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The Impact of Phosphorus Management Today on Quality of Life: Patient Perspectives



Derek Forfang, Dawn P. Edwards, and Kamyar Kalantar-Zadeh

Patients with kidney failure and early stages of chronic kidney disease often develop hyperphosphatemia, which is associated with negative outcomes. The reduction of phosphate levels is the established clinical practice. However, achieving and maintaining target phosphate levels is challenging, and the current methods of phosphate management lead to poor quality of life (QoL) in patients receiving dialysis, particularly because patients might not receive adequate education on phosphate control. Patients receiving dialysis are advised to maintain stringent dietary restrictions and might experience anxiety and depression due to the constant burden of dietary self-management. The lack of nutritional information on food labels makes adhering to dietary restrictions even more confusing and difficult. Phosphate binders are the only pharmacologic treatment currently indicated for hyperphosphatemia. However, phosphate binders have a limited binding capacity and are difficult to incorporate into patients' daily routines. Because of the suboptimal efficacy of phosphate binders and the negative impact of dietary restrictions on patient QoL, novel therapies for more effective phosphate control are needed. New treatment options that control phosphate levels would enable patients to eat a more normal, healthy diet and potentially improve their QoL.

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INTRODUCTION

Patient-centered care—ie, care that is respectful of and responsive to individual patient preferences, needs, and values—should be an important part of kidney medicine. Patients receiving dialysis, in particular, may be negatively affected by their treatment regimen because of rigid dietary restrictions and the high burden of phosphate binder therapy. Thus, considering a more patient-centered approach is a crucial part of ensuring good quality of life (QoL) in patients receiving dialysis. This review discusses the limitations of currently available phosphorus management strategies, incorporating quotes from 3 patients, including 2 patient authors (D.F. and D.P.E.), on their experiences with hyperphosphatemia treatment to describe and illustrate a specific barrier or challenge.

IMPORTANCE OF PHOSPHATE REGULATION IN CHRONIC KIDNEY DISEASE

Elevated serum phosphate levels, or hyperphosphatemia, are seen in a very large proportion of patients with kidney failure and early stages of chronic kidney disease.¹ The negative clinical outcomes of hyperphosphatemia are established: hyperphosphatemia is associated with a number of disorders, such as cardiovascular disease, vascular calcification, and secondary hyperparathyroidism.^{1,2} Guidelines recommend the reduction of phosphate levels toward normal levels^{3,4}; furthermore, phosphate control is a standard, established part of treatment for patients with kidney failure and early stages of chronic kidney disease. However, achieving and maintaining target phosphate levels remains a clinical challenge: over 40% of patients receiving dialysis treated for hyperphosphatemia had serum phosphorus levels of >5.5 mg/dL in the most recent

month, and over 70% had levels of >4.5 mg/dL.⁵ In a prospective cohort study of patients receiving hemodialysis enrolled in the Dialysis Outcomes and Practiced Patterns Study, 4,286 (93%) US patients were unable to consistently maintain their serum phosphate levels at <4.5 mg/dL during a 6-month evaluation period.⁶ The current methods of phosphate management lead to poor QoL in patients receiving dialysis.⁷

EDUCATION GAP IN THE IMPORTANCE OF PHOSPHATE CONTROL AND ITS LINK WITH CARDIOVASCULAR OUTCOMES

Patients receiving dialysis do not have adequate knowledge of the importance of phosphate control (Box 1). They are often given instructions regarding dietary phosphate restriction.⁸ However, patients may not understand why phosphate restriction is important or the negative impact of poor phosphate control. A study of US patients receiving dialysis found that their health literacy about phosphate control was lower than their knowledge of other nutrients.⁸ Even when patients do understand the negative effects of high phosphate levels, they may not understand the parameters of a “low-phosphate” diet or be aware of “hidden phosphates.”⁹ Patients should be taught the importance of phosphate control and be educated on dietary phosphate restriction.

DIETARY RESTRICTION IMPACT ON PATIENT QOL

Dietary restrictions may negatively affect patient QoL, leading to negative clinical outcomes and difficulties in social interactions (Box 2). Patients receiving dialysis are advised by dietitians and nephrologists to adhere to a diet low in phosphate, potassium, sodium, and liquids to avoid

Box 1. Patient Quotes About the Lack of Education for Phosphorus Control

- “Two hours with a renal dietician, although something, doesn’t make up for 50 years of 0 nutrition education. I have bothered and pestered every dietician I’ve come in contact with, but the nutrition information is a very slow trickle. Nutrition education is a significant gap for patients, and that gap is coupled with the frank inability to find appropriate healthy foods and the easy access of processed foods with very high hidden sodium, potassium, and phosphate.”
- “When they say, ‘don’t eat too much phosphorus,’ well, how much is too much? Maybe some will learn less than 1,000 mg a day. Well, what does 1,000 mg of phosphorus look like? Four bell peppers? Nutrition labels don’t list phosphorus, so it’s all hidden. It’s very frustrating because even if you are trying hard, and we do try hard, everything seems stacked against you.”
- “No one told me how important phosphate control was and how it was tied to my chances to have a heart attack, stroke, and other cardiovascular events.”
- “I felt that education for patients on dialysis was focused on fluid restriction, hemoglobin, and potassium. Very rarely was phosphate mentioned and certainly not emphasized in my dialysis center.”

severe negative consequences associated with electrolyte overload.¹⁰ For example, the National Kidney Foundation–Kidney Disease Outcomes Quality Initiative guidelines recommend that phosphate intake should be limited to 800–1,000 mg/d.³ The burden of constant dietary self-management and dietary restrictions can lead to anxiety and depression. The recommended dietary restrictions do not allow flexibility, and patients might struggle to find foods that they are allowed to eat.¹⁰ The lack of nutritional information on food labels makes adhering to dietary restrictions even more confusing and difficult (eg, manufacturers are not required to include the quantity of phosphate due to food additives on labels).^{10,11} Furthermore, consuming a diet different from others’ diets in the household is difficult because preparing multiple meals within 1 household is expensive and time-consuming.¹² Consuming a separate diet may also create social, physical, and timing distances between patients and their family members. Patients may not be able to participate in social activities, which may result in a feeling of isolation at home and/or with friends. Moreover, patients may not be able to adhere to dietary restrictions at social gatherings and/or restaurants because the nutritional content of foods prepared in restaurants is unknown and processed foods containing additives often lack labeling.¹¹

PHOSPHATE BINDER IMPACT ON PATIENT QOL

The patient quotes regarding phosphate binders are shown in **Box 3**. Phosphate binders have been the only approved

Box 2. Patient Quotes About Dietary Restrictions

- “Managing my diet requires a spreadsheet and a certain amount of obsession, that not all patients have, to make sure all the chemicals balance as far as a renal diet is concerned.”
- “I am exhausted because I need to spend a lot of time cooking at home and trying to calculate phosphate intake.”
- “I have a hard time finding anything to eat within this restricted diet, and I’m not sure I totally understand which foods are allowed and which are not. I am always stressed about meals and have trouble enjoying spending time with my family and friends.”
- “I’m in a more rural or suburban area, and it’s a healthy food desert. Minority and lower socioeconomic communities make up a large portion of dialysis patients, but it also makes access to healthy fresh foods almost impossible, especially during a pandemic. I couldn’t even find a fresh head of lettuce within miles at the supermarket. In some areas, they have groceries delivered, but they won’t deliver to my area. However, right around the corner, I had fast food and dollar stores with all the processed foods in a box or can. It’s disgusting. Many of us don’t eat the right foods because we are just worn out from trying to find them.”
- “I know what it is that I need to eat, but if I can’t find it, what can I do? I’m just going to eat what I’m going to eat. I’m hoping the dialysis machine sucks out the majority of it and just deal with the backlash consequences. Many patients don’t know what the consequences are, that it could put you in a lot of pain or a wheelchair or walker from the heart attack and stroke that’s coming.”
- “When I go to someone’s house for dinner, it’s a huge stress. They are trying to be nice by offering lots of food. I want to be gracious and accept the food they are offering instead of being rude and saying that I can’t eat it. It makes them feel bad. It makes me feel bad. More often than not, I secretly have to throw it away and pretend I loved it. I probably would have loved it too. Social and family gatherings are a difficult time.”
- “Just try to go to a restaurant. I’ll order a cheeseburger. Hold the bun and hold the cheese.”

therapeutic option for hyperphosphatemia for decades.^{13–17} Phosphate binders complex with dietary phosphate in the gastrointestinal tract to reduce the quantity of available absorbable phosphorus.^{13–17} The binders’ mechanism of action does not target or affect the primary paracellular phosphate absorption pathways.^{13–17}

Phosphate binders are difficult to incorporate into patients’ daily lives and can negatively affect and/or limit social interactions. Because binders must be present in the gut when dietary phosphorus is present in the gut, these must be taken every time a patient eats.^{13–17} If patients do not have phosphate binders with them, they cannot eat anything because phosphate binders must be taken with every meal or snack.^{13–17} As a result, patients may feel stressed or burdened by always having to carry phosphate

Box 3. Patient Quotes About Phosphate Binders

- “I take about 1,100 pills a month. Five hundred of those are phosphate binders. If I could get those 500 pills down to 50 or so, that would be enormous. I am chugging down 5 or 6 binders with every meal, which I'd rather not do.”
- “It's stressful to constantly remind myself to take the binders every time I eat, it really makes spontaneous activities difficult, and I can't enjoy social activities as much. Sometimes I forget and feel really anxious and guilty.”
- “The size and number of pills are hard to deal with every day. Sometimes I have trouble swallowing them, and I'm worried about taking them in public in case I can't swallow successfully on the first try.”

binders or being unable to have impromptu meals or snacks. Because each pill can only bind so much phosphorus,^{18,19} phosphate binders tend to be large and require to be taken in a high quantity and at frequent dosing.¹³⁻¹⁷ Because phosphate binders tend to be large and can be difficult to swallow and because patients have to often take multiple pills with each meal or snack, they sometimes need to try multiple times to successfully take the pills, leading to discomfort and potentially traumatizing memories for friends and families. The daily pill burden in patients receiving dialysis is one of the highest reported to date in any chronic disease state.²⁰ By far, phosphate binders are the single largest contributor to this pill burden, accounting for approximately 50% of total daily pills.²⁰

Capsules and large tablets are difficult to swallow because of their size,²¹ whereas chewable tablets have a bad taste and may still be difficult to swallow.²¹ Frequent dosing with each meal and snack¹³⁻¹⁷ can result in difficulty in consistently incorporating the binders into the patient's existing schedule, difficulty in remembering to take the pill, and a negative impact on the patient's social life. With the high number of pills,¹³⁻¹⁷ repeated swallowing or chewing of pills is uncomfortable, and large amounts of water might be needed to accompany the pills among patients who are fluid restricted. Moreover, the total dosage of binders needed depends on the amount of phosphate ingested in the diet¹³⁻¹⁷; the pill requirement increases as the intake increases.

SUBOPTIMAL EFFICACY OF PHOSPHATE BINDERS AND THEIR IMPACT ON THE PATIENT–CLINICIAN RELATIONSHIP

The inability to achieve and maintain target phosphate levels is frustrating for patients and can damage the patient–clinician relationship (Box 4). Patients may follow phosphate binder dosing instructions and still have hyperphosphatemia. They may also feel ashamed and guilty and feel like they are being blamed for above-target phosphate levels. These negative emotions and the lack of

Box 4. Patient Quote About Negative Clinician–Patient Relationship

“I get harassed. I get a finger waved in my face by my doctor or dietician. They will say that I need to do better. I don't wanna get harassed, so I just need to do better. All of this makes me feel like it's my fault for not eating a near-perfect kidney-friendly diet. Once in a while, I get that smiley face next to my phosphorus lab. I look forward to that smiley face. The tradeoff for that smiley face is I'm not allowed to enjoy life if I want to have a little ice cream.”

trust can impair the patient–clinician relationship. In addition, monitoring and treating hyperphosphatemia takes up time that clinicians would otherwise spend on treating the disease itself and other important comorbidities. Patients may get angry or frustrated with clinicians because they may perceive that they are not receiving adequate resources, care, and support. The constant, ongoing burden of dietary restrictions and medication may erode the relationship between patients and dietitians, nurses, doctors, and other medical professionals.

STRATEGIES TO OVERCOME PHOSPHATE MANAGEMENT BARRIERS

Patient Education

To address the low level of health literacy about phosphate management, clinicians should clearly communicate the negative effects of not adhering to phosphorus management strategies and educate patients on which foods can be safely consumed.²² First, clinicians should make sure that patients understand that not adhering to phosphate control strategies (eg, eating processed foods high in phosphate additives) might lead to above-target phosphate concentrations, which can negatively affect health outcomes.²² Second, increased dietary education on which foods are safe and which are not safe to eat can improve phosphate control,^{23,24} although extended consultations with a dietician (eg, 20-30 minutes) might not be practical in real-world facilities because of staffing issues. Patient education that incorporates both of the abovementioned components has been shown to be beneficial for phosphate control: in patients who completed an education program consisting of modules on diet, phosphate additives, and the complications of hyperphosphatemia, the phosphate concentration decreased from 2.1 to 1.7 nmol/L (6.5-5.7 mg/dL; $P < 0.001$).²⁵

Dietician Support and Visual Aids

The ways to reduce the negative impact of dietary restrictions on patient QoL include support from dietitians and the use of visual aids that lighten the day-to-day burden of phosphorus management. Dietitians can help reduce the stress of adhering to a restricted diet by

Box 5. Patient Quote About Novel Phosphorus Control Approaches

“There are so many reasons that phosphorus is difficult to manage in kidney patients like me. I’m really excited about hearing what’s new on the horizon. The possibility of just blocking the phosphates; well, that was just like the bee’s knees for me.”

providing practical, achievable recommendations rather than by compelling patients to give up their favorite foods.²⁶ For example, patients can be advised to eat fresh, nonprocessed egg whites instead of entirely cutting out eggs from their diet.²⁶ Visual aids that allow patients to quickly check which foods are safe to eat, without needing to memorize the phosphate load for each item, help alleviate the stress and anxiety of adhering to a restricted diet. One such example is the phosphorus pyramid, which was designed to easily display the phosphate load of various foods.⁶ The pyramid consists of 6 tiers and categorizes foods based on their phosphorus content, phosphorus-to-protein ratio, and phosphorus bioavailability.⁶ Foods at the base of the pyramid have very low phosphorus content, progressing to foods at the top of the pyramid that contain phosphorus additives.⁶ Novel therapies under development that improve current phosphate management strategies may also allow patients to consume a more liberal diet, potentially improving their QoL.

Novel Therapies for Efficient Phosphate Control

The negative impact of phosphate binders on patient QoL can be reduced by novel therapies, including pills that are smaller in size, making them easier to swallow, and/or pills that can achieve proper phosphate control, with lower daily pill burdens (Box 5). The pan-phosphate transport inhibitor EOS789 is administered at a dose of 50 mg 3 times per day (with meals), compared with thousands of milligrams for phosphate binders; furthermore, a phase 1 trial showed encouraging results in patients receiving hemodialysis.²⁷ The paracellular phosphate absorption inhibitor tenapanor is administered twice daily (30 mg).²⁸ When tenapanor was coadministered with phosphate binders, the daily phosphate binder pill burden decreased from 15 to 3 pills, and 30% of patients were able to switch to tenapanor only while maintaining effective phosphate control.²⁸ Thus, novel nonbinder phosphate control therapies can decrease the negative impact of phosphate binders on patient QoL.

Increased clinician–patient interactions and treatment approaches that can improve phosphate control are strategies to address the negative impact of suboptimal phosphate binder efficacy on the patient–clinician relationship. In a study assessing satisfaction with dialysis facilities, all patients emphasized the importance of nurse-

patient interactions.²⁹ The single most important thing that a dialysis unit can provide, according to patients, is attentiveness to individual patient concerns.²⁹ New phosphate management approaches and therapies that can more consistently achieve and maintain proper phosphate control can also improve the patient–clinician relationship by reducing the shame patients feel for not achieving their phosphate goals and freeing up time that clinicians would otherwise spend on managing hyperphosphatemia.

CONCLUSION

Considering the negative impact of the current treatment approach to phosphorus management on patient QoL, novel therapies and approaches are needed that provide effective phosphate control with more reasonable requirements of patients.

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