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

Manjuprasad M S¹, Padmaja Udaykumar²*, Shreya Hegde³

¹²PG. Resident, ³Professor and HOD, Department of Pharmacology, A Block, Father Muller Medical College, Mangalore-575002, Karnataka, INDIA.
Email: manjuprasadms@gmail.com, padmajaudaykumar@gmail.com, shramikahegde@gmail.com

Abstract

Introduction: Hyperphosphataemia 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 sevelamer, calcium carbonate and calcium acetate and their baseline serum phosphate levels were compared with serum phosphate levels after 8weeks of treatment and found that at the end of 8th week the difference in control of phosphate levels in sevelamer 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 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.

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

INTRODUCTION

With worldwide increase in morbid conditions such as hypertension, diabetes and malignancy, patients with renal disease also are growing in number.²² It was found that the prevalence rate of end stage kidney disease has increased by 8% over past 5years because of which end stage kidney disease reflects itself to be one of the major health problems.¹⁹,²⁰ 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.²¹ 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.¹

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.⁴,⁶ When the glomerular filtration rate (GFR) falls below 25 to 40 mL/min/1.73 m², hypophosphatemia develops.⁵ 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. In patients with eGFR<60 mL/min/1.73 m² 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. 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-calcium containing agents are advised. 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 3 months in FMCI
- 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)

RESULTS

Of the total 107 patients, 52 were females and 55 were male patients, 42 were in control group, 11 were in calcium acetate, 39 were in carbonate, 15 were in sevelamer 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 8th week, the difference in control in serum phosphate levels in sevelamer 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 8th 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 sevelamer 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

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

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

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.
### 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.\(^1\) Caravaca. \(^F\) et al and few other studies suggests that in patients treated with calcium acetate have less chances of developing hypercalcaemia.\(^12, 1\) However, few other studies found no difference in calcium acetate compared to calcium carbonate.\(^14, 15\) 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.\(^16\) 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.\(^17\)

### 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.

### REFERENCE


Source of Support: None Declared
Conflict of Interest: None Declared