Clinical Evaluation of Niacin in Hemodialysis Patients with Hyperphosphatemia as Adjuvant to Calcium Carbonate
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Abstract

Background: The complications of End Stage Renal Disease ESRD attributed to high morbidity and mortality such as hyperphosphatemia and vascular disease. Vascular smooth muscle cells (VSMCs) are sensitive to elevation in serum phosphate levels and have the ability to modify their functions in response to this elevation through many processes that promote calcification. Vascular calcification is highly correlated with the major events of cardiovascular mortality which are included heart failure, sudden cardiac death, and ischemic heart disease. The control of hyperphosphatemia in HD patients remains poor in spite of the effectiveness of all the available phosphate binders. However, calcium based binder may promote the aggravation of vascular calcification while Aluminum-based binder associated with osteomalacia, and encephalopathy. Calcium/aluminum free phosphate binder may cause gastrointestinal adverse effect in addition to their high cost of treatment. The active phosphate transport inhibitors are the newest interesting agents in the management of hyperphosphatemia alone or as add-on therapy to the existing phosphate binders. Niacin is one of this novel drug classes that has been demonstrated to show promising therapeutic potential in the treatment of hyperphosphatemia in HD patients.

Aim of study: This study is designed to evaluate the efficacy of niacin as adjuvant therapy to calcium carbonate (as a phosphate binder) in hemodialysis patients.

Method: In this prospective, randomized interventional study, 56 patients confirmed with end stage renal disease (ESRD) and hyperphosphatemia on regular hemodialysis were included. Only 40 patients completed the study and were classified randomly into two groups: group (1); composed of 19 patients who received 1500 mg/day of calcium carbonate tablets, and group (2); composed 21 patients who received 1500 mg/day calcium carbonate tablets plus niacin both for 2 months’ duration. Blood sample was taken thrice, at baseline, after 1 month and at the end of month 2 for measurement of serum study parameters: (inorganic phosphorus (Pi), calcium (Ca), Calcium-Phosphorus product (Ca x P).

Results: Results of this study showed that the patients who administered orally niacin as adjuvant to calcium had the superiority over using calcium alone in the reduction of serum phosphorus level (-20.3% and -13.5%) respectively after 2 months of treatment in respect to baseline levels. Meanwhile, there was a marked increase in serum Ca level in both groups after 2 months of treatment however, it was non-significant. In addition, treatment with combination of calcium and niacin resulted in more reduction in serum (Ca x P) product level at the end of
الخلاصة:

الخلاصة: تُعتبر مضاعفات المرحلة المنتهية لمريض الفشل الكلوي إلى إزالة معدلات المراضا والوفيات مثل فوسفور الدم وأمراض الأوعية الدموية، خلايا العضلات النموذجي وعملية إزالة الفعال من مستويات الفوسفور في المصل، لننوعية، وتزن أولويات الفوسفور في تلك الأدوية. بنظام تكلس الأدوية، تقوم في الأدوية، وهي تشمل قصور القلب والسكتة القلبية المفاجئة، وأمراض تقصي القلب. السيطرة على فوسفور الدم في مرضى الفشل الكلوي لا تزال ميتا. على الرغم من الفعالية جمع روابط الفوسفور المتوفرة، وعلى الرغم من ذلك، قد يؤدي روابط الفوسفور المتوفرة على الكالسيوم إلى تقليل التركيز بينما روابط الفوسفور المتوفرة على الاموسوموماً تقليل تأثيره، وتم تقييم مساعدات الفلسوب خارج الكالسيوم/الفوسفور على أهمية هذا الموضوع، فضلاً عن ارتفاع تكلفة الفعالية، وتوافق الفوسفور المستخدمة في بعض الخصائص المثيرة للألم في علاج فوسفور الدم وحدة، وعندما يصبح مضاعف فوسفور الدم. في هذه الدراسة، تم تقييم فعالية النباتين كمساعد لرابط الفوسفور (كربيونات الكالسيوم) في علاج فوسفور الدم في مرضى الفشل الكلوي.

الهدف من الدراسة: تم تصميم هذه الدراسة لتنبأ فعالية النباتين كمساعد لرابط الفوسفور (كربيونات الكالسيوم) في علاج فوسفور الدم في مرضى الفشل الكلوي.

الطريقة: في هذه الدراسة الاستنباطية العشوائية التنازلية، تم تضمين 79 مريضاً في المرحلة المنتهية لمريض الفشل الكلوي، مع فوسفور الدم والìn. في الدراسة، تم تقييم فعالية النباتين كمساعد لرابط الفوسفور (كربيونات الكالسيوم) في علاج فوسفور الدم وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بمدى التأثير الفعال في مرضى الفشل الكلوي، وجدت هذه الدراسة أن فعالية النباتين قويةً، حيث تأثيره على استخدم الكالسيوم، وجدت في مرضى الفشل الكلوي في المصل -6.1% - 5.3%. ومع ذلك، في حالة التدخل المتوازن، لا يمكن إجراء التدخل المتوازن، نسبياً، إلى أن يكون معييناً، فضلاً عن ذلك، أدى الالتباس بين الكالسيوم والتبسيط بأول لدموية موضوعية في مرضى الفشل الكلوي. هذه الدراسة، تم تقييم فعالية النباتين كمساعد لرابط الفوسفور (كربيونات الكالسيوم) في علاج فوسفور الدم في مرضى الفشل الكلوي.
### Introduction:
Chronic kidney disease is a global public health problem that places an enormous strain on both patients and healthcare providers [1]. Globally, CKD is ranked to be the 18th major cause of death (increased from 27th in 1990) and the 12th cause of disability [2]. The progression of CKD will lead to end stage renal disease (ESRD), it defines as “loss of kidney function such that life is unsustainable in the absence of renal replacement therapy (RRT)” [3].

Universally, the increase in prevalence of ESRD over the period from 2003 to 2016 was 43% [4]. Over the next few decades, ESRD may rise sharply, induced by population ageing and an increasing prevalence of diabetes and hypertension [5].

The complications of ESRD attributed to high morbidity and mortality such as hyperphosphatemia and vascular disease [6]. In addition, cardiovascular disease in patients with ESRD is 10-30 folds greater than in a patient without kidney disease, which considered the major causes of deaths for approximately 40% of ESRD patients undergoing dialysis [7].

Hyperphosphatemia is a serious abnormality that affected almost ESRD patients undergoing maintenance hemodialysis [8]. There is a strongly associations between incidence of vascular calcification and hyperphosphatemia in dialysis patients [9].

Vascular calcification is highly correlated with the major events of cardiovascular mortality which are included heart failure, sudden cardiac death, peripheral arterial disease, and ischemic heart disease [10]. Vascular smooth muscle cells (VSMCs) are sensitive to serum phosphate levels and have the ability to modify their functions in response to this elevation through many processes that promote calcification [11]. For each 0.323mmol/L serum phosphorus increment, the calcification in coronary artery and thoracic aorta increased by 21% and 33% respectively, and increased in the risk of death by 20% among ESRD patients [12].

The control of hyperphosphatemia in HD patients remains poor, in spite of the effectiveness of all the available phosphate binders in decreasing serum phosphate level [13]. However, calcium-based binder may promote the aggravation of vascular calcification by achievement a positive calcium balance [14], while the use of Aluminum-based binder associated with osteomalacia, cognitive disturbances, dementia, and encephalopathy [15]. Calcium/aluminum free phosphate binder such as lanthanum and sevelamer may cause gastrointestinal adverse effect in addition to their high cost of treatment [16]. Consequently, new therapies or adjunctive treatments to the currently phosphate binders that increase the effectiveness well-tolerated and cost-effective are needed [17].

Niacin (generic name of nicotinic acid), also known as vitamin B3, is a naturally occurring water-soluble vitamin that is essential in different biological activities [18]. The active phosphate transport inhibitors are the newest interesting agents in the management of hyperphosphatemia alone or as add-on therapy to the existing phosphate binders [19]. Niacin is one of this novel drug classes that has been demonstrated to show promising therapeutic potential in the treatment of hyperphosphatemia in HD patients [20]. It decreases phosphorus absorption in the GIT, result in lowering serum phosphorus level [20]. The first study that was performed to assess the safety and effectiveness of niacin (extended-release) as a phosphate reducing agent was done in Indian HD patients; this study found that a niacin single dose can produce significantly reduction in both serum phosphorus and Ca-P product level [21].

Niacin administered once or twice/ day with no need to be taken at the meal time that may increase patient compliance, and provides a cost-effective treatment compared to the expensive non-calcium-based binders [22]. Thereby, it can be valuable for the niacin to be added to the...
treatment of hyperphosphatemia in HD patients.\cite{23}

**Aim of the study:** This study is designed to evaluate the efficacy of niacin as adjuvant therapy to the phosphate binder, calcium carbonate, in HD patients.

**Methods:**
In this prospective, randomized interventional study, 56 patients with age range from 18-60 years confirmed with end stage renal disease (ESRD) on regular hemodialysis in the dialysis center of Al Karama Teaching Hospital were included. The inclusion criteria were patients who scheduled to three sessions of hemodialysis per week (4 hours each) for more than six months, also patients received stable dose of calcium carbonate for 2 weeks prior to the study and had serum inorganic phosphorus level > 5.0 mg/dl. Patients with +ve hepatitis C virus or active liver disease were excluded from the study. Patients with DM and those with active malignancy or with diagnosed peptic ulcer disease were also excluded. Pregnant and lactating women, as well as patients allergic to any of the study medications were excluded. Only 40 patients completed the study and were classified randomly into two groups: Group (1); composed of 19 patients who received 1500 mg/day of calcium carbonate tablets, and group (2); composed 21 patients who received 1500 mg/day calcium carbonate tablets plus niacin (extend release tablet) both for 2 months’ duration. At the first week, niacin was administered at a starting dose of 500 mg once daily, and then at week 2 to the end of the study, it was increased to be 1000 mg at bedtime to ensure tolerance. Advised the patients to take 100 mg aspirin 30 minutes before niacin in case of flush symptom, and calcium carbonate were administered with meals. Blood sample was taken thrice, at baseline, after 1 month and at the end of month 2 for measurement of serum study parameters: (inorganic phosphorus (Pi), calcium (Ca), calcium-phosphorus product (Ca x P)). The analysis, description, and presentation of data were executed using SPSS (version 25). Data were represented as mean, standard division, standard error of mean and parentage. Shapiro-wilk test was done to assess if continuous variables follow normal distribution. Pearson's chi-square test was applied to check the association between two categorical variables. Paired t-test to compare pre and post treatment variables in same group. One-way analysis of variance (ANOVA) used to determine the difference among independent samples. Analysis of covariance (ANCOVA) used to correct the initial group differences that exist on the dependent variable.\(P\) values >0.05 considered not significant, whereas \(P < 0.05\) considered significant and \(P <0.01\) considered highly significant.

**Results**
Forty patients completed the 2 months of study and were included in the final analysis. The mean values of gender, age, BMI, and duration of symptoms between the study group's patients were statistically non-significant differences.

Study results showed that there was a statistically high significant difference in the level of Pi between both groups after 1 month of the treatment (\(P<0.01\)) and significant difference (\(P<0.05\)) at the end of month 2. Meanwhile there was highly significant reduction within each group after two months of treatment (\(P<0.01\)) in respect to the baseline levels. Table (2), figure (1).

A non-significant change in serum Ca levels was demonstrated after each period interval of treatment between the study groups (\(P>0.05\)) compared to pre-treatment level. There was a marked increase in serum Ca level in both groups after 2 months of treatment compared to baseline, nevertheless, was not significant (\(P >0.05\)). Table (3), figure (2). The changes in serum (Ca x P) level showed a non-significant difference between groups 1 and 2 patients.
throughout the whole study intervals compared to the pre-treatment level, the change in \((\text{Ca} \times \text{P})\) product was not significant at the end of the study, however, treatment with combination of calcium and niacin resulted in more reduction in serum \((\text{Ca} \times \text{P})\) product level after 2 months of treatment than with calcium alone compared to baseline, as showed in table (4), figure (3).

### Table 1: Patient’s demographic data and disease characteristics

<table>
<thead>
<tr>
<th>variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (42.1)</td>
<td>10 (47.6)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (57.9)</td>
<td>11 (52.4)</td>
<td>0.48(^{NS})</td>
</tr>
<tr>
<td>Total</td>
<td>19 (100)</td>
<td>21 (100)</td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>47.8 (13.05)</td>
<td>48.8 (14.46)</td>
<td>0.82(^{NS})</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>24.69 (4.29)</td>
<td>23.74 (4.16)</td>
<td>0.48(^{NS})</td>
</tr>
<tr>
<td>Duration (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>6 (31.6)</td>
<td>5 (23.8)</td>
<td></td>
</tr>
<tr>
<td>1-5</td>
<td>12 (63.2)</td>
<td>16 (76.2)</td>
<td>0.45(^{NS})</td>
</tr>
<tr>
<td>&gt;1</td>
<td>1 (5.3)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Number of patients (n), Percentage (%), \(NS\): No significant differences \((P>0.05)\). One way anova is used for statistical analysis of (age, BMI). Chi-square test is used for statistical analysis of (gender, duration of symptoms).

### Table 2: Effect of phosphate binder alone and in combination with niacin on serum inorganic phosphorus level.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study groups</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pi (mmol/L)</td>
<td>Group 1</td>
<td>Group 2</td>
<td>(P) value</td>
</tr>
<tr>
<td>Adjusted baseline</td>
<td>2.66</td>
<td>2.66</td>
<td></td>
</tr>
<tr>
<td>After 1 month</td>
<td>2.42±0.044</td>
<td>2.23±0.041</td>
<td>0.003(^{**})</td>
</tr>
<tr>
<td>After 2 months</td>
<td>2.30±0.060</td>
<td>2.12±0.056</td>
<td>0.04(^{*})</td>
</tr>
<tr>
<td>(P)-value</td>
<td>0.001(^{**})</td>
<td>0.001(^{**})</td>
<td></td>
</tr>
</tbody>
</table>

Data expressed as mean ±SEM (standard error of mean). * significant difference \((P<0.05)\), ** Highly Significant difference \((P<0.01)\). One-way ANCOVA test used to compare pre or post treatment between group 1 and group 2 patients. Paired \(t\)-test used to compare between pre- and post-treatment results in same group. Reference range of Pi for adults is (0.81-1.45 mmol/L).

### Table 3: Effect of phosphate binder alone and in combination with niacin on serum calcium level

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study groups</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca (mmol/L)</td>
<td>Group 1</td>
<td>Group 2</td>
<td>(P) value</td>
</tr>
<tr>
<td>Adjusted baseline</td>
<td>2.09</td>
<td>2.09</td>
<td></td>
</tr>
<tr>
<td>After 1 month</td>
<td>2.21±0.040</td>
<td>2.19±0.038</td>
<td>0.4(^{NS})</td>
</tr>
<tr>
<td>After 2 months</td>
<td>2.24±0.066</td>
<td>2.25±0.062</td>
<td>0.9(^{NS})</td>
</tr>
<tr>
<td>(P)-value</td>
<td>0.07(^{NS})</td>
<td>0.06(^{NS})</td>
<td></td>
</tr>
</tbody>
</table>

Data expressed as mean ±SEM (standard error of mean), Ca: serum calcium level. \(NS\): Not significant \((P>0.05)\), one-way ANCOVA test used to compare pre or post treatment between
group 1 and group 2 patients. Paired t-test used to compare between pre- and post-treatment results in same group. Reference range of Ca for adults is (2.15-2.50 mmol/L).

Table (4): Effect of phosphate binder alone and in combination with niacin on serum calcium-phosphorus product level

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study groups</th>
<th>P value</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca x P (mmol/L)</td>
<td>Group 1</td>
<td>Group 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.6</td>
<td>5.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 1 month</td>
<td>5.42±0.148</td>
<td>5.13±0.120</td>
<td>0.1NS</td>
<td></td>
</tr>
<tr>
<td>After 2 months</td>
<td>5.45±0.295</td>
<td>5.37±0.239</td>
<td>0.8NS</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.6NS</td>
<td>0.1NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data expressed as mean ±SEM. NS: Not significant (P>0.05). One-way ANCOVA test used to compare pre or post treatment between group 1 and group 2 patients. Paired t-test used to compare between pre- and post-treatment results in same group. Target range of Ca x P is(< 4.44 mmol²/L²).

Figure (1): Effect of phosphate binder alone and in combination with niacin on serum inorganic phosphorus level

Figure (2): Effect of phosphate binder alone and in combination with niacin on serum calcium level.
Figure (3): Effect of phosphate binder alone and in combination with niacin on serum calcium-phosphorus product

Discussion

The present study and other studies revealed that hemodialysis patients of both genders have higher phosphorus serum level with slight predominance towards female patients in this study and others [24], or towards male patients in other study [25]. Regarding to the age, hyperphosphatemic patients tended to be younger in the current study with a mean age 47.8 years in group 1 and 48.8 years in group 2, comparable results were found in other studies where hyperphosphatemia was inversely correlated with age in dialysis population, Salhab et al. (2019), and Mohamed Koya et al. (2019), reported a mean of age 48.8 and 46 years, respectively [26,27]. This association can be attributed to the reduced in renal phosphate reabsorption and increased under nutrition with age [24]. Most patients in the present study were slightly underweight among the study groups where BMI <25 kg/m², a similar finding has been found in other studies [28]. Meanwhile, another study by Gray et al. (2019) reported a high BMI values among hyperphosphatemic patients on maintenance hemodialysis [29]. Majority of patients in the current study presented with duration of hemodialysis between 1-5 years while only 1 patient presented with duration of more than 5 years. Hyperphosphatemia have been shown to be associated with increased risk of cardiovascular mortality, and considered the “silent killer” for HD patients [30]. The risk of death increased by 18% with each 0.323 mmol/L increase in the phosphorus level [31]. Cardiovascular mortality risk is mainly due to vascular calcification that promoted and induced by high serum phosphate levels, elevated (Ca x P) product, and high calcium serum level [7]. The risk of death due to CVD in HD patients is about 10 to 30 times than general population [32]. In the present study, the patients who administered oral niacin as adjuvant to calcium had the superiority over using calcium alone in the reduction of serum phosphorus level (-20.1%, -13.5% respectively), while (Ca x P) product level that although was statistically not significant in patients treated with calcium and niacin (-4.1%) but higher than using calcium alone (-2.7%). Meanwhile, there was a notable increase in the calcium serum level in both groups; nevertheless, it was non-significant (P>0.05). In line with these results, Zahed et al. (2016), in a study on dialysis patients, reported a significant reduction in the level of serum phosphorus after 8 weeks use of niacin [33]. Furthermore, previous study by Ahmadi et al. (2012) stated that the level of both serum phosphorus and (Ca X P) product dropped in HD patients after 4-weeks treatment with niacin [34]. On the other hand, these two studies showed that the reduction of serum phosphorus level by niacin was achieved without significant change in serum
calcium level [33, 34], that is in consistence with the current study. More recently, a study by Khalid et al. (2019), demonstrated that serum phosphorus level decreased significantly after 4 weeks with low dose niacin therapy (100 mg/day) on HD patients [35]. While the exact mode of action remains unknown, the observed reduction in serum phosphorus level is mostly attributed to the decreasing effect of niacin to the active transport-mediated phosphorus absorption in GIT [36]. Hence, niacin seems to have mechanistic basis distinct from the traditional phosphate binders. In vitro and in vivo studies have indicated that niacin can suppress the sodium-dependent intestinal phosphate absorption through inhibiting the expression of phosphate co-transporter (NaPi2b) in the brush border of intestine [37, 38]. The intestinal NaPi2b co-transporter has been shown to be responsible for up to 50% of total phosphate uptake [39]. In addition, numerous animal in vitro studies observed that administration of niacin (or its metabolite nicotinamide) was associated with a decrease in renal co-transporter (NaPi2a) level with noticeable increase in renal phosphate excretion [40,41]. The intestinal NaPi2b found to be strongly upregulated as a compensatory mechanism in response to situations of phosphate depletion like using of phosphate binder or phosphate dietary restriction [42]. Therefore, inhibition of intestinal NaPi2b activities can provide greater phosphate controlling efficacy in patients when adding to phosphate binders [43]. This may explain why niacin treated group appeared to be more effective in lowering serum phosphate concentrations in the current study. As noted above, the both groups of current study revealed an increase in serum calcium level; this finding is consistent with other studies used calcium as a phosphate binder for hyperphosphatemia treatment that reported similar results [44,45]. Calcium overload with persistent hyperphosphatemia may directly activate vascular calcification by inducing extra-skeletal (calcium-phosphate) deposition [46,47].

In addition, it has a central role in induction of apoptosis and matrix vesicle release that is also leading to activation of vascular calcification [48]. Nevertheless, due to their low cost, calcium-containing binders can be useful for hypo-calcemic HD patients who have no evidence of a dynamic bone disease or vascular calcification although with careful monitoring for serum calcium level [49].

Elevation in Ca x P product may increase the risk of mortality in HD patients mainly due to aortic valve calcification that is directly associated with the level of this product [50], it’s accelerated the calcium deposition in the valve and inducing valvular heart insufficiency [51]. Cheema et al (2017) demonstrated that the risk of death increased by 34% more in HD patient with Ca x P level >5.8 mmol²/L² than patients with value of (4–4.2 mmol²/L²) [52]. Thus, an appropriate control of the Ca x P product level may prevent the progression of aortic valve calcification and improve survival in HD patients [51].

Conclusion

The effect of niacin to suppress the sodium-dependent intestinal phosphate absorption, and thereafter serum phosphate and calcium-phosphorus product levels was obvious in this study. Using niacin as adjuvant therapy to conventional phosphate binder for hemodialysis patients is a promising strategy to reduce the prospective risks of both hyperphosphatemia and long-term use of phosphate binder.

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