p-value <0.05 is considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

There was no significant (p>0.05) difference in all the biochemical parameters between the groups at 0 month except for Serum intact PTH and TSH. At 6 month, only Serum intact PTH and TSH were observed to be significantly (p=0.003) different between the groups. Serum intact PTH and TSH also significantly (p=0.003) different between the groups at 9 month. Gromerular filtration rate was found to be significantly higher in Group 2 (22.73±10.87) compared to Group 1 (16.46±6.54) (Table-1).

The Hb was significantly decreased in both Group 1 (p=0.008) and Group 2 (p=0.001) from 0 month to 9 month. The mean change in Hb was almost similar in both the groups from 0 to 9 month. TLC was significantly decreased in Group 1 only from 0 to 6 month (p=0.03) and 9 month (p=0.02) with higher mean change in Group 1 than Group 2. Similar pattern was observed for serum sodium, however, this was increased. Serum potassium was found to be significantly increased in both the groups from 0 to 9 month. Urea, serum creatinine, serum intact PTH and gromerular filtration rate were found to be significantly increased in both the groups from 0 to 6 month and 9 month. The TSH was significantly increased in both the groups only from 0 to 9 month (Table-2).

Table-1: Comparison of biochemical parameters between the groups at time intervals

	Time period		
	0 month	**6 month**	**9 month**
Hb			
Group 1	9.24±1.93	8.94±1.41	8.54±1.40
Group 2	8.79±1.93	8.50±1.51	8.14±1.53
p-value[1]	0.40	0.28	0.33
TLC			
Group 1	12061.54±3554.83	10992.69±2353.87	10511.15±2482.57
Group 2	10465.38±4307.01	10084.62±2588.07	10123.08±3199.66
p-value[1]	0.15	0.19	0.62
Serum sodium			
Group 1	135.69±6.58	140.38±6.19	139.65±7.69
Group 2	137.62±4.90	137.92±4.85	137.31±5.91
p-value[1]	0.23	0.11	0.22
Serum potassium			
Group 1	4.44±0.84	4.50±0.76	4.84±0.59
Group 2	4.26±0.78	4.51±0.64	4.87±0.68
p-value[1]	0.43	0.98	0.85
Urea			
Group 1	99.50±29.64	116.08±40.82	138.50±57.19
Group 2	103.29±51.69	111.00±47.11	120.00±47.34
p-value[1]	0.74	0.68	0.21
Serum creatinine			
Group 1	3.39±1.31	3.89±1.47	4.72±1.64
Group 2	3.99±2.54	4.42±2.65	4.86±2.72
p-value[1]	0.29	0.37	0.81
Serum intact PTH			
Group 1	148.15±64.07	184.58±82.02	245.96±98.72
Group 2	233.62±130.76	298.42±164.60	388.46±242.02
p-value[1]	0.004*	0.003*	0.008*
TSH			
Group 1	3.03±1.31	3.07±1.30	3.62±1.23
Group 2	2.49±0.72	2.79±0.98	2.94±0.68
p-value[1]	0.004*	0.003*	0.008*
Gromerular filtration rate			
Group 1	23.35±10.75	20.45±10.18	16.46±6.54
Group 2	30.35±15.21	26.08±12.95	22.73±10.87
p-value[1]	0.06	0.08	0.01*

Group 1=Sevelamer, Group 2=Phostat, [1]Unpaired t-test, *Significant

Table-2: Comparison of mean change in biochemical parameters in Group I and Group 2 from 0 month to subsequent follow-ups

	Mean change, p-value[1]	
	0 to 6 month	**0 to 9 month**
Hb		
Group 1	-0.29, 0.13	-0.70, 0.008*
Group 2	-0.28, 0.05	-0.65, 0.001*
TLC		
Group 1	-1068.84, 0.03*	-1550.38, 0.02*
Group 2	-380.76, 0.53	-342.30, 0.67
Serum sodium		
Group 1	4.69, 0.0001*	3.96, 0.03*
Group 2	0.30, 0.75	-0.30, 0.82
Serum potassium		
Group 1	0.06, 0.61	0.40, 0.02*
Group 2	0.24, 0.008*	0.60, 0.001*
Urea		
Group 1	16.57, 0.005*	39.00, 0.0001*
Group 2	7.70, 0.001*	16.70, 0.0001*
Serum creatinine		
Group 1	0.49, 0.001*	1.32, 0.0001*
Group 2	0.43, 0.001*	0.87, 0.001*
Serum intact PTH		
Group 1	36.42, 0.0001*	97.80, 0.0001*
Group 2	64.80, 0.0001*	154.84, 0.0001*
TSH		
Group 1	0.04, 0.74	0.58, 0.0001*
Group 2	0.30, 0.18	0.45, 0.03*
Gromerular filtration rate		
Group 1	2.89, 0.001*	6.88, 0.0001*
Group 2	4.26, 0.001*	7.61, 0.0001*

Group 1= Sevelamer, Group 2=Phostat, [1]Paired t-test, *Significant

DISCUSSION

Chronic Kidney Disease (CKD) is defined by National Kidney Foundation (NKF) as kidney damage for ≥ 3 months associated with structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR), manifested by either pathological abnormalities or markers of kidney damage. The NKF has classified chronic kidney disease into 5 stages. [11]

In our study, we have taken 74 patients were taken out which 16 were lost to follow up and 6 had to undergo dialysis and were subsequently not included in the study. Out 52 remaining patients various parameters like intact PTH, serum urea, serum creatinine, TSH, serum potassium and serum sodium were compared. After 6 months these 52 patients were divided into 2 groups randomly group 1 was given sevelamer and Group 2 conventional phosphate binder calcium acetate.

There was no significant (p>0.05) difference in the urea between the groups at 0 month 6 and 9 month. There was no significant (p>0.05) difference in the creatinine between the groups at 0 month 6 and 9 month. This finding was comparable to study by and George et al. [11]

There was significant (p<0.01) difference in the serum intact PTH between the groups at 0 month, 6 and 9 month. A significant change in serum intact PTH level was observed from 0 month (148.15±64.07) to 6 month (184.58±82.02, p=0.0001) and 9 month (245.96±98.72, p=0.0001) in Group 1. However, the change was also significant (p<0.01) in Group 2 from 0 month to 6 and 9 month. The mean change in serum intact PTH was lower in Group 1 than Group 2 from 0 month to 6 and 9 month suggesting that sevelamer was much more effective in maintaining calcium homeostasis in Group 1. Farkouh et al had also reported similar results. [12]

There was significant (p<0.01) difference in the TSH between the groups at 0 month, 6 and 9 months. A significant change in TSH level was observed from 0 month (3.03±1.31) to 9 months (3.62±1.23, p=0.0001) in Group 1. However, the change was also significant (p<0.01) in Group 2 from 0 month to 9 months. The mean change in TSH was lower in Group 1 than Group 2 from 0 month to 6 and higher at 9 months. These findings are in agreement with the by Chertow et al. [13]

There was significant (p<0.01) difference in the gromerrular filtration between the groups at 9 month. A significant change in gromerrular filtration level was observed from o month (23.35±10.75) to 6 month (20.45±10.18, p=0.001) and 9 month (16.46±6.54, p=0.0001) in Group 1. However, the change was also significant (p<0.01) in Group 2 from 0 month to 6 and 9 month. The mean change in glomerular filtration was lower in Group 1 than Group 2 from 0 month to 6 and 9 month. Farkouh et al had also reported similar results. [12]

CONCLUSION

We found significant effect of both sevelamer and conventional phosphate binder calcium acetate on biochemical parameters.

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