

# A comparative study of phosphate binders in patients of end stage kidney disease undergoing haemodialysis

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## Abstract

**Introduction:** Hyperphosphatemia is one of the complication in patients with chronic kidney disease on long term haemodialysis which will add on to the morbidity and mortality of the patient. This study was conducted in an attempt to compare the efficacy of phosphate binders prescribed to the patients of end stage kidney disease undergoing haemodialysis. It was a retrospective study in which medical records of patients with ESKD who received phosphate binders over past 2 years (2013 and 2014) were included in the study and divided into groups receiving sevelemer, calcium carbonate and calcium acetate and their baseline serum phosphate levels were compared with serum phosphate levels after 8 weeks of treatment and found that at the end of 8th week the difference in control of phosphate levels in sevelemer group compared with control group was highly significant with a p value of 0.003. The difference in control of phosphate levels in the calcium carbonate group compared with control group also had a significant result with p value 0.039. There were no significant differences in calcium acetate and control group with respect to serum phosphate level difference at the end of 8th week. There were no statistically significant differences between individual groups.

**Conclusion:** Our study confirms that phosphate binders significantly control the serum phosphate levels over a period of eight weeks treatment in ESKD patients on haemodialysis. However sevelemer was found to be more effective in controlling the serum phosphate levels but its high costs limits its use for the poor socioeconomic population.

**Keywords:** hyperphosphataemia, end stage kidney disease, phosphate binders, haemodialysis.

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## INTRODUCTION

With worldwide increase in morbid conditions such as hypertension, diabetes and malignancy, patients with renal disease also are growing in number.<sup>18</sup> It was found that the prevalence rate of end stage kidney disease has increased by 8% over past 5 years because of which end stage kidney disease reflects itself to be one of the major

health problems.<sup>19,20</sup> For the patients of end stage kidney disease, though haemodialysis helps in improvement of health and enhances survival, on long term, it will lead to decline in, quality of life as one of the reason for it being hyperphosphataemia.<sup>21</sup> Elevation in serum phosphate levels is one of the most common complications found in patients with late stage kidney disease which can affect up to 70% of the patients undergoing haemodialysis.<sup>1</sup> Large observational studies have proven that hypophosphatemia alone or in combination with high serum calcium levels in dialysis patients is associated with cardiovascular disease and mortality.<sup>4,6</sup> When the glomerular filtration rate (GFR) falls below 25 to 40 mL/min/1.73 m<sup>2</sup>, hypophosphatemia develops.<sup>5</sup> In accordance to Kidney Disease Improving Global Outcomes (KDIGO) guidelines, the frequency at which serum phosphate and calcium levels to be monitored depends upon the rate at which kidney function declines i.e. eGFR.<sup>7</sup> In patients with eGFR < 60 mL/min/1.73 m<sup>2</sup> not

on dialysis, the suggested serum phosphate level to be maintained is <4.5mg/dl and in dialysis patients the advised serum phosphate levels should be in between 3.5 and 5.5mg/dl.<sup>8</sup> Phosphate binders can broadly be classified as calcium containing and non-calcium containing. The choice of phosphate binders depends upon the serum calcium levels of the patient. In hypocalcaemic and normocalcemic patients, it is advised to give calcium containing agents but increase in serum calcium levels should be kept in mind. Hence should be monitored. In patients with hypercalcemia, non-calciumcontaining agents are advised.<sup>9,10</sup> There are studies done comparing different phosphate binders prescribed to the patients of end stage kidney disease undergoing hemodialysis but very few studies are done in the Indian population. Hence our study is being undertaken where we attempt to compare the efficacy of phosphate binders.

## MATERIALS AND METHODS

### Aims and objectives

To study the efficacy of phosphate binders in patients with end stage kidney disease undergoing haemodialysis

### Inclusion Criteria

- Patients of stage 5 ESKD maintained on haemodialysis for at least 3months in FMC
- S. Phosphorus levels >5mg/dl
- Without significant hyper/hypocalcaemia

### Exclusion Criteria

- History of any cancer
- Drug abuse
- Transplanted kidney
- Parathyroidectomized patients

### Methodology

- This is a retrospective study in which 120 patients (of either sex) were involved.
- The study was carried out from Jan 01, 2013 to Feb 28 2015 in Father Muller Medical College, Mangalore.
- Patients were randomly selected who were on dialysis for at least 3 months and were divided

into 4 groups in whom phosphate binders were prescribed namely Calcium acetate (667 mg), calcium carbonate (500 mg), sevelamer hydrochloride (400 mg)

- Data was recorded in a specific record form over a period of 3 months from patient’s records including Serum phosphorus and serum alkaline phosphatase.
- Data was analyzed by mean frequency, percentage, standard deviation and Fishers exact test

## RESULTS

Of the total 107 patients, 52were females and 55were male patients, 42 were in control group, 11 were in calcium acetate, 39 were in carbonate, 15 were in sevelemer group. Among these, 45% of the patients had co morbidities the commonest of them being type2 diabetes mellitus and hypertension and 2 patients had left ventricular dysfunction and 1 patient was HBsAg positive. The number of study subjects was more in age group of 51 to 65 years. Demographic data of the patients involved in the study is shown in the Table 1 and 2. The baseline phosphate levels in the study groups were comparable. At the end of 8<sup>th</sup> week, the difference in control in serum phosphate levels in sevelemer group compared with control group was highly significant with a p value of 0.003. The difference in phosphate level control in the calcium carbonate group compared with control group also had a significant result with p value 0.039. There were no significant differences in calcium acetate and control group with respect to serum phosphate level difference at the end of 8<sup>th</sup> week (Table 5). There were no statistically significant differences between individual groups (Table 6). Comparing the cost of phosphate binders by MRP labels on respective drugs, calcium acetate (Phostat) costing 2.6 rupees / tablet found to be cheapest, calcium carbonate (Shelcal) i.e. 4.13 rupees / tablet being the second cheapest and sevelemer found to be almost 5 to 6 times costlier than the other two i.e. 18 rupees / tablet.

**Table 1:** Table showing the sex distribution in the treatment groups

		Binders				Total
		Control	Calcium Acetate	Calcium Carbonate	Sevelamer	
Sex	F	14 33.3%	9 81.8%	23 59.0%	6 40.0%	52 48.6%
	M	28 66.7%	2 18.2%	16 41.0%	9 60.0%	55 51.4%
<b>Total</b>		<b>42</b> <b>100.0%</b>	<b>11</b> <b>100.0%</b>	<b>39</b> <b>100.0%</b>	<b>15</b> <b>100.0%</b>	<b>107</b> <b>100.0%</b>

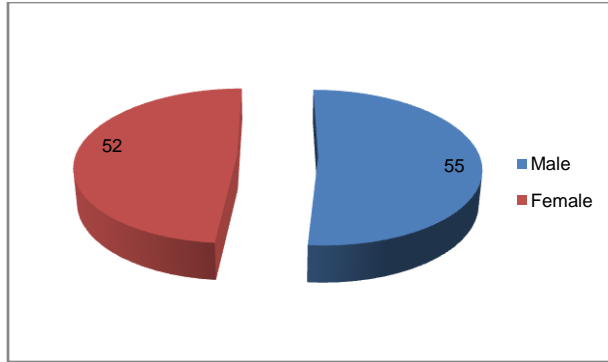


Figure 1: Graph showing the sex distribution, 48.2% females and 51.4% males

Table 2: Table showing the age distribution in the treatment groups

	Binders				Total	
	Control	Calcium Acetate	Calcium Carbonate	Sevelamer		
Age	36-50	11 26.2%	2 18.2%	7 17.9%	0 0.0%	20 18.7%
	51-65	22 52.4%	8 72.7%	25 61.1%	12 80.0%	67 62.6%
	Above 65	9 21.4%	1 9.1%	7 17.9%	3 20.0%	20 18.7%
<b>Total</b>	<b>42 100.0%</b>	<b>11 100.0%</b>	<b>39 100.0%</b>	<b>15 100.0%</b>	<b>107 100.0%</b>	

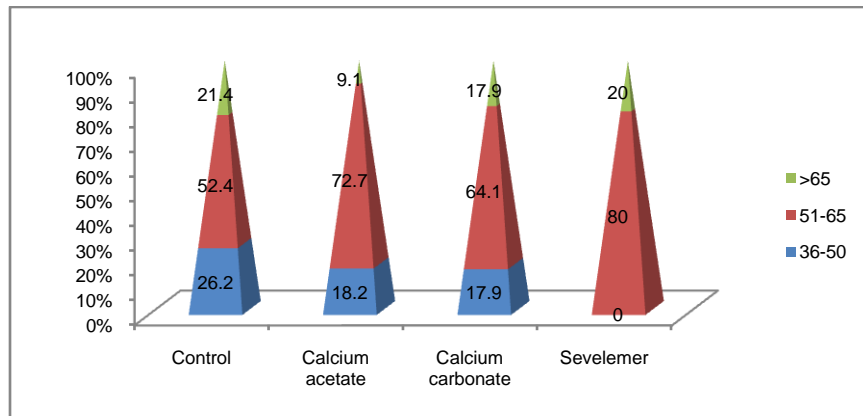


Figure 2: Graph showing the age distribution in the treatment groups

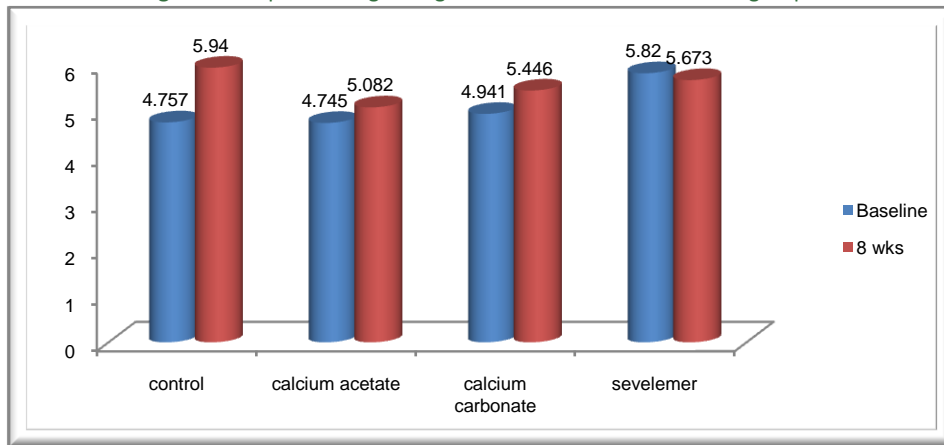


Figure 3: Graph showing the comparison between serum phosphate levels at baseline and after 8 weeks of phosphate binders treatment

**Table 3:** Table showing the serum phosphate levels at baseline

Binders	N	Minimum	Maximum	Mean	Std. Deviation	Median	ANOVA F	p
Control	42	1.7	6.4	4.757	.9860	4.900	2.866	.040
Calcium acetate	11	3.2	6.4	4.745	1.3589	4.600		sig
Calcium carbonate	39	3.0	7.3	4.941	1.2584	4.600		
Sevelamer	15	4.1	9.2	5.820	1.7150	5.300		
<b>Total</b>	<b>107</b>	<b>1.7</b>	<b>9.2</b>	<b>4.972</b>	<b>1.2776</b>	<b>4.850</b>		

**Table 4:** Table showing the serum phosphate levels at 8<sup>th</sup> week of phosphate binders treatment

Binders	N	Minimum	Maximum	Mean	Std. Deviation	Median	ANOVA F	p
Control	42	3.7	9.2	5.940	1.4754	6.450	1.301	.278
Calcium acetate	11	4.3	6.5	5.082	.9432	4.500		NS
Calcium carbonate	39	2.6	9.3	5.446	1.6204	5.000		
Sevelamer	15	3.2	8.5	5.673	1.4864	5.600		
<b>Total</b>	<b>107</b>	<b>2.6</b>	<b>9.3</b>	<b>5.634</b>	<b>1.4969</b>	<b>5.400</b>		

**Table 5:** Table showing the difference in serum phosphate levels over 8week duration

Binders	N	Minimum	Maximum	Mean	Std. Deviation	Median	Kruskal Wallis test value	p value
Control	42	-5.10	1.00	-1.1824	1.42056	-1.1000	5.130	.002
Calcium acetate	11	-1.90	1.70	-.3364	1.40945	-1.3000		HS
Calcium carbonate	39	-4.00	1.30	-.5051	1.14741	-.3500		
Sevelamer	15	-.30	.90	.1467	.48934	-1.1000		
<b>Total</b>	<b>107</b>	<b>-5.10</b>	<b>1.70</b>	<b>-.6622</b>	<b>1.30056</b>	<b>-.3000</b>		

**Table 6:** Table showing the multiple comparisons between the groups

		p
Control	Calcium acetate	.270
	Calcium carbonate	.039
	Sevelamer	.003
Calcium acetate	Calcium carbonate	1.000
	Sevelamer	1.000
Calcium carbonate	Sevelamer	.506

## DISCUSSION

In this study the efficacy of four different phosphate binders were compared by measuring the phosphate levels at two different time points. Results in this study suggest that the phosphate binders significantly controlled the serum phosphate levels with respect to control group. Our results are similar to other reported studies. Results of several studies on phosphate binders conclude that there is an increased frequency of hypercalcaemia in patients treated with calcium containing phosphate binders.<sup>11</sup> Caravaca. F *et al* and few other studies suggests that in patients treated with calcium acetate have less chances of developing hypercalcaemia.<sup>12, 13</sup> However, few other studies found no difference in calcium acetate compared to calcium carbonate.<sup>14,15</sup> Chertow GM *et al* and few other studies conclude that development or progression of cardiovascular diseases reduces significantly with the use of phosphate binders in dialysis patients.<sup>16</sup> Also, it has been suggested that in the management of uremic hyperphosphatemia calcium acetate should be considered as the choice of calcium based phosphate binder of use. On comparing the cost of comparable doses of phosphate binders, it was found that

calcium carbonate was the cheapest and sevelamer was much costlier than the others i.e. about six times costlier than the other two. A pharmacoeconomic analysis of phosphate binders in RISCAVID study concluded that, used over a period of 7years,sevelamer reduced risk of stroke with a saving of disease related costs.<sup>17</sup>

## CONCLUSION

Our study confirms that phosphate binder's treatment significantly control the serum phosphate levels over a period of eight weeks in ESKD patients on hemodialysis. Though sevelamer was found to be more effective in controlling the serum phosphate levels, but its high costs limits its use for the poor socioeconomic population. Calcium acetate can be used in patients with hyperphosphatemia and hypocalcemia.

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