

Phosphate-control adherence in hemodialysis patients: current perspectives

Ebele M Umeukeje¹⁻³

Amanda S Mixon^{3,4}

Kerri L Cavanaugh¹⁻³

¹Vanderbilt Center for Kidney Disease, Nashville, TN, USA; ²Division of Nephrology, Department of Medicine, Vanderbilt University Medical Center, Nashville TN, USA;

³Vanderbilt Center for Health Services Research, Nashville, TN, USA; ⁴Section of Hospital Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

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Correspondence: Ebele M Umeukeje
Division of Nephrology, Department of Medicine, Vanderbilt University Medical Center, 1161 21st Avenue South, MCN S-3223, Nashville, TN 37232, USA
Email ebele.m.umeukeje@vanderbilt.edu

Objectives: This review summarizes factors relevant for adherence to phosphate-control strategies in dialysis patients, and discusses interventions to overcome related challenges.

Methods: A literature search including the terms “phosphorus”, “phosphorus control”, “hemodialysis”, “phosphate binder medications”, “phosphorus diet”, “adherence”, and “nonadherence” was undertaken using PubMed, PsycInfo, CINAHL, and Embase.

Results: Hyperphosphatemia is associated with cardiovascular and all-cause mortality in dialysis patients. Management of hyperphosphatemia depends on phosphate binder medication therapy, a low-phosphorus diet, and dialysis. Phosphate binder therapy is associated with a survival benefit. Dietary restriction is complex because of the need to maintain adequate protein intake and, alone, is insufficient for phosphorus control. Similarly, conventional hemodialysis alone is insufficient for phosphorus control due to the kinetics of dialytic phosphorus removal. Thus, all three treatment approaches are important contributors, with dietary restriction and dialysis as adjuncts to the requisite phosphate binder therapy. Phosphate-control adherence rates are suboptimal and are influenced directly by patient, provider, and phosphorus-control strategy-related factors. Psychosocial factors have been implicated as influential “drivers” of adherence behaviors in dialysis patients, and factors based on self-motivation associate directly with adherence behavior. Higher-risk subgroups of nonadherent patients include younger dialysis patients and non-whites. Provider attitudes may be important – yet unaddressed – determinants of adherence behaviors of dialysis patients.

Conclusion: Adherence to phosphate binders, low-phosphorus diet, and dialysis prescription is suboptimal. Multicomponent strategies that concurrently address therapy-related factors such as side effects, patient factors targeting self-motivation, and provider factors to improve attitudes and delivery of culturally sensitive care show the most promise for long-term control of phosphorus levels. Moreover, it will be important to identify patients at highest risk for lack of control, and for programs to be ready to deliver flexible person-centered strategies through training and dedicated resources to align with the needs of all patients.

Keywords: hyperphosphatemia, adherence, phosphorus binders, low-phosphorus diet, dialysis

Plain language summary

Management of end-stage renal disease (ESRD) is complicated by hyperphosphatemia. This is the accumulation of phosphorus in the body due to the inability of dialysis patients to excrete phosphorus. This increases the risk of spontaneous bone fractures from abnormal mineral metabolism and risk of death from cardiovascular disease. Management of hyperphosphatemia depends on three approaches: use of medications known as phosphate binders, dietary phosphorus restriction, and removal of phosphorus through dialysis. Adherence to each of these approaches is a challenge for dialysis patients due to medication- or dialysis-treatment-associated burden, complexity of the diet, as well as patient-specific factors. Patient factors associated with phosphate-control adherence behaviors include age, gender, and race. In preliminary research,

psychosocial autonomy-centered or self-motivation patient factors contribute to phosphorus-control adherence, and suggest that aligning with a person's value system may be the key to optimizing medication, diet, and dialysis care. Existing strategies to improve phosphate control include educational and behavioral interventions delivered by multidisciplinary dialysis providers. Emerging research implicates that dialysis providers have varying attitudes and poor perceptions of their support of self-motivation in dialysis patients for adherence to prescribed phosphate binder medication therapy. Improvement in phosphorus-control adherence will require enhanced provider-level training strategies integrated into existing patient-level interventions, with a focused effort to identify patients at high risk of nonadherence who may benefit from more personalized solutions.

Introduction

Hyperphosphatemia is common in end-stage renal disease (ESRD) because of impaired renal phosphate excretion.¹ It is a critical component of mineral and bone disease (MBD) that increases the risk of fractures and osteoporosis,² and is associated with greater cardiovascular and all-cause mortality in dialysis patients.³ Hyperphosphatemia may be effectively managed with phosphate binder medication therapy, dietary restriction, and dialysis prescription.¹

Phosphate binder medication therapy is the cornerstone of therapeutic management in hyperphosphatemia,⁴ and it has been associated with survival benefits. The existing evidence, although robust, is from observational studies,⁵ and this could be a possible opportunity for a pragmatic trial design in the future.⁶ Optimization of phosphate binder use by patients with ESRD to achieve target serum phosphorus levels toward the normal range of 3.5–5.5 mg/dL is of utmost importance to minimize morbidity and mortality risks.^{7,8} However, it is estimated that up to 74% of ESRD patients are noncompliant to phosphate binder medication therapy.^{9,10} Challenges to adherence include 1) medication-related factors such as high pill counts, complex adjustable schedules, adverse side effects, and financial burden;¹¹ 2) patient-specific factors such as limited knowledge about the importance of taking binder medications;^{11,12} 3) recurrent hospitalizations disrupting the usual daily approaches to binder medications, and concomitant comorbidities such as diabetes and hypertension compounding medication complexity and overall burden;¹² and 4) provider-level factors related to educational and emotional support for patients.¹¹

High dietary phosphorus intake and increased dietary phosphorus-to-protein ratio have been associated with mortality in ESRD.¹¹ A low-phosphorus diet is insufficient to control the serum phosphorus level in the well-nourished

ESRD patient, and has not been associated with improved survival.¹³ Dietary phosphorus restriction is complex because it is challenging to maintain the adequate protein intake needed in ESRD patients to prevent malnutrition and simultaneously restrict phosphorus intake. Perhaps even more importantly, many processed foods contain a significant amount of phosphate additives that are often undisclosed and difficult for patients to identify.¹¹ In ESRD, the ideal daily phosphorus intake is 700 mg/day; however, the usual intake commonly averages 1,000–2,000 mg/day.¹⁴ Approximately 60% of the phosphorus is absorbed,¹⁵ which results in a significant daily excess of phosphorus. Adherence to a low-phosphorus diet could be as low as 43%,¹⁶ and is influenced similarly by 1) diet-specific factors such as menu selections, impact of the diet on social outings, and acceptance of the diet by friends and family;¹⁶ 2) patient factors such as depression, limited self-efficacy, and poor coping skills;¹⁶ and 3) provider factors including inadequate support,¹⁶ infrequent contact with dietitians, and conflicting phosphorus diet advice from different health professionals.¹⁷

Thrice-weekly conventional dialysis removes phosphorus in the range of 1,800–3,600 mg and, thus, does not provide enough clearance of the daily amount of ingested phosphorus to maintain balance.¹⁸ This is due to the kinetics of phosphorus removal during hemodialysis, whereby serum phosphorus levels plateau after an initial drop within the first 2 hours of treatment, followed by a rebound, resulting in up to 40% rise in serum phosphorus levels after dialysis.¹⁹ Dialysis treatments are complicated by nonadherence, and it is estimated that up to 35% of patients miss treatments entirely whereas another 32% shorten their treatment time.²⁰ Reasons for nonadherence to the prescribed dose of dialysis include treatment- and patient-related factors. Dialysis vintage and schedule assignment, both, are associated with treatment nonadherence.²¹ Patient factors associated with dialysis treatment nonadherence include younger age^{21,22} and non-white race²³ as well as psychosocial factors including negatively perceived effects of kidney disease on daily life and lack of perceived control over future health.²² Nonadherence to the dialysis procedure contributes to significant morbidity and increases mortality risk – in part, due to uncontrolled mineral bone disease.^{9,24}

There are unique drivers of adherence behaviors for medications, diet, and dialysis in the effort to control phosphorus, but there are also common themes that can be leveraged to simultaneously optimize all approaches. This review discusses current perspectives and challenges contributing to low adherence to phosphate control, and examines

effective and emerging strategies for patient-centered care with hemodialysis.

Phosphate-control methods in hemodialysis patients

Phosphate binder medication therapy

An overview of phosphate binder medications is presented in Table 1. Phosphate binders regulate calcium–phosphate homeostasis and mitigate the metabolic abnormalities resulting from hyperphosphatemia.²⁵ They prevent phosphate absorption from the gastrointestinal tract through varied mechanisms. These medications can be broadly classified into 1) calcium-based and 2) non-calcium-based phosphate binders.

Calcium-based phosphate binders including calcium acetate, citrate, and carbonate dissociate in the gastrointestinal tract and bind phosphate to form insoluble precipitates. They are less expensive than the non-calcium binders,¹⁰ but are associated with greater risk of vascular calcification due to a positive calcium balance.²⁶

Non-calcium-based binders include sevelamer, lanthanum, and iron-based binders (eg, ferric citrate and sucroferri oxyhydroxide).²⁶ Sevelamer is an anion exchange resin that exchanges chloride ions for phosphate ions whereas lanthanum binds phosphate through its trivalent cation. Both are associated with gastrointestinal side effects such as abdominal bloating, diarrhea, and constipation. Lanthanum has a low pill burden compared to sevelamer. Sevelamer carbonate is available as a powder for patients who may benefit from a different formulation;¹¹ however, patients often get tired of taking it and usually request a change of phosphate binder preparation.²⁷ The pill form of sevelamer is comparatively large in size and, given its accompanying high pill burden, it requires the ingestion of large quantities of water.⁷

Iron-based phosphate binders include ferric citrate and sucroferri oxyhydroxide. Ferric citrate is partially absorbed and, therefore, is ideal for the management of hyperphosphatemia in patients who are also iron deficient; however, the citrate content increases the potential for aluminum absorption and possible toxicity.²⁸ Sucroferri oxyhydroxide is better suited for dialysis patients who do not require iron supplementation and has the added benefit of low pill burden.²⁸ Findings from a recent meta-analysis suggest that nicotinic acid, a major form of vitamin B3, may be a novel effective alternative or adjunct for lowering serum phosphorus concentrations in dialysis patients.²⁹ It lowers the absorption of phosphorus from

the gastrointestinal tract, has unique antilipemic effects, and warrants further investigation of its long-term safety and efficacy.²⁹

Patient tolerance of different phosphate binders varies, and patient-reported reasons for discontinuation of these medications also vary by the type of binder.³⁰ Patients with ESRD may be nonadherent to phosphate binder therapy because of the misconception that nonadherence results in no immediate symptoms or risks.^{10,11} A systematic review of nonadherence to medications in hemodialysis patients described medication side effects, pill burden, large tablet size, unpalatable taste, medication regimen complexity, difficulty opening the medication container, and prescription refilling as key contributors to nonadherence.¹² These medication-based factors are particularly characteristic of phosphate binders and, therefore, represent targets for control strategies.

Epidemiology of phosphate binder adherence

Nonadherence to phosphate binders ranges from 13% to 99%, with an average of 53%.¹² This range is wide partly due to heterogeneity in the methods of characterizing nonadherence.¹² Current methods of assessing nonadherence to phosphate binders include 1) subjective measures, 2) objective measures, and 3) biochemical assessment of serum phosphorus levels. Estimated rates of nonadherence, assessed by subjective and objective measures as well as biochemical assessment of serum phosphorus levels, are 48%, 78%, and 29% respectively.¹²

Subjective measures using validated scales^{31,32} or non-validated scales or interviews^{33,34} are the most widely used methods of nonadherence assessment.¹² Objective measures including pill count,³⁵ bottle-use devices such as Medication Event Monitoring System (MEMS) caps^{36,37} and medication possession ratio³⁸ are the least utilized methods of assessment.¹² The biochemical assessment of serum phosphorus levels is frequently conducted as a part of routine dialysis care, but is complicated by variable definitions of the upper limit of the acceptable range.^{31,39} Moreover, these assessment methods have been used in combination in the absence of universally agreed upon standards for assessment of phosphate binder adherence.⁴⁰

KDIGO guidelines for phosphate binder use

The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease – Mineral

Table 1 Overview of currently available phosphate binders

Phosphate binder	Mechanism of action	Typical daily pill burden*	Advantages	Disadvantages
Aluminum salts	Aluminum binds to phosphates and forms insoluble precipitate in the GI tract; aluminum hydroxide also forms compounds with phosphate ions in the blood	No safe dose identified	Effective, inexpensive	Associated with cognitive disturbances, osteomalacia, and anemia. Patient requires careful monitoring
Calcium acetate (eg, Phosex)	Dissociates in the GI tract; calcium binds to phosphates and forms insoluble precipitate	4–6 pills (1,000 mg each, equivalent to 250 mg calcium) per day	Effective and inexpensive	Potential for increased hypercalcemia; could lead to vascular calcification; high pill burden
Calcium carbonate (eg, CalciChew)	Dissociation in the GI tract; calcium binds to phosphates and forms insoluble precipitates	Pill number as prescribed per day, (1,250 mg each, equivalent to 500 mg calcium)	Effective and inexpensive	Potential for increased hypercalcemia; could lead to vascular calcifications; high pill burden
Calcium acetate/magnesium carbonate	Dissociation of the active compounds calcium acetate and magnesium carbonate in the GI tract; each binds to phosphate and forms insoluble precipitates	Total: 3–10 pills per day (each pill contains 435 mg calcium acetate/235 mg magnesium carbonate)	Lower calcium uptake versus calcium-based binders; effective; moderate costs	Monitoring of magnesium level required; in some circumstances, moderate increase in serum magnesium level
Sevelamer HCl	Anion exchange resin that exchanges chloride ions for phosphate ions	3 pills (800 mg each) three times daily (total: 9 pills/days)	Effective; lipid-lowering effect; potential cardioprotective effect	Expensive; high pill burden; associated with GI side effects such as abdominal bloating, diarrhea, and constipation. Potential development of metabolic acidosis
Sevelamer carbonate	Anion exchange resin that exchanges chloride ions for phosphate ions	3 pills (800 mg each) three times daily (total: 9 pills/day)	Effective; lipid-lowering effect; potential cardioprotective effect; available as a powder, which may reduce pill burden	Expensive; high pill burden; associated with GI side effects
Lanthanum carbonate	Dissociation in the upper GI tract; lanthanum then binds to phosphates and forms insoluble, nonabsorbable lanthanum phosphate complexes	1 pill (500, 750, or 1,000 mg) three times daily (total: 3 pills/day)	Effective, low pill burden	Expensive; associated with GI side effects such as nausea, vomiting
Sucroferric oxyhydroxide	Ligand exchange between the hydroxyl groups in the sucroferric oxyhydroxide and phosphorus in food lead to elimination of bound phosphate in the stool	3 pills (1,500 mg daily)	Effective, reduced pill burden relative to sevelamer Iron is not absorbed; does not lead to iron overload	Discolored feces, diarrhea, nausea Does not affect the hemoglobin level
Ferric citrate	Increases stool phosphate excretion and reduces intestinal phosphate absorption	6 pills (6,000 mg daily)	Effective, positive hematologic effects; Iron is absorbed	Discolored feces, diarrhea, nausea; Risk of iron overload; Potential risk of aluminum absorption

Notes: *Timing and dose of phosphate binder to be adjusted in line with timing of meal/snacks and the phosphorus content thereof. Copyright ©2013. Covic and Rastogi; licensee BioMed Central Ltd. Reproduced with permission from Covic A, Rastogi A. Hyperphosphatemia in patients with ESRD: assessing the current evidence linking outcomes with treatment adherence. *BMC Nephrol.* 2013;14(1):153.¹¹

Abbreviations: GI, gastrointestinal; HCl, hydrochloride.

and Bone Disorder (CKD-MBD) was updated in 2017. The current recommendation for serum phosphorus control in dialysis patients is that decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate (Not graded), and elevated serum phosphorus levels should be lowered toward the normal range (3.5–5.5 mg/dL) (Grade 2C recommendation). However, implementation of this recommendation is challenging because of laboratory variability in the normal range of phosphorus and diurnal variations in serum phosphorus levels. Furthermore, the KDIGO guidelines recommend restricting the dose of calcium-based phosphate binders (Grade 2B recommendation).⁴¹

Economics of phosphate binder use

In the USA, phosphate binder use for US dialysis patients and patients with non-dialysis chronic kidney disease enrolled in Medicare Part D accounted for more than USD 1.5 billion in 2015.⁴² Phosphate binder-associated costs outweigh the costs associated with all other Part D-covered drugs for patients on dialysis.⁴² As of 2013, it cost Medicare five times as much for sevelamer carbonate and lanthanum carbonate, compared to calcium acetate, to achieve the same degree of phosphate control in a patient.⁴² When adjusted for the costs of binders, calcium binders have lower Medicare per member per month costs.⁴³ Data from a recent systematic review suggest that calcium acetate is the most cost-effective therapy for first-line use in dialysis patients, although these conclusions were limited due to the heterogeneity of study quality.⁴⁴

The enormous costs associated with the use of phosphate binders in dialysis patients in the absence of conclusive evidence of their impact on end points has been a source of controversy.⁴² There is controversy over the best way to determine the most cost-effective phosphate binder therapy, and much of the debate is due to the quality of existing data. One approach could be to look at overall expenses. It has been suggested that sevelamer is associated with a lower risk of stroke⁴⁵ as well as reduced Medicare inpatient and total costs as compared with calcium-based binders, which makes it more cost effective overall.⁴³ This continues to be a source of debate and may contribute to mixed messaging to patients about risks/benefits of the various choices.

Factors affecting phosphate binder adherence

Medication factors

Multiple factors have been implicated in nonadherence to phosphate binders (Table 2). Medication-related factors responsible

for nonadherence to phosphate binders are well studied, and the most commonly acknowledged is pill burden. Phosphate binders are often the single largest contributor to the excessive pill burden for dialysis patients, constituting half of their daily pill burden.³⁵ Dialysis patients take a mean 11 ± 4 medications, with a median daily pill intake of 19 (interquartile range: 12).¹¹ The total number of phosphate binders prescribed⁴⁶ and total pill burden for other chronic conditions are associated with nonadherence to phosphate binders.^{35,47,43} The frequency of dosing of phosphate binders with all food intake, including meals, beverages, and snacks, increases its complexity and worsens adherence.^{12,47} Unfortunately, nonadherence leads to poorer phosphate control and results in an increase in the number of prescribed tablets.¹⁰ In addition to pill burden, the form, taste, and side effects – as discussed earlier – are also associated with nonadherence to these medications.⁴⁶

Patient factors

Patient-related factors associated with phosphate binder nonadherence¹² include 1) sociodemographic and 2) psychosocial variables. Younger age^{10,12,31–33,46–49} has been most consistently linked to phosphate binder nonadherence. Perhaps, younger people are prioritizing other activities over their health⁵⁰ or, alternatively, they may be more willing to report nonadherence than older patients.¹⁰

Non-Caucasian race^{12,23,32,36,37,49} has been associated with phosphate binder nonadherence (odds ratio [OR 0.76]; $p < 0.05$)⁴⁹ and may be confounded by lower socioeconomic status.⁵⁰ Other sociodemographic variables associated with phosphate binder nonadherence include lack of marital support^{12,52,53} (OR 1.21; $p < 0.05$)⁴⁹ and unemployment^{12,52} (OR 1.21; $p < 0.05$),⁴⁹ although findings across studies are not consistent.

Psychosocial factors have been identified as the most influential and potentially modifiable determinants of phosphate binder nonadherence (Figure 1). These include 1) patients' health beliefs and 2) social support related to hyperphosphatemia treatment.¹⁰ These health beliefs include concerns about the potential side effects of phosphate binders (OR = 3.17; 95% CI: 1.87–5.37; $p < 0.001$);³² reduced beliefs in personal need for phosphate binder medications (OR = 0.34; 95% CI: 0.14–0.83; $p < 0.05$);³² and low self-efficacy or perceived competence of taking phosphate binders ($t(71) = 2.55$, $p < 0.02$).⁵⁴ Knowledge about the purpose of phosphate binders has been found to be an important factor influencing adherence ($r = 0.22$; $p < 0.05$).⁵⁵ However, knowledge of treatment instructions does not correlate with adherence, suggesting that knowledge alone is insufficient to drive adherence to phosphate binders.¹⁰

Table 2 Factors associated with nonadherence and summary of relevant associations (N=38)

Factors	No of studies	Significant association with measures of nonadherence ^a		
		Pre-dialysis phosphorus	Patient self-report	Pill count/medication event monitoring system
Sociodemographic variables				
Age	27			
Younger		8	8	
Older		1	2	1
Gender	22			
Male			1	
Female			2	
Low education (high school)	15		1	
Ethnicity (non-Caucasian)	7	1	1	2
Marital status (single, divorced, or widowed)	6		2	
Employment status (unemployed)	6		1	
Support from healthcare provider	2		2	
Family problems (illness interfering with family life)	2		1	
Smoker	1	1		
Clinical variables				
Long-term on hemodialysis	16		3	
Comorbidity (DM, HTN)	9	1	1	
Number of hospitalizations	2		1	
Psychosocial variables				
Depressive symptoms	6		4	
Beliefs about medicine	5			
Concern		1	2	
Benefit		1	1	
Necessity		1	3	
Necessity–concern differential score			2	
Health locus of control ^b	3	2	1	
Autonomous			1	
Doctors			1	
Emotional representation	1	1		
Medication-related factors				
Knowledge about medicine	5	1	1	
Number of prescribed medicines	3			1
Daily tablet count	2	1	1	
Total number of PB prescribed	2	1	1	
Total pill burden	2			
Pill burden from PB	1			1
PB equivalent dosage	1		1	
Regimen complexity (frequency and dosage)	1	1		
Drug coverage by insurance	1			1
Healthcare cost (inpatient)	1			1

Notes: ^aLevel of significance ($p < 0.05$, $p < 0.01$, and $p < 0.001$) varies between studies. ^bDefined as having high expectation that one's actions will have a causal relationship with the consequences produced. Copyright ©2015. PLOS. Reproduced from Ghimire S, Castelino RL, Lioufas NM, Peterson GM, Zaidi ST. Nonadherence to medication therapy in haemodialysis patients: a systematic review. *PLoS One*. 2015;10(12):e0144119.¹²

Abbreviations: DM, diabetes mellitus; HD, hemodialysis; HTN, hypertension; PB, phosphate binders.

Whereas marital support may be associated with adherence, the support of other family and friends has not yet been demonstrated to have a significant impact on phosphate binder nonadherence.⁵⁵ Rather, the patient's perception of illness and its disruption of their family life contributes significantly to phosphate binder nonadherence ($r = -0.35$; $p < 0.05$).⁵⁵

Depressive symptoms, furthermore, have been linked to nonadherence to phosphate binder therapy (OR = 1.11;

95% CI, 1.04–1.18; $p = 0.001$).^{52,56,57} Factors such as forgetfulness, lack of interest, and monotony have been identified as contributing to nonadherence.¹² Intentional phosphate binder nonadherence behavior exists in dialysis patients⁵⁸ and, in order to understand it, it is important to understand the patients' personal values and level of motivation. This addresses the call for patient-centered care in dialysis management that aligns patients' values to their therapy

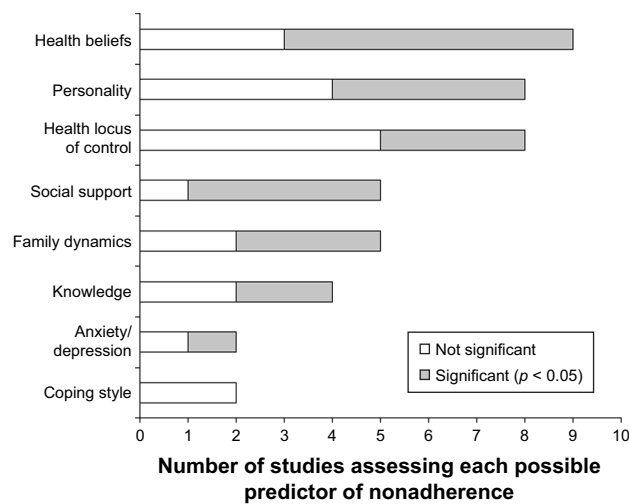


Figure 1 Psychosocial predictors of nonadherence to phosphate-binding medication assessed by two or more studies.

Note: ©2008. BioMed Central Ltd. Adapted from Karamanidou et al; licensee BioMed Central Ltd. Karamanidou C, Clatworthy J, Weinman J, Horne R. A systematic review of the prevalence and determinants of nonadherence to phosphate binding medication in patients with end-stage renal disease. *BMC Nephrol.* 2008;9:2.¹⁰

while taking into account their side-effect and tolerability profiles.⁵⁹

Emerging research has identified that novel motivation and autonomy-centered factors are associated with phosphate binder nonadherence. These psychosocial factors are based on the self-determination theory (SDT), which posits that autonomy is an essential factor for achieving durable positive change.⁶⁰ The SDT distinguishes between autonomous or self-motivated behavior and controlled behavior. It includes three unique psychosocial factors: autonomous regulation, autonomy support, and perceived competence.⁶⁰ Higher autonomous regulation of phosphate binder therapy or more positive attitudes toward phosphate binder use has been associated with phosphate binder adherence.^{47,61} Similarly, the perception of dialysis patients with regard to their providers' support of autonomy for phosphate binder therapy and patient empowerment are associated with adherence to binders.⁶² Moreover, perceived competence or self-efficacy has been associated with adherence to phosphate binder therapy.⁶³ These factors show great promise to better understand nonadherence as they are associated with self-reported phosphate binder adherence,^{61,62} and are potentially modifiable using patient-centered approaches, such as motivational interviewing.^{60,64}

Racial differences in the relationship between these novel psychosocial factors, phosphate binder adherence, and phosphorus control suggest that they may be more important in non-whites. Non-white dialysis patients have a lower perception of provider support for phosphate binder adherence as

compared to whites.⁶² Furthermore, the association between autonomous regulation of phosphate binder therapy and serum phosphorus control is significant in non-whites (β 95% CI: -0.38 [-0.74 to -0.02]; $p = 0.04$) but not in whites (β 95% CI: 0.49 [-0.00 to 0.99]; $p = 0.05$).⁶¹

Phosphate binder adherence in the elderly

Polypharmacy has been identified as a geriatric-related syndrome that is associated with medication nonadherence,⁵¹ and it is exacerbated when the regimen includes phosphate binders. There are currently no guidelines for achieving a balance between phosphate adherence and health-related quality of life for the elderly, or others with predicted poor survival. Therefore, the overarching principle for phosphate-control adherence is the delivery of patient-centered care, with individualization of phosphorus-control regimens to optimize health-related quality of life in the elderly.

Provider factors

The World Health Organization (WHO) highlights provider factors as important determinants of patient adherence to prescribed medication and emphasizes that 1) "patients need to be supported by providers, not blamed", 2) providers need to be able to assess adherence and factors that influence it, and 3) providers must be adequately trained in adherence management.⁶⁵ Provider factors relevant to phosphate binder nonadherence have not been fully investigated. Interview and focus-group data from hemodialysis patients suggested the presence of adversarial interactions between dialysis patients and their providers that impact their adherence.⁶⁶ In particular, dialysis providers do not 1) individualize their patients' care, but rather, deliver "assembly line" treatment, 2) recognize patients' knowledge based on their unique expertise on their bodies and experience gained from their chronic illness, or 3) engage in shared decision making.⁶⁶

Provider attitudes have been shown to correlate with clinical outcomes. For instance, facilities with providers that have more positive attitudes toward transplants have better wait-listing performance.⁶⁷ The phosphate binder prescription patterns of dialysis providers are highly variable, and some dialysis units prescribed phosphate binders for a significantly smaller proportion of their dialysis patients.⁵ This suggests differences in the preferences of dialysis providers for, or attitudes toward, phosphate binders.⁵ Patients who positively characterize their interactions with their dialysis providers have a lower odds for nonadherence to phosphate binders (OR = 0.52; 95% CI, 0.30–0.90).³³ Further, support by

dialysis staff is associated with phosphate binder adherence ($r = 0.20$; $p < 0.05$).⁵⁵ Provider interventions show promise of a positive and sustained impact on medication adherence in dialysis patients.

Dialysis treatment and hospitalizations affect medication adherence

Longer duration on hemodialysis therapy of 5 years or more has been found to be the most consistent ESRD factor associated with phosphate binder nonadherence.^{17,47,68} Perhaps, the longer duration on hemodialysis leads to more boredom and frustration over the need for continued adherence to this challenging medication regimen.¹⁷ Another important consideration is the relatively frequent acute illnesses leading to hospitalization. This disrupts the rigorous routine of day-to-day phosphate binder medications and increases the perception of burden of therapy.⁴⁷ In general, hospitalizations also have an adverse impact on medication adherence due to errors in medication reconciliation⁶⁹ and patients' limited understanding of the post-discharge treatment plan.^{70,71}

Interventions to improve phosphate binder adherence

Patient education

Knowledge about the rationale for phosphate binders is associated with improved patient adherence to phosphate binder therapy.³³ Patients need to be effectively educated about the risk associated with phosphate binder nonadherence and, specifically, its association with increased morbidity and mortality.^{14,19,72} Patient education about appropriate timing of dosing toward the end of each meal, as well as adjusting dosing to the phosphorus content of the food, is important to ensure binder efficacy.¹⁴

Effective approaches for phosphate binder education utilize tools such as pamphlets, posters, websites, and videos.¹⁴ However, the readability of many available patient-education materials remains a concern, with text written at above the ninth-grade levels and formatting that does not meet standards for optimal usability.^{73,74} Delivery of education occurs in all formats, including face-to-face individual consultations, group education, telephonic consultations, and practical demonstrations¹⁹ such as lobby days in dialysis units. Individual educational sessions for binder adherence have the benefit of providing personalized education, but are resource and time intensive. Education in small groups promotes interaction among dialysis patient peers, and has been shown to improve phosphate binder knowledge, as well as adherence, when facilitated by a dietitian.^{19,75}

Incorporation of patient preferences

Dosing regimens can be simplified by reducing pill burden and adjusting phosphate binder prescriptions to accommodate the patient's dialysis preferences.¹¹ For instance, some patients favor calcium acetate gel caps over the tablets because of ease of swallowing⁷⁶ whereas others have a preference for lanthanum because it requires fewer tablets.⁷⁷ Adopting an individualized strategy that takes into account patient preferences with regard to phosphate binders resulted in significant improvement in intentional nonadherence, phosphorus control, and even costs related to phosphate binder use.²⁷ This strategy empowers patients to request a change in binder type if they have had problems with the prescribed phosphate binders. It is recommended to offer alternate options to patients who object to a particular dosing method.¹⁴

Patient empowerment techniques

Counseling interventions that incorporate a cognitive or behavioral component could be most effective for improving phosphate binder adherence.^{19,78} Cognitive behavioral interventions are psychological strategies that focus on the association between thoughts, feelings, and emotions and assist patients in identifying and modifying negative thoughts, feelings, and behaviors to facilitate coping. They may include education or relaxation training delivered in different settings and formats. Motivational interviewing – an autonomy-promoting style of communication – has been shown, in a small study, to improve phosphate binder adherence and phosphorus control.⁷⁹ This style of communication effectively engages patients to focus on a behavioral change; resolve ambivalence; and make plans that are specific, measurable, action-based, realistic, and time-based (Table 3). Motivational interviewing uses strategies such as open-ended questions, affirmations, reflections, and summaries.⁸⁰ Similarly, self-affirmation – which involves reflection on one's personal values in order to reduce resistance to health-risk information – has been successfully used to improve adherence.⁸¹ These patient empowerment techniques address the most influential factors of phosphate binder adherence, including beliefs and attitudes.¹⁰

Other potential novel approaches for patient empowerment in improving medication adherence include the use of electronic monitoring devices. These can be used to remind patients to take their medications at prescribed times and may be helpful in empowering patients to improve phosphate binder medication adherence.⁸² The Phosphate Education Program (PEP) is a novel program that incorporates patient

Table 3 Motivational interviewing

Motivational factor	Objective	Example	Follow-up
1. Express empathy	To establish rapport and avoid resistance by demonstrating understanding of the patient's situation	Patient expresses difficulty making all these changes	Remind the patient that current levels put them at risk for more serious diseases
2. Roll with resistance	Avoid magnifying resistance by allowing patient to explore their barriers in a nonjudgmental supportive manner	Patient is reluctant to continue medication since it is hard to remember to take and they no longer feel unwell	Ask the patient where they see themselves in 6 months if they stop taking the medication
3. Elicit/provide reminder/elicit	Find out what the patient already knows, fill in the gaps or correct misconceptions, and explore how the change you suggest will fit into the patient's life	Elicit: ask patient what they know about managing their CKD	Reminder: for example, to take statins and closely monitor blood pressure Elicit: "what do you think the biggest barrier is for you right now in managing this condition?"
4. Support autonomy	To reduce resistance by assuring patients you know you can't make them do anything – it is their choice	Emphasize to patient that it is their choice but as their doctor you are concerned if they do not try medication	Reiterate that it is the patient's choice and they need to consider all the options. Reassure patient that if they do decide to try a particular medication they will be regularly monitored for side effects and dose adjusted accordingly
5. Explore ambivalence	Help patient consider pros and cons of change in a relaxed yet systematic manner	Encourage a discussion about the pros and cons, eg, eating egg whites as part of a low-phosphorus diet	Summarize current situation with the patient and explain that the benefits will outweigh the potential drawbacks associated with an egg-white diet
6. Elicit change talk	To evoke the patient's reasons, desire, ability, and need for change. This predicts increased commitment to the lifestyle change and good clinical outcome	"What makes it important to you to start an exercise program?" "What benefits would come from losing weight?" "Why do you want to quit smoking?"	Remind patient of the benefits of regular exercise and how well it made them feel previously. These measures will help patient become a good role model for their children and allow them to play sports together
7. Develop an action plan	To help the patient develop a plan that is realistic and suitable for their life	Enquire about the next step for the patient. Ask what they think they can do or are willing to do to improve health and make a difference	Motivate patient to follow plan and reiterate the steps agreed, ie, eat more vegetables, avoid fast foods, exercise more, etc

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Abbreviation: CKD, chronic kidney disease.

empowerment by teaching patients how to estimate the phosphorus content of their food and adjust their phosphate binder therapy using a prescribed binder/unit ratio.⁸³ This program equips patients for "eye-estimating" the phosphorus content of various foods to guide these real-time adjustments. It assigns similar phosphorus units to similar whole food groups whereby 1 phosphorus unit is equivalent to 100 mg per serving.⁸⁴ Informed by similar approaches in diabetes management, this approach seems promising; however, additional complexities of dietary recommendations for phosphorus management must be acknowledged.

Dietary approaches to phosphorus control

Epidemiology of adherence to low-phosphorus diet

An integrative review of studies on adherence to the renal diet reports a wide variation in dietary adherence.¹⁶ This is related

to differences in how dietary adherence was measured – ranging from subjective approaches involving self-reported adherence to indirect approaches using serum phosphorus levels or a combination of approaches. Adherence to a low-phosphorus diet from 15 studies of 12,571 ESRD patients ranges from 43% to 84% and the majority of these studies measured low phosphate dietary adherence using serum phosphorus levels.¹⁶ Interestingly, one study that measured the rates of low phosphate dietary adherence using two different methods reported a self-reported adherence rate of 33% as compared to an adherence rate of 44% when using serum phosphorus levels.⁸⁵

Types of dietary phosphorus

Dietary phosphorus is obtained from three different sources: 1) organic phosphorus in plant foods; 2) organic phosphorus in animal protein; and 3) inorganic phosphorus from additives

in processed food.¹⁴ The phosphorus content in plant foods has only 20%–40% bioavailability whereas the phosphorus content in animal protein has 40%–60% bioavailability.¹⁴ In sharp contrast, the phosphorus content from food additives has 100% bioavailability and has the most impact on hyperphosphatemia.¹⁴

Phosphorus additives

The “hidden” phosphorus content from phosphate additives found in processed foods^{86,87} increases the complexity of dietary phosphorus management. The presence of unlabeled phosphorus content in many foods, in addition to the wide array of foods high in natural phosphorus content, contributes to nonadherence to a low-phosphorus diet. More recently, emphasis has been placed on the reduction of phosphate additives by avoidance of processed, high-phosphorus protein sources.¹⁴

Balancing the protein-to-phosphorus ratio

Dietary phosphorus restriction is complex because of the delicate balance between ensuring adequate protein intake and simultaneously restricting phosphorus intake.^{11,14} Achieving this balance is a high priority because higher protein intake (up to 1.4 g/kg/day) has been linked to increased survival in dialysis patients, regardless of a simultaneous increase in serum phosphorus levels.⁸⁸ Yet, higher levels of dietary phosphorus intake and higher dietary phosphorus-to-protein ratios increase the 5-year mortality rates in hemodialysis.⁸⁹ Interestingly, prior research has not yet demonstrated a survival benefit as a result of prescribed dietary phosphorus restriction.¹³ This may be explained, in part, because dietary phosphorus restriction is insufficient to reduce serum phosphorus load.⁹⁰ A daily low-phosphorus diet includes approximately 371 mg of absorbed phosphorus each day. Therefore, phosphorus control inherently requires strategies in addition to dietary restriction.^{11,14}

Factors affecting adherence to low-phosphorus diet

Table 4 presents factors affecting adherence to a low-phosphorus diet. A recent integrative review of dietary adherence in dialysis, including adherence to low-phosphorus diet, provides a detailed overview of contributory factors.¹⁶ Longer dialysis vintage has been associated with nonadherence to a low-phosphorus diet,^{16,17,49} perhaps due to the burden of managing such complex dietary recommendations for an extended time.¹⁶ Poor dietary knowledge has been linked to nonadherence to phosphorus-restricted diet.^{17,91,92}

Table 4 Factors associated with dietary adherence in adults with ESRD on hemodialysis categorized according to WHO criteria

Study	Patient numbers	Socioeconomic factors	Condition-related factors	Therapy-related factors	Healthcare team and system-related factors	Patient-related factors
Agondi et al ¹²³	117	Higher education level, older age		Shorter dialysis vintage, Dietary knowledge		Positive beliefs regarding the benefits of the diet
Ahrari et al ¹²⁴	237					Social and family support
Baraz et al, 2010	63	Higher education level, being employed, younger age				
Chan et al ¹⁷	188	Retired or not working, female gender, older age		Dietary knowledge, short dialysis vintage, diet complexity		Self-efficacy
Clark-Cutaja et al ¹²⁰	122	Male gender, older age		Self-monitoring		
Dowell et al ¹²⁵	4			Dietary knowledge		
Durose et al ¹²⁶	71		Knowledge of medical complications of dietary nonadherence			
Elliott et al ¹⁸⁵	95	Minimum of high school education	Better quality of life	Shorter dialysis vintage		Perceived benefits of dietary adherence, self-efficacy
Ford et al ¹⁹⁷	70	White ethnicity			Intensive patient education	

Kara et al ⁹⁴	160	Older age, being married			Dietary knowledge	Adequate dietitian staffing, experienced renal dietitian	Presence of family support; presence of social support
Karavetian and Ghaddar ⁹¹	570						
Khalil et al ¹⁰⁰	100						Absence of depression
Kugler et al ¹¹⁸	456	Lower education level, female gender, being married					Non-smoking status
Kugler et al ⁹⁵	916	Female gender, old age			Short dialysis vintage		Family support, non-smoker, non-diabetic status
Lee et al ¹²⁷	62	Unemployment or non-working status			Shorter dialysis hours per week		Positive attitudes to diet, high residual renal function > 300 mL/day
Lindberg et al ¹³⁴	4,498	Older age			Short dialysis vintage		Higher BMI
Mellon et al ⁹⁶	50	Older age					Perception that diet fits into lifestyle strategies to manage the diet at social events; positive beliefs and attitudes about the diet
Molaison et al ¹²⁸	316	Older age, female gender			Self-monitoring		
Mok et al ¹²⁹	50				Long dialysis vintage		
Morales López et al ¹⁰¹	34	Adequate finances			Culturally appropriate format of patient education, dietary knowledge	Presence of a dietitian on staff	Presence of family support
O'Connor et al ⁶⁸	73	Female gender, older age					Adequate psychological coping ability
Pang et al ¹³⁰	92	Lower family income					Lower comorbid disease burden, presence of social support
Park et al ⁹⁸	160	Older age					Malnutrition
Poduval et al ¹³¹	117	College education			Education about food composition		
Sagawa et al ¹³²	10				Self-monitoring		
Saran et al ⁴⁹	7,676	Unemployed, male gender, older age, married			Long dialysis vintage	Presence of a dietitian on staff	Family support, non-smoking status
Sharp et al ¹³³	56					Intensive patient education	Higher self-efficacy
Thomas et al ⁹²	276	White ethnicity, female gender			Dietary knowledge, practical shopping skills		Family support, positive beliefs, and attitudes about the impact of the diet
Tsay et al ¹³⁴	62				Self-monitoring		High self-efficacy
Welch et al ¹³⁵	148						Positive beliefs & attitudes about the impact of the diet
Yokoyama et al ¹³⁶	72					Dialysis staff encouragement	Lower perceived burden of the diet, high self-efficacy, good mental health
Zrinyi et al ⁹⁹	107	Female gender					High self-efficacy

Note: Adapted from Lambert K, Mullan J, Mansfield K. An integrative review of the methodology and findings regarding dietary adherence in end stage kidney disease. *BMC Nephrol.* 2017;18:318. Creative Commons license and disclaimer available from: <http://creativecommons.org/licenses/by/4.0/legalcode>.¹⁴

Abbreviations: BMI, body mass index; ESRD, end-stage renal disease; WHO, World Health Organization.

Furthermore, dialysis patients have acknowledged that the diet is challenging to incorporate into social occasions and dietary advice, preferably from renal dietitians or nephrologists, is of utmost importance.⁹³

Patient factors associated with nonadherence to low-phosphorus diet include age, gender, race, and education level.¹⁶ Younger age ($r = 0.19$; $p < 0.05$) and male gender are more likely to predict dietary nonadherence ($r = 0.25$; $p < 0.05$). Non-whites have been found to have more dietary nonadherence,^{85,92} and this may be driven by lower socioeconomic status. Employment status has been associated with dietary nonadherence in dialysis patients ($r = -0.36$; $p < 0.01$), and this may be because it is challenging to juggle the demands of the diet with the rigors of employment. Lower education level has been consistently associated with dietary nonadherence.^{17,94–98}

Several psychosocial factors have been consistently associated with dietary nonadherence in dialysis. Negative beliefs and attitudes were strongly linked to dietary nonadherence.^{92,96} Moreover, patients with lower self-efficacy or depressive symptoms experienced dietary nonadherence.^{17,85,99,100} Poor coping skills have correlated with nonadherence to a low-phosphorus diet.⁶⁸ Negative peer pressure or lack of acceptance of the prescribed diet by family or friends⁹³ worsen dietary nonadherence.

Poor interaction between patients and dialysis providers is associated with dietary nonadherence,¹⁶ and conflicting dietary advice from different dialysis clinicians is also associated with nonadherence.¹⁷ Limited dietary education and support from renal dietitians^{49,91,101} was associated with dietary nonadherence, and this has largely been attributed to suboptimal staffing ratios.^{49,91}

Interventions to improve adherence to low-phosphorus diet

Patient education

Effective education on dietary phosphorus restriction should include specific recommendations of foods with minimal inorganic phosphorus content, foods without phosphorus additives, low phosphorus-to-protein ratios, and adequate protein content (Table 5).¹⁴ Patients need to understand that plant foods, animal-derived foods, and food additives have a range of low to high phosphorus bioavailability.¹⁴ Examples of food options that have the lowest phosphorus-to-protein ratio include non-dairy products and animal foods with high protein content such as egg whites.⁸⁹ These food selections can effectively lower serum phosphorus level while simultaneously increasing the albumin level.¹⁰² In addition, education should include cooking methods that preserve protein content while reducing phosphorus content (eg, boiling chicken) to promote the low-phosphorus diet.^{14,103}

Food fatigue or getting tired of eating the same allowed food has been identified as a larger problem than food intolerance or allergies in dietary management of chronic kidney disease, including ESRD.¹⁴ Food fatigue can be ameliorated by diversifying the diet to include additional low-phosphorus, high-protein food options such as poultry.¹⁴ Phosphate binder medication therapy, when taken effectively, also reduces food fatigue by permitting the patient's preferred mainstream foods while controlling their serum phosphorus levels.¹⁴

Ideal patient education tools include information estimating the phosphorus content of food with glossaries of additives to guide the interpretation of food labels; comprehensive labeling of phosphorus additives; and use

Table 5 Strategies to improve control of dietary phosphorus intake and adherence to phosphate binders in ESRD

Patient education	<ul style="list-style-type: none"> • Introduce education programs, led by nurses or other ancillary healthcare providers, focusing on the: <ul style="list-style-type: none"> ◦ physiologic role of phosphate and its presence in different foods ◦ role of phosphate in ESRD-associated cardiovascular disease ◦ importance of phosphate binders and their role in lowering serum phosphorus concentrations ◦ importance of dietary adherence • Involve patients' families and friends in educational initiatives • Tailor education to patients' lifestyle, environment, career, ethnicity, cultural background, and socioeconomic status • Educate patients on appropriate food choices and provide training on preparing suitable meals
Patient empowerment	<ul style="list-style-type: none"> • Introduce initiatives such as the "Phosphate Education Program" which enable patients with hyperphosphatemia to estimate the phosphate content of their meals and adjust their phosphate binder dose accordingly
Improve properties of phosphate binders	<ul style="list-style-type: none"> • Reduce pill size and burden • Improve palatability • Reduce associated adverse effects • Introduce electronic monitoring devices, which may help patients remember to take their medications and support adherence

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Abbreviation: ESRD, end-stage renal disease.

of a “traffic light” scheme to classify foods based on low, intermediate, or high phosphorus content.¹⁰⁴ Educational interventions to improve phosphorus control through dietary restriction have demonstrated improvements in patient knowledge, adherence to the low-phosphorus diet, as well as serum phosphorus levels.^{19,91,105} More recent educational initiatives, such as the Phosphate Education Program described earlier, empower patients to tailor the phosphorus content of food to their phosphate binder use per meal, leading to improved control of hyperphosphatemia.^{14,83,84}

Dietitian-led interventions have been successful.^{75,106,107} Systematically delivered nursing instruction on low-phosphorus diet using a nursing instruction pamphlet, pictures, and reminder cards has also been shown to improve adherence, reduce serum phosphorus levels, and improve pruritus.¹⁰⁸ Although comprehensive low-phosphorus dietary education, developed and delivered by dialysis nurses and physicians, was effective in improving serum phosphorus levels,¹⁰⁹ dietitian involvement has been found to be more effective.¹⁰⁹

Behavioral interventions

Behavioral interventions to improve dietary phosphate adherence also commonly employ counseling delivered by dietitians.¹⁹ Some interventions have been grounded in theoretical frameworks such as self-regulation theory⁹¹ and self-efficacy theory.¹¹⁰ Individualized self-management dietary counseling—especially in combination with patient education—improves patient knowledge, dietary adherence, and serum phosphorus level.⁹¹ Use of a phosphate management protocol incorporating dietary counseling as well as patient education and pharmacotherapy delivered by a dialysis dietitian and a dialysis pharmacist, respectively, has led to greater improvement in serum phosphorus control compared to usual care.¹¹¹ A motivational interviewing pilot study, focusing on dietary, medication, and dialysis attendance, demonstrated a positive impact on serum phosphorus control.⁷⁹

Other potential strategies

Patients have expressed frustration about insufficient psychosocial support and information from providers that affects their self-care.¹¹² Provider communication skills as well as the provider–patient relationship and interactions may have an impact on adherence to the prescribed low-phosphorus diet.¹⁶ Providers need to recognize that patients have limited self-efficacy^{17,85} and suboptimal attitudes^{92,93} that contribute to poor adherence to a low-phosphorus diet and are potential modifiable targets. Staffing ratios in the dialysis unit has been linked to adherence metrics and need to be optimized.

For instance, a ratio of no more than 60 dialysis patients per dietitian with monthly consultations has been shown to be more effective in improving phosphate binder adherence and serum phosphate control.¹⁴ Provider-level strategies may be an important opportunity to complement ongoing patient-focused interventions to improve dietary adherence in dialysis patients, and all members of the multidisciplinary team should be equipped to deliver phosphate binder adherence education and counseling.¹⁴

Dialysis

Conventional 4-hour thrice-weekly hemodialysis is limited in its ability to lower the phosphorus levels associated with the average dietary intake of phosphorus.^{19,113} Phosphorus removal through conventional hemodialysis occurs primarily during the first half of treatment, after which the serum phosphorus levels either plateau or even increase again (by up to 30%–40%) due to a rebound effect.¹¹⁴ The daily phosphorus intake of dialysis patients can average 1,500 mg/day or 10,500 mg/week and, if 50% of that is absorbed, the phosphorus excess for removal by dialysis could be greater than 5,000 mg.¹⁵ However, conventional hemodialysis removes an average of 1,800–3,600 mg of phosphorus per week. Therefore, conventional hemodialysis alone is usually insufficient for phosphorus control.¹⁹ Optimal dialytic clearance of phosphorus is dependent on slow flow rates in addition to a longer dialysis time. Daily or extended nocturnal hemodialysis leads to greater phosphorus clearance compared with conventional thrice-weekly hemodialysis sessions.¹¹⁵

Dialysis treatment nonadherence

Dialysis treatment nonadherence is a significant problem.⁴⁹ As much as 35% of patients miss treatments entirely whereas another 32% shorten their treatment time.²⁰ In addition to its direct impact on hyperphosphatemia management, dialysis treatment nonadherence has been linked to increased hospitalizations^{116,117} and mortality.^{23,49} This high rate of treatment nonadherence has persisted and is linked to age,^{23,36} gender,¹¹⁸ marital status,¹¹⁸ ethnicity,^{23,119} and education¹¹⁸ as well as comorbidities and logistical barriers such as holidays that alter the dialysis unit scheduling.¹¹⁶ As with other chronic diseases requiring self-management, autonomy-centered psychosocial factors may be important, modifiable determinants of dialysis adherence.¹²⁰ Deliberate multidisciplinary strategies to increase patient engagement in dialysis^{59,121,122} is increasingly recognized as a high-value opportunity to impact adherence behaviors and outcomes.

Conclusion

Phosphate-control adherence is a fundamental component of care in dialysis, and adherence rates to phosphate binder therapy, low-phosphorus diet, and dialysis attendance remain suboptimal. Factors responsible for nonadherence include those related to the therapy (eg, medications, diet, dialysis); patient-specific factors including demographic, clinical, and psychosocial determinants, and provider-level factors. Psychosocial factors are the most influential determinants of adherence because they can be effectively modified using strategies that incorporate cognitive behavioral interventions to change negative beliefs, attitudes, and behaviors across treatment approaches to optimize phosphorus control. Provider-level factors are critical determinants of phosphate-control adherence in dialysis patients. Thus, provider-patient relationships must be enhanced by ensuring positive provider attitudes, adequate staffing ratio, and improved staff effectiveness by role clarification and training. All dialysis providers must be skilled in the delivery of culturally sensitive, patient-centered care using a novel combination of effective strategies and protocols. Optimal phosphate-control adherence rates will require multilevel interventions that recognize and address the preferences and unique attitudes of dialysis patients, enhance their self-regulation behaviors, and empower them to achieve sustained phosphate binder adherence.

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