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Phosphate Elimination in Modalities of Hemodialysis and Peritoneal Dialysis

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Key Words
Hyperphosphatemia · Phosphate elimination · Hemodialysis · Peritoneal dialysis

Abstract
Hyperphosphatemia is highly prevalent in hemodialysis (HD) and peritoneal dialysis (PD) patients and is a major risk factor for cardiovascular mortality. Elimination of inorganic phosphate by dialysis is a cornerstone of the management of hyperphosphatemia. Phosphate clearance during HD is affected by various factors of dialysis prescription, such as blood and dialysate flow rate, dialyzer membrane surface area and ultrafiltration volume. Phosphate mass removal can be improved by hemodiafiltration, increased dialysis frequencies and extended treatment times. Short daily or extended daily or 3 times weekly nocturnal HD allow higher phosphate mass removal and potentially complete discontinuation of phosphate binder medication. In PD, phosphate mass removal appears to be correlated with peritoneal creatinine but not urea clearance. In hyperphosphatemic PD patients, the decision on the optimal PD modality should be based on peritoneal creatinine and ideally also on peritoneal phosphate transport characteristics.

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Introduction

Both hemodialysis (HD) and peritoneal dialysis (PD) patients are at an increased risk for cardiovascular mortality. Besides classical cardiovascular risk factors, hyperphosphatemia has been identified as one of the most important risk factors for mortality [1, 2]. Hyperphosphatemia differs from many other cardiovascular risk factors in one important aspect: it appears potentially well controllable. However, since hyperphosphatemia is still widely prevalent among HD and PD patients worldwide, there is a lot of room for improvement in the strategies currently applied to manage hyperphosphatemia. These are based on three principles, namely dietary phosphorus restriction, use of phosphate binder substances and phosphate elimination by one of several dialysis modalities. An innovative approach to the integrative use of the first two principles, i.e., patient self-adjustment of phosphate binder dose in relation to eye-estimated meal phosphorus content, has been discussed recently by the author [3]. This review will focus on strategies to optimize the removal of inorganic phosphate (P_i) by the various modalities of HD and PD.

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HD Modalities

Based on its molecular weight of 96 Da alone, P_i clearly falls into the category of water-soluble low-molecular-weight uremic toxins. However, due to its hydrophilic characteristics, the phosphate molecule is surrounded by an aqueous cover, which considerably increases the effective molecular weight. Phosphate is mainly distributed in the intracellular space with a slow intra-/extracellular solute transfer rate and with a distribution volume which is assumed to be equal to total body water. It needs to be stressed that in contrast to urea, phosphate is not freely diffusible across cell membranes and about 5% of circulating phosphate has been shown to be a component of sodium, calcium and magnesium salts. All these factors contribute to the fact that the elimination characteristics of phosphate in HD and PD are dissimilar to those of urea and other small-molecular-weight toxins and much more similar to those of typical middle molecules [4].

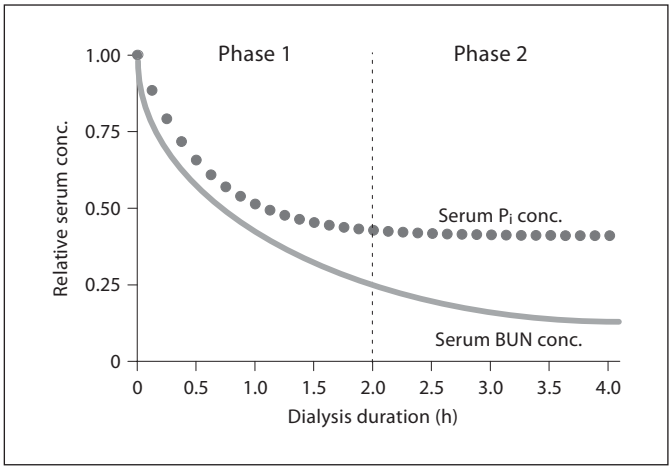

Fig. 1. Comparison of intradialytic phosphate and blood urea nitrogen (BUN) kinetics. Serum P_i concentration sharply drops during the first phase of dialysis (phase 1) and, after reduction of serum P_i to about 40% of predialysis levels, stabilizes throughout the rest of the treatment (phase 2). In contrast, BUN levels steadily decline during dialysis without reaching a plateau.

Phosphate Kinetics during HD

The kinetics of intradialytic phosphate removal differ significantly from classic urea kinetics. During HD, blood urea nitrogen concentrations continuously decline and, following a short rebound period immediately after termination of the treatment, steadily return to predialysis values in relation to protein intake and endogenous urea generation during the interdialytic interval. Intradialytic plasma P_i kinetics show a characteristic 2-phase pattern (fig. 1): the first phase is determined by a relatively steep decline of plasma P_i levels and lasts for about 2–2.5 h after start of the treatment. This is followed by the second phase, during which plasma P_i levels do not further decline or even slightly increase towards the end of the dialysis session. This characteristic stabilization of serum P_i levels despite ongoing P_i elimination reproducibly occurs when plasma P_i levels have dropped to about 40–50% of baseline predialysis levels. Within a couple of hours after termination of dialysis, plasma P_i levels rebound to almost predialysis values [5, 6]. These kinetics suggest that during the first phase of dialysis predominantly the P_i available in the extracellular plasma compartment is removed, while during the second phase P_i removal occurs from the intracellular space with the rate of change in plasma P_i levels determined by the rate of P_i transfer from one or more intracellular compartments to the plasma compartment [7]. The strong postdialytic P_i rebound is representative for this transfer rate. It can be concluded from these kinetics, that the P_i mass removal *rate* (P_i mass removed per time unit) is highest during the first phase of HD. On the other hand, since the P_i diffusion gradient between plasma and dialysate is maintained stable during the second phase of treatment, the *absolute* P_i mass removed during the second phase may be higher than during the first phase, depending on the duration of the second treatment phase. This stands in contrast to urea kinetics, where fractional urea mass removal during dialysis steadily declines due to the constant reduction of the concentration gradient across the dialyzer membrane. With these characteristics of intradialytic phosphate kinetics in mind, several strategies to optimize HD P_i removal can be formulated:

(i) optimizing dialysis prescription to maximize P_i removal with conventional 3 times a week HD regimens;

(ii) increasing dialysis frequency with shorter treatment times (short daily HD, SDHD); with this strategy a focus is put on the first phase of phosphate kinetics;

(iii) extending dialysis treatment time (nocturnal HD, NHD, with variable frequency); with this approach, the constant P_i mass removal during the second phase of dialysis is maximized.

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Table 1. Weekly P_i mass removal with various HD and PD treatment modalities

Modality and ref.	P_i mass removal mg/week	Dialysis schedule	Flow rates ml/min	Treatment specifications
Hemodialysis				
HD high-flux [8]	2,356 ± 864	3 × 230 min	Q_B: 323 ± 22 Q_D: 500	UFV 1.8 ± 0.8 liters
HD + passive muscle activity [9]	PCM: 3,515 ± 945 TEMS: 3,591 ± 795	3 × 195–240 min	Q_B: 300–400 Q_D: 600	S-P_i 5.1 ± 0.9 mg/dl
HD – double dialyzer [10]	2,970 mg	3 × 4 h	Q_B: 350–400 Q_D: 800	F80A or F160 dialyzers S-P_i 5.3 mg/dl
Postdilution HDF [11]	3,570 ± 270 mg	3 × 4 h	Q_B: 315–345 Q_D: 500	F8 dialyzer, MSA 1.8 m^2 Q_{UF} 25–35 ml/min
Mixed-dilution HDF [12]	975 ± 272 mg/Tx (2,975 mg/week)	231 ± 18 min	Q_B: 385 ± 20 Q_D: 625 ± 16	Q_{UF} 181 ± 12 ml/min MSA 1.8 m^2
SDHD [13]	2,452 ± 720 mg	6 × 3 h	Q_B: 400 Q_D: 800	high-flux dialyzer S-P_i 4.2 mg/dl
NHD [14]	8,000 ± 2,800	6 × 6–8 h	Q_B: 150–300 Q_D: 300	high-flux dialyzer F80
	P_i mass removal mg/week	Dwell time h	Flow rates ml/min	Treatment specifications
Peritoneal dialysis				
APD, CCPD [8]	2,739 ± 1,042	18.5 ± 7.3	–	DV 13.2 ± 3.5 liters ex. 5.5 ± 1.1 S-P_i 5.0 ± 1.4 mg/dl
CAPD [8]	2,790 ± 1,022	24.0	–	DV 10.5 ± 2.1 liters ex. 4.2 ± 0.5 S-P_i 4.2 ± 0.9 mg/dl

HDF = Hemodiafiltration; APD = automated PD; CCPD = continuous cycling PD; CAPD = continuous ambulatory PD; Tx = treatment; PCM = passive cycling movements; TEMS = transcutaneous electrical muscle stimulation; Q_B = blood flow rate; Q_D = dialysate flow rate; S-P_i = serum P_i concentration; Q_{UF} = ultrafiltrate flow rate; MSA = membrane surface area; DV = peritoneal fluid drainage volume; UFV = ultrafiltration volume; ex. = number of PD fluid exchanges.

Conventional HD Regimens

With plasma P_i levels at the end of dialysis reaching about 40% of predialysis levels, it is evident that the absolute phosphate mass removed per treatment depends mainly on predialysis P_i levels. For a standard HD treatment of 240 min duration, an average phosphate mass removal of 700–900 mg has been reported. This amounts to a weekly P_i removal of 2,100–2,700 mg with a conventional 3 × 4 h HD regimen (table 1). Considering a daily dietary phosphorus consumption of 1,000 mg with a gastrointestinal absorption rate of 70%, the weekly P_i burden of roughly 5,000 mg is inadequately removed by conventional HD strategies. Phosphate removal with conventional HD regimens can be maximized by the means described below.

Dialyzer Membrane and Surface Area

For any dialyzer membrane P_i clearance is generally lower than urea clearance. This is due to a higher diffusive resistance for phosphate in full blood, with blood cells acting as diffusion barrier. From specification sheets it appears that low-flux membranes have a lower P_i clearance than high-flux membranes, but studies have shown that low-flux and high-flux membranes apparently do not differ if corrected for membrane surface area [5]. Membrane surface area itself has a potentially important impact on phosphate mass removal. In a recent study in 18 patients over a period of 6 weeks, doubling of membrane area by the use of 2 dialyzers in parallel (with blood flow equally split between the dialyzers) resulted in a 1.34 mg/dl decline in predialysis serum P_i levels compared with conventional HD [10]. The somehow surprising ob-

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servation that absolute phosphate mass removal was not different from standard dialysis was explained by hypothetical larger phosphate adsorption to dialyzer membranes. It may be concluded that, in order to optimize P_i removal, a dialyzer with a large membrane surface area should be used.

Blood Flow Rate and Dialysate Flow Rate

For any substance, dialyzer clearance depends on the effective blood flow rate (Q_B). However, in contrast to urea and potassium removal, increasing Q_B to >250–300 ml/min has only limited effects on P_i removal [15]. On the other hand, raising the dialysate flow rate (Q_D) from 300 to 500 ml/min is associated with a 10% increase in P_i clearance [16]. A rise of Q_D from 500 to 800 ml/min apparently does not significantly increase P_i clearance [10].

Hematocrit

The dialyzer clearance of any substance also depends on the effective distribution volume within the bloodstream. While for urea this is total blood water and for creatinine it is plasma water volume and 61% of erythrocyte volume, for phosphate it is plasma water volume alone. Since plasma water volume depends on hematocrit and albumin levels, dialyzer P_i clearance declines with increasing hematocrit [16]. Therefore, in hyperphosphatemic patients with high predialysis hematocrit, mixed-dilution hemodiafiltration (HDF) may be a better alternative than conventional HD (see below).

Choice of Anticoagulant

Even with the use of heparin, unnoticed clotting of dialyzer fibers and membrane pores often occurs. This subtle clotting, while not interfering with the completion of the treatment, reduces the efficiency of dialytic removal of phosphate and other solutes. A recent study indicates that acidifying bicarbonate-based dialysate with citrate instead of acetate may be associated with increased solute removal including phosphate. Possible explanations include the local anticoagulant activity of dialysate citrate at the site of the dialyzer, thereby preventing the clogging of larger pores and maintaining effective dialyzer surface area throughout the treatment [17].

Physical Activity

Physical activity before or during HD increases muscle perfusion and facilitates blood/tissue equilibration for urea, phosphate and other solutes. Predialytic or intradialytic short active physical activity has been shown to increase P_i mass removal by 6–9% [18]. Repetitive muscle activity may further enhance P_i removal substantially. Intradialytic motor-driven passive leg cycling movements or transcutaneous electrical muscle stimulation of both thighs and calves increased P_i removal by 31% (1,172 ± 315 vs. 895 ± 202 mg) and 34% (1,197 ± 265 vs. 895 ± 202 mg), respectively. This translates into an increase in weekly P_i removal from 2.6 to 3.5 g with passive leg cycling movements and to 3.6 g with transcutaneous electrical muscle stimulation, effects similar in size to an additional HD treatment per week (table 1) [9].

Hemodiafiltration

Online HDF allows a greater fraction of uremic middle molecules and phosphate to be removed by convection. HDF can be delivered in a predilution or postdilution mode. The latter may cause hemoconcentration and an increase in blood viscosity resulting in increased diffusive resistance for phosphate, high transmembrane pressure, loss of membrane permeability and eventually filter clotting. Predilution HDF, in contrast, is associated with reduced efficiency due to dilution of the solute concentration gradient across the membrane. In direct comparison, postdilution HDF has been shown to be more effective than predilution HDF, and an increase in P_i removal by 30–40% has been reported for postdilution HDF by several groups [11, 19]. Mixed-dilution HDF is a relatively new modality where blood dilution is split between pre- and postfiltering and which was developed to achieve the best possible rheological and hydraulic conditions within the dialyzer and to optimize the fluid exchange rate and convective solute removal. However, a significant advantage of mixed-dilution over postdilution HDF in regard of P_i removal still needs to be demonstrated [12]. Mixed dilution may be of special advantage in patients with high predialysis hematocrit and an increased risk of filter clotting with postdilution HDF due to hemoconcentration.

Increased Dialysis Frequency

Increasing dialysis frequency from 3 to 5 or 6 times per week appears an attractive alternative treatment schedule which may be associated with an increased quality of life and potentially better outcome and phosphate control [20]. Increased dialysis frequencies with shorter treatment times take advantage of the high P_i mass removal rate during the first phase of dialysis.

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Short Daily HD

The concept of SDHD offers more frequent dialysis at shorter treatment duration. Effective control of phosphate levels, however, depends on the duration of each HD session. With a regimen of 6 × 2–2.5 h, only about 400–500 g of phosphate are removed per session. In almost all studies on SDHD with treatment durations between 2.0 and 2.5 h, patients had to continue to take phosphate binders [20, 21]. In order to achieve phosphate control without the use of phosphate binders, longer treatment duration, such as 6 × 3 h, may be necessary. This was demonstrated in a study by Ayus et al. [13] where 77 patients were treated with either conventional 3 times weekly dialysis (3 × 4 h; n = 51) or with SDHD (6 × 3 h; n = 26). Total weekly P_i removal was 56% greater in the SDHD group, and serum phosphate levels decreased from 6.3 ± 2.57 to 4.0 ± 1.19 mg/dl. Phosphate binder medication was withdrawn in 73% of the SDHD group. Improved phosphate removal and a reduction in phosphate binder dose have also been reported for short daily HDF (6 × 2–2.5 h) [22].

Extended Treatment Times

With extended treatment times, the benefits of the sustained blood/dialysate concentration gradient during the second phase of dialysis are maximized. Extending weekly dialysis time from 12 (3 × 4) to 15 (3 × 5) h without changing treatment Kt/V significantly increases phosphate mass removal by 13% [18]. Eloot et al. [23] have recently demonstrated that applying even longer treatment times of 6 and 8 h without increasing urea Kt/V resulted in increased phosphate mass removal compared to conventional treatment times of 4 h. This is in line with intradialytic phosphate kinetics discussed above and the advantage of the sustained phosphate diffusion gradient during the second phase of dialysis. It appears that with longer dialysis times, phosphate is removed more efficiently from deeper body compartments.

Nocturnal HD

With NHD, treatment times are even further extended. Several small studies report the effects on P_i removal by NHD with treatment times of up to 8 h of varying frequency. Pierratos et al. [24] demonstrated in a study comparing 3 × 4 h standard HD with 6 × 8 h NHD (with Q_D of 100 ml/min) significantly improved P_i elimination despite unchanged urea mass removal. In addition, prescription of phosphate binders was completely stopped despite significantly increased dietary protein and phosphorus intake[24]. Daily NHD with higher Q_D would even further increase phosphate removal, which may then be well in excess of daily dietary phosphorus intake [25]. In a recent randomized controlled trial of 52 patients comparing NHD 6 times weekly with conventional HD 3 times weekly, NHD was significantly more effective at lowering serum phosphate levels. Average predialysis serum phosphate levels were reduced from 5.5 ± 1.5 to 4.4 ± 1.7 mg/dl, and phosphate binder medication was reduced or completely discontinued in 73% of patients [26]. NHD with a frequency of only 3 times a week, such as in-center 3 times weekly NHD, has also been shown to improve phosphate management. In a retrospective study of 39 patients switched from 3 times weekly conventional HD to 3 times weekly in-center NHD, median phosphate values decreased from 5.9 to 3.7 mg/dl, and the mean daily dose of phosphate binders declined from 6.2 to 4.9 pills/day [27]. Data on phosphate removal are not available from these two recent studies. Nevertheless, all published data on extended treatment times demonstrate the advantage of long treatment times for adequate P_i removal.

PD Modalities

Similar to HD patients, hyperphosphatemia is highly prevalent in PD patients and is strongly associated with overall and cardiovascular mortality [28, 29]. Although detailed knowledge about the kinetics of phosphate removal appears essential for optimizing phosphate removal in PD, peritoneal P_i clearance has not been well studied in the past. This may be due to the fact that, in general, ion transport across the peritoneal membrane is complex and influenced by a whole multitude of factors, which are difficult to take into account and even more difficult to control. Among the various cations and anions subjected to transmembranous peritoneal transport, phosphate has been studied only in a minority of cases. Even in a recently published excellent comprehensive review of the principles of fluid and ion transport across the peritoneal membrane in continuous ambulatory PD (CAPD), phosphate transport only plays a minor role [30]. According to the simplified 3-pore model of peritoneal clearance, the peritoneal membrane consists of a large number of small endothelial pores of a radius of 43 Å in the peritoneal capillaries, which account for 99.7% of the total surface area available to small solute diffusion. Less than 0.01% of the total number of pores is represented by large pores of a radius of 250 Å, across which proteins are transported by convection. The rest mainly consists of

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water-conductive ultrapores (aquaporin 1) which are responsible for the osmotic water flow during the first few hours of the dwell but do not contribute to solute removal. On top of that, transmembranous active phosphate transporters exist in endothelial cells. When discussing transmembrane phosphate elimination in PD, several aspects of phosphate specific to PD need to be considered: the phosphate anion is negatively charged and so are capillary walls and interstitial matrix. About 15–20% of phosphate is bound to proteins and about 5% is complexed to other ions. Furthermore, because phosphate is not freely diffusible through cell membranes, the diffusion resistance at the capillary vessel membrane is higher than for highly diffusible substances like urea. While the molecular weight of phosphate (96 Da) lies right between those of urea (60 Da) and creatinine (13 Da), the molecular radius of phosphate (2.8 Å) is closer to that of creatinine (3.0 Å) than urea (1.8 Å). Finally, the hydrophilic phosphate molecule is surrounded by an aqueous cover which increases the effective molecular weight. Taken together, phosphate transport across the capillary walls into the peritoneal cavity is influenced by osmotic, chemical and electrical gradients, as well as by transmembranous active phosphate transporters and thus is more complex than peritoneal urea or creatinine transport [4, 30]. Principally, diffusion occurs through the small endothelial pores, while convective phosphate transport occurs through the larger pores.

Peritoneal and Renal Phosphate Clearance versus Creatinine and Urea Clearance

Peritoneal P_i clearance in average PD patients is considerably lower than clearance of small water-soluble substances. In a direct comparison, peritoneal P_i clearance (35.9 ± 2.7 l/week/1.73 m^2) was reported to be about 20% lower than creatinine clearance (45.3 ± 3.5) and almost 50% lower than urea clearance (66.6 ± 4.8) but about 8-fold higher than β_2-microglobulin clearance (4.7 ± 0.5) [4]. Various clinical studies have demonstrated that peritoneal P_i removal is more closely related to creatinine than to urea removal [31, 32]. In a retrospective analysis of urea, creatinine and phosphate clearances in 129 PD patients, a strong correlation between peritoneal P_i clearance and creatinine clearance was observed. In a multivariate regression analysis, peritoneal creatinine clearance, but not peritoneal urea Kt/V, was independently associated with peritoneal P_i clearance, indicating that peritoneal creatinine clearance may serve as a surrogate marker for peritoneal P_i clearance [31].

Renal clearance, on the other hand, has a higher relative impact on total clearance for P_i than for urea and creatinine [4]. At the start of dialysis therapy, residual renal function may contribute up to 65% of total P_i clearance, which declines over time. Interestingly, the loss of renal P_i clearance may be compensated for by an increase in peritoneal P_i clearance due to 3 potential mechanisms: first, prescription of higher dialysate volume; second, structural changes in the peritoneal membrane with increased transport of small substances caused by the exposure to dialysis fluid components, and third, an increase in 24-hour ultrafiltration volume with concomitantly increased convective P_i removal [33].

Influence of Membrane Transport Characteristics on Peritoneal Phosphate Elimination

Only recently has it been shown that membrane transport characteristics influence peritoneal P_i clearance. This is not a surprise considering the association between peritoneal P_i and creatinine clearance and the fact that membrane transport types are characterized by peritoneal creatinine equilibration kinetics [34]. Some studies have reported that patients in the low-average and low membrane transport categories have lower peritoneal P_i clearance than those in the high-average or high membrane transport categories [31, 32].

Other studies, however, question the validity of the peritoneal membrane transport category as a predictor of peritoneal P_i handling. In children on PD, the association of the 2- and 4-hour dialysate-to-plasma (D/P) ratio for P_i with the D/P ratio for creatinine was strong, while the association of peritoneal P_i clearance with the D/P ratio of creatinine was much weaker. From these data the authors concluded that creatinine is an inadequate surrogate marker of peritoneal P_i transport and argued for an individual assessment of peritoneal P_i handling. They also proposed the definition of an individual peritoneal membrane P_i transport status by defining a D2/P of P_i <0.27 and D4/P of P_i <0.41 as low P_i transport status [35]. No other studies have so far tried to define peritoneal membrane P_i transport status, but those studies appear to be urgently needed.

Phosphate Elimination in Various PD Modalities

Independently of the membrane transport category, weekly average P_i removal in adults with CAPD has been reported to be around 70 mmol (2,170 mg) with an inlet volume of 4×2 liters and 105 mmol (3,250 mg) with an inlet volume of 4×3 liters of daily PD fluid [36]. In a cross-sectional comparative study between automated

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PD and CAPD, weekly total P_i mass removal was similar with 2,790 mg in CAPD and 2,739 mg in automated PD (table 1) [8]. Phosphate mass removal in CAPD and continuous cycling PD (CCPD), however, appears to be affected by membrane transport type. For patients in the high-average, low-average and low membrane transport categories, peritoneal P_i clearance is higher with CAPD than with CCPD, while creatinine clearance does not differ. For patients in the high category of membrane transport, in contrast, no difference between CAPD and CCPD was observed [31].

Based on currently available data, the following recommendations for the improvement of P_i removal can be made.

(i) For patients in the high type membrane category, phosphate elimination may be viewed as similar to the clearance of small-molecular-weight solutes. Phosphate mass removal in these patients may benefit from automated PD or CCPD with high nighttime fluid turnover and high number of cycles. However, it should be kept in mind that the diffusion of uremic toxins through the peritoneal membrane resembles a parabola and that if dialysate flow is increased beyond the individual turning point of the parabola, clearances may decrease, as the time spent for inflow and outflow becomes a significant part of the entire treatment period, which is less effective for diffusion [37]. The shape of the parabola for P_i elimination may be markedly different from that for creatinine.

(ii) For high average, low average and low membrane category type patients, peritoneal P_i clearance much more resembles the removal of middle molecules and small proteins which generally need longer dwell times to diffuse from peritoneal capillaries into the peritoneal cavity and do not depend on the number of exchanges of PD fluid. Phosphate mass removal in these patient groups will be higher with CAPD than with CCPD and may be further optimized with increasing dialysate outlet volume without reducing dwell time by using larger PD fluid volumes and higher dialysate glucose concentration.

(iii) All patient groups, independently of the PD modality used, may benefit from increased convective peritoneal P_i clearance through higher ultrafiltration rates. This is achieved by the use of higher dialysate glucose concentration or the use of icodextrin with or without shorter dwell times. However, no detailed studies on the effects of increased ultrafiltration rates on peritoneal P_i clearance are available.

These recommendations are based on the assumption that peritoneal membrane transport characteristics are predictive of peritoneal P_i removal. However, as pointed out earlier, peritoneal P_i clearance may follow its own characteristics, different from those of creatinine [35]. If that is the case, PD prescription needs to be adapted to the individual P_i-based and not only to the creatinine-based membrane transport types. Future studies should explore peritoneal P_i transport types in more detail. In hyperphosphatemic PD patients, the decision on the optimal PD modality should not solely be based on urea Kt/V but mainly on peritoneal creatinine and especially peritoneal phosphate transport characteristics.

In conclusion, comparing the various PD and conventional HD modalities, it can be stated that all remove about the same amount of phosphate per week (table 1) [31]. However, with all these HD and PD modalities, weekly phosphate removal is inadequate in relation to weekly dietary phosphate intake, and prescription of phosphate binders remains an essential component of phosphate management. The daily phosphate binder tablet burden can be reduced by optimizing the dialysis prescription for PD and HD. Modern HD treatment schedules with higher dialysis frequencies or extended treatment times, such as SDHD, or daily or 3 times weekly NHD, allow higher phosphate mass removal and potentially complete discontinuation of phosphate binder medication.

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