Title

Inadequate Awareness among Chronic Kidney Disease Patients Regarding Food and Drinks Containing Artificially Added Phosphate

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Citation

Issue Date

2014-03-20

URL

http://hdl.handle.net/10129/5380

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Inadequate Awareness among Chronic Kidney Disease Patients Regarding Food and Drinks Containing Artificially Added Phosphate

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Abbreviation

CKD: Chronic Kidney Disease
Introduction

Dysregulation of phosphate balance can affect the functionality of most organ systems. Several studies have shown that hyperphosphatemia is the single most important determinant of mortality in chronic kidney disease (CKD) patients undergoing hemodialysis, perhaps due to cardiovascular damage. Excessive retention of phosphate can cause extensive cellular and tissue damage, and a higher incidence of vascular calcification related to hyperphosphatemia is found in patients with CKD. Phosphate toxicity has been associated with cardiovascular calcification in various genetically modified mouse models. More importantly, reduction of serum phosphate levels in these models can markedly suppress vascular calcification, despite the presence of significantly higher serum calcium and 1,25-dihydroxyvitamin D levels. In patients with CKD, hyperphosphatemia and low serum vitamin D levels are independent risk factors for high mortality. Therefore, reducing serum phosphate in patients with CKD is a therapeutic priority, and these patients are often asked to consume a low-phosphate diet, in addition to taking phosphate-lowering drugs. Hence, it is important for CKD patients to be aware of food items and beverages that are rich in artificially added phosphates.

Organic and inorganic forms of phosphate are present in meat, fish, eggs, milk/dairy products, and vegetables. These foods are required for maintaining normal nutritional balance and avoidance of these foods is not a suitable option. However, CKD patients may need to reduce intake of some of these food items as required to minimize phosphate intake. Of particular importance, processed food items and beverages are rich in phosphate. Therefore, total phosphate ingestion is likely to be increased significantly by consumption of processed food and soda.

Developing awareness of food items and drinks containing artificially added phosphate is becoming more important because of widespread use of phosphate as a preservative in processed food items, which complicates the ability of CKD patients to reduce
phosphate intake. To assess the level of awareness of CKD patients regarding food and drinks containing artificially added phosphate, we conducted a survey of CKD patients undergoing hemodialysis in multiple dialysis centers in Hirosaki, Japan. We also assessed the immediate effects of consumption of carbonated soda with a high-phosphate content in overnight fasted healthy volunteers by determining urinary calcium, phosphate, protein and sugar contents before and 2 hours after consumption of 350 ml of soda.
Methods

1. Survey population
The subjects were 153 randomly selected CKD patients (77 males, 76 females) undergoing hemodialysis who are currently enrolled at the Dialysis Center in Hirosaki City, Japan. The average age of the subjects was 56±11 years old. All patients participated voluntarily on the assurance of anonymity, and none refused to answer the survey questions. A questionnaire consisting of seven questions was used to assess each patient's level of awareness about food and drinks containing artificially added phosphate (Table S1). The survey was conducted in June 2011. Informed consent was collected from each subject. All participation was on a volunteer basis and no financial compensation was offered. The results of the survey were analyzed using Microsoft Excel 2007 and IBM SPSS Statistics 19. A Mann-Whitney U test was used for comparison between groups.

2. Effects of consumption of carbonated soda
The subjects in this study were 55 Hirosaki University students (average age 20.7±0.3 years old; 20 males, 35 females) who were randomly divided into a group that drank 350 ml of carbonated soda (n = 35; average age 21.2±0.4 years old; 13 males, 22 females) and a control group (n = 20; average age 19.9±0.3 years old; 7 males, 13 females) who drank 350 ml of water, both after an overnight fast. Urine samples were collected before and 2 hours after drinking the soda or water. Urinary protein contents and glucose were determined qualitatively in both samples of urine using test paper, and the amounts of urinary phosphate, calcium and creatinine were measured in both samples using an auto-analyzer. The urinary phosphate and calcium levels were normalized using the urinary creatinine concentration. Data were analyzed using a Wilcoxon signed-rank test and a Pearson correlation test, with a value of p<0.05 considered to be significant. The survey and the carbonated soda study were approved by the Committee for Medical Ethics of Hirosaki University, Japan.
Result and discussion

To determine the level of awareness of food and drinks containing artificially added phosphate, we conducted a survey on CKD patients undergoing hemodialysis at the Dialysis Center in Hirosaki City, Japan. Since patients with CKD are required to maintain a low-phosphate diet, it is important that they are fully aware of food items (hamburgers and pizza) and beverages (soda) that contain artificially added phosphate. Based on this survey, 93% of the CKD patients were aware of the high sugar content in soda, but only 25% were aware of the presence of phosphate (phosphoric acid) in similar drinks. Similarly, 46% of the CKD patients were not aware that phosphate, in the form of a preservative, is routinely added to processed foods such as hamburgers and pizza (Figure 1). The survey results, categorized by gender, are shown in Table S2. It is clear from the survey that the CKD patients were often uninformed about the phosphate content in food and drinks, and therefore did not understand the detrimental effect of consuming such items.
### Table S1

**List of questioner**

1) Do you know carbonated Soda drinks contain high levels of sugar?  **Yes / No**
2) Do you know carbonated Soda drinks contain high levels of phosphate?  **Yes / No**
3) Do you know “fast foods” contain high levels of phosphate?  **Yes / No**
4) Do you know consuming too much phosphate may be harmful for the body?  **Yes / No**
5) How many cans of carbonated Soda do you drink a week?
   1- None,
   2- 1-5,
   3- 6-10,
   4- >10,
6) How often do you eat “fast food”? 
   1- Do not eat,
   2- Once a week,
   3- Once a month,
   4- Almost every day,
7) After knowing that too much phosphate consumption might be harmful, what do you think you should do?
   1+ I want to get more information about phosphate.
   2+ I want to reduce consumption of phosphate-containing food/drink.
   3+ I have no further Interest on phosphate-related issues.

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*Fast food in this survey is restricted to the commercially available hamburgers, pizza or fried chicken*
Figure 1. The survey participant CKD patients were asked whether they were aware of the sugar and phosphate content in commercially available soda drinks. Almost 93% of the participants were aware of the presence of sugar, while only 25% were aware of the presence of phosphate (phosphoric acid) in such drink, showing a noticeable awareness gap related to phosphate-contenting drinks among the patients.
Table S2
Survey results categorized by gender.

<table>
<thead>
<tr>
<th></th>
<th>n=153</th>
<th>Male n=77</th>
<th>Female n=76</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.3±9.4</td>
<td>56.4±11.6</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Q1 YES</td>
<td>72(93.5%)</td>
<td>71(93.4%)</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>5(6.5%)</td>
<td>5(6.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2 YES</td>
<td>21(27.3%)</td>
<td>18(23.7%)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>56(72.7%)</td>
<td>58(76.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q3 YES</td>
<td>40(51.9%)</td>
<td>47(61.8%)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>37(48.1%)</td>
<td>29(38.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q4 YES</td>
<td>59(76.6%)</td>
<td>60(78.9%)</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>18(23.4%)</td>
<td>16(21.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q5</td>
<td>1</td>
<td>36(46.8%)</td>
<td>39(52.0%)</td>
<td>0.2</td>
</tr>
<tr>
<td>2</td>
<td>32(41.6%)</td>
<td>33(44.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5(6.5%)</td>
<td>3(4.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4(5.2%)</td>
<td>0(0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q6</td>
<td>1</td>
<td>46(60.5%)</td>
<td>47(61.8%)</td>
<td>0.14</td>
</tr>
<tr>
<td>2</td>
<td>13(17.1%)</td>
<td>20(26.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>17(22.4%)</td>
<td>9(11.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q7</td>
<td>1</td>
<td>21(28.8%)</td>
<td>30(42.3%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2</td>
<td>31(42.5%)</td>
<td>33(46.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21(28.8%)</td>
<td>8(11.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
More importantly, despite 78% of the surveyed patients being aware of the detrimental effects of consumption of a high phosphate diet, 43% drank at least 1 to 5 cans of soda per week, while another 5% consumed 6 to 10 cans of soda per week. About 17% of the surveyed patients ate fast food (hamburgers, pizza, etc.) once each week and another 22% consumed these items once each month (Figure 2). The survey results categorized by age groups are shown in Table S3.

Figure 2. The participants were asked to describe their soda drink and fast food consumption habits.

Almost half (51%) of the CKD patients drink soda, while 39% patients eat fast food.
Table S3

Survey results categorized by different age groups.

<table>
<thead>
<tr>
<th></th>
<th>n=153</th>
<th>Under 60</th>
<th>Over 60</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=75</td>
<td>n=78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>YES</td>
<td>72(96.0%)</td>
<td>71(91.0%)</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>3(4.0%)</td>
<td>7(9.0%)</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>YES</td>
<td>23(30.7%)</td>
<td>16(20.5%)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>52(69.3%)</td>
<td>62(79.5%)</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>YES</td>
<td>58(77.3%)</td>
<td>29(37.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>17(22.7%)</td>
<td>49(62.8%)</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>YES</td>
<td>66(88.0%)</td>
<td>53(67.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>9(12.0%)</td>
<td>25(32.1%)</td>
<td></td>
</tr>
<tr>
<td>Q5</td>
<td>1</td>
<td>36(49.6%)</td>
<td>39(50%)</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>29(39.2%)</td>
<td>36(46.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6(8.1%)</td>
<td>2(2.7%)</td>
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</tr>
<tr>
<td></td>
<td>4</td>
<td>3(4.1%)</td>
<td>1(1.3%)</td>
<td></td>
</tr>
<tr>
<td>Q6</td>
<td>1</td>
<td>30(40.5%)</td>
<td>63(80.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>24(32.4%)</td>
<td>9(11.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>20(27.0%)</td>
<td>8(7.7%)</td>
<td></td>
</tr>
<tr>
<td>Q7</td>
<td>1</td>
<td>16(23.2%)</td>
<td>35(46.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>45(65.2%)</td>
<td>19(25.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>8(11.6%)</td>
<td>21(28.0%)</td>
<td></td>
</tr>
</tbody>
</table>
The majority (78%) of the CKD patients in the survey did appreciate the risk of consuming high phosphate-containing food and drinks (Figure 3). These responses differed significantly from those of medical and nursing students, since only 32% of the students were aware of the risks associated with uncontrolled phosphate consumption\textsuperscript{23}. Despite 87% of the CKD patients recognizing the impact of phosphate on disease progression, only 25% were aware that most soda contains a phosphate compound (phosphoric acid).

Figure 3. The survey participant CKD patients were asked whether they were aware of the possible harmful effects of unrestricted consumption of a high phosphate diet, and the majority (78%) of the participants was aware of detrimental effects related to high phosphate diet.
The results of the survey clearly suggest that many CKD patients lack awareness of the presence of phosphate in food and drinks. However, after explaining this issue to the patients, 35% were eager to obtain information related to food containing phosphate and 45% were willing to consider reducing their phosphate intake by minimizing consumption of processed food and soda (Figure 4). These findings show the potential benefits of education of patients. Such educational guidance of CKD patients to make healthier food choices is likely to help in reducing complications related to abnormal mineral ion metabolism \(24-27\), which is particularly important, given that the global prevalence of CKD may be as high as 500 million \(28\).

Figure 4. The survey participant CKD patients were asked whether they were willing to modify their diet to reduce phosphate intake.

Around 35% of the participants wanted to have more information related to artificially containing-food and drinks, and another 45% were willing to reduce their phosphate intake by minimizing consumption of processed food and soda drinks.
Notably, almost half of the surveyed Japanese patients did not consume any soda (Figure 2). One reason for this result may be their strong preference for green tea, since almost 87% of Japanese adults (40 to 69 years old; n = 13,916) have been found to consume green tea every day \(^{29}\). Therefore, availability of an alternative healthy drink may reduce consumption of soda with high levels of sugar and phosphate.

The awareness of a majority (78%) of the subjects regarding effects related to a high-phosphate diet (Figure 3) indicates that healthcare providers, including doctors, nurses, and nutritionists, have been effective in informing patients of phosphate-related complications. However, an important finding in the survey was that about half (51%) of the CKD patients drank soda and 39% ate fast food (Figure 2), despite the high level of awareness of phosphate-related harmful effects. This may be explained by the fact that 75% of the surveyed patients did not realize that carbonated soda contains high levels of phosphate (Figure 1). Similarly, half of the surveyed patients were not aware of the high phosphate content in fast food and processed food items.
Conclusion

In summary, our results make it clear that there is an awareness gap among CKD patients regarding phosphate-containing foods and drinks. An issue that needs further evaluation, but is not within the scope of this survey, is the level to which healthcare providers are informing patients of the risk of a high-phosphate diet without providing sufficient details of the kind of foods and drinks that contain high phosphate. The results of this survey highlight a gap between the patients and healthcare providers, in terms of education of patients on foods with high phosphate levels. Of particular importance, the absence of listing of phosphate content in the nutritional ingredients makes it harder for patients to avoid food containing higher levels of phosphate.

A limitation of the study is that most of the surveyed patients drank soda and/or ate fast food due to lack of awareness of the phosphate content, and therefore we did not have enough patients to form a control group of non-consumers of these products. However, studies in overnight-fasted healthy volunteers show excretion of significantly increased amounts of urinary calcium at two hours after drinking soda, suggesting that the high phosphate content in the drink can influence other mineral metabolism. In the current study, the mean level of urinary calcium (adjusted using urinary creatinine) in 35 overnight fasted volunteers increased significantly from before to 2 hours after consuming 350 ml of carbonated soda (0.09±0.01 vs. 0.15±0.01, p = 0.001). In contrast, there was no such change in urinary calcium excretion from before to after drinking water in 20 control subjects. Urinary phosphate levels (adjusted using urinary creatinine) showed a slight, but not significant, increase from before to 2 hours after soda consumption (0.33±0.03 vs. 0.36±0.03, p = 0.252), and was unchanged in samples collected from the controls. A urinary analysis did not detect abnormal excretion of urinary protein and sugar in samples collected before and after drinking soda or water (data not shown).
The long-term effects of soda consumption on mineral ion metabolism were not examined in this study. This issue requires further study to show that increased serum phosphate levels in patients consuming fast food and soda are not harmless, and that the high-phosphate diet cannot be justified. In fact, it is becoming more evident from experimental and human studies that features of phosphate toxicity can appear after consumption of a high-phosphate diet, even when serum phosphate levels are within the normal range\textsuperscript{30,31}.

The results of the survey highlight two important points. First, CKD patients are not sufficiently aware of food items and drinks that contain artificially added phosphates. Second, there is a need for an educational initiative to raise awareness of the risks posed by dietary items with hidden phosphate content.
References


要旨
弘前大学大学院保健学研究科健康支援科学領域健康増進科学分野
出頭 佳子

リンは細胞を構成する成分であり、人体にとって必須の栄養素の一つである。その反面、過剰に摂取することは人体に悪影響を及ぼす可能性がある。過剰摂取になり得るのは、慢性腎疾患(CKD)患者などの本来過剰なリンを排出する臓器である腎臓に障害があるケースであることが多い。リンは肉や魚、芋やその他でんぷん質を多く含む食品に自然に含まれているものの他に、近年では肉の加工食品や炭酸飲料などに食品添加物としてリン酸塩の形で多く用いられており、本来必要とされる以上のリンを摂取しやすい現状がある。しかも現在では、自然に食品に含まれるリンよりも、食品添加物のリンは吸収率が良いことが明らかとなっている。CKD患者はリンを抑えた食事を摂取するよう指導され、多くの場合はリン酸塩下治療薬を処方される。しかし、加工食品や炭酸飲料に添加物として含まれているリン酸は、通常成分表で表示されていないため、CKD患者は適切に食品を選択できない。本研究ではまず弘前市内で血液透析を受けているCKD患者153名(age56±11, Male:77 Female:76)に対し、リン酸が添加された食品/飲料についての無記名自記式質問紙を用いた知識調査を実施した。つぎに健常成人を対象として学生ボランティア35名(age21.2±2.35, Male:13 Female:22)に食品添加物としてリンが含まれる炭酸飲料350mlを摂取してもらい、飲料前と飲料後の尿のリン及びカルシウムを測定した。結果として、炭酸飲料に砂糖が多く含まれていることを知っているCKD患者は93%であった。対して炭酸飲料にリン酸が多く含まれていることを知っているCKD患者は25%であった。また、リン酸の過剰摂取が有害であることを知っているCKD患者は78%であったが、43%の炭酸飲料を少なくとも週に1〜5缶、17%はファストフードを少なくとも週に1度は摂取すると回答した。次に健常成人では尿中カルシウム(クレアチニン補正)が炭酸飲料飲用前0.099±0.01、飲用後0.15±0.017で有意差がみられた。
研究の調査結果は、血液透析を受けているCKD患者において食事中のリン酸について十分な認識がないことを示唆した。CKD患者に対しリン酸への認識を高めるための教育の取り組みをより強化していく必要性があると考えた。