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Phosphate end dialysis value : a misleading parameter of hemodialysis efficiency

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Abstract. Despite low end dialysis serum phosphate levels (P_e) the control of phosphate retention remains often unsatisfactory in dialyzed patients. In order to assess the value of P_e in dialyzed children as an indicator of dialytic phosphate removal, we studied serum phosphate kinetics over the period of dialysis and post dialysis and compared these with urea kinetics. A multicenter study was conducted in the 21 French pediatric hemodialysis units and included 144 children under 15 years of age. Blood urea and phosphate concentrations were measured at the beginning, at 45 min later, at the end of dialysis, and 30 min post dialysis. At 60 min and at 360 min post dialysis measurements were made only for a subgroup of 12 children. From the serum levels, reduction ratios for urea (URR) and phosphate (PRR) and post dialysis rebound for urea (PDUR) and phosphate (PDPR) were calculated. URR (over the dialysis session, 72%±9%) was higher than PRR (47%±12%). Moreover, urea removal continued throughout the dialysis period, while most of the reduction in phosphate occurred in the initial dialysis period. Post dialysis urea rebound was limited to the 60th min post dialysis, whereas post dialysis phosphate rebound occurred until the 360th min post dialysis; by this time the serum phosphate levels had almost reached the predialysis levels. In summary, serum phosphate kinetics over dialysis and post dialysis periods in children appear to be misleading for the quantification of phosphate removal, i. e., phosphate clearance is a poor indicator of dialytic phosphate removal.

Key words: Phosphate - Reduction ratio - Post dialysis phosphate rebound - Dialysis efficiency

Introduction

Adequacy of dialysis as estimated by urea kinetics is now widely used to manage patients on maintenance hemodialysis. The urea kinetics model usually used is derived primarily from the post- and predialysis serum urea reveals. Despite the knowledge of the post dialysis urea rebound phenomenon [1], the urea reduction ratio (URR), and so the end dialysis urea serum value, is used as an indicator of dialysis efficiency. Despite low end dialysis serum phosphate values (P_e), the control of phosphate retention remains often unsatisfactory in dialyzed patients [2–4]. The phosphate mass removal during dialysis appears to be more dependent on the predialysis serum phosphate level than on the end dialysis serum phosphate value [5, 6]. In order to assess the value of serum phosphate levels as an indicator of the efficiency of dialytic phosphate removal in dialyzed children, we studied serum phosphate kinetics over the dialysis period, the reduction rate, and the post dialysis, rebound.

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Materials and methods

A multicenter survey was conducted in the 21 French hemodialysis units during February 1994 in order to study urea and phosphate kinetics during and after a midweek bicarbonate hemodialysis session conducted as usual in terms of blood flow and membrane prescriptions. A total of 144 patients were included, 41 aged from 1 to 7 years (mean age 5.6±1.3 years) 102 aged from 8 to 15 years (mean age 12.8±2.9 years). Vascular dialysis access was obtained in 139 cases through a fistula ponction and in 5 cases through a central catheter, with a mean blood flow of 5.8±1.9 ml/min per kg body weight (range 60–300 ml/min). Capillary membranes were used for 93% of the children, from 0.3 to 2.1 m^2 area. Mean dialysis duration was 3 h and 45 min (range 2 h to 5 h and 30 min). No phosphate binders were given on the day of dialysis. Serum urea and phosphate levels were measured at the beginning (U_i, P_i), then at 45 min (U_{45}, P_{45}), at the end (U_e, P_e) and finally at 30 min after the dialysis session (U_{+30}, P_{+30}). The end value sample was taken after 3 min low blood flow rate (50 ml/min) in order to minimize vascular access and cardiopulmonary recirculations. After the dialysis session, the extracorporeal blood flow was maintained at a low rate (50 ml/min) without dialysate flow in order to avoid variation in urea and serum phosphate concentrations secondary to saline line flush. All the samples were taken from the arterial limb of the dialysis circuit.

One hundred and forty sessions from the 144 children were available for analysis. For 12 children (from the same unit, two

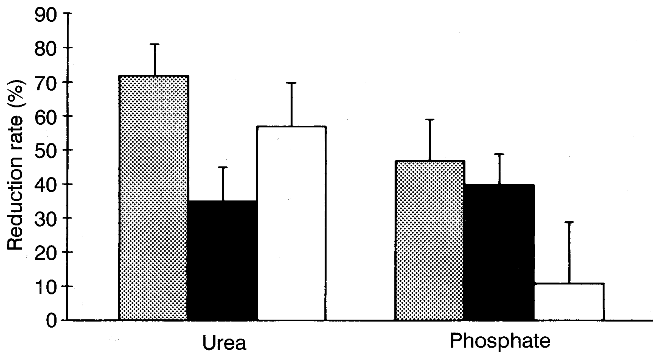

Fig. 1. Reduction ratio for urea and for phosphate over the different dialysis times (mean ±SD of 140 dialysis sessions). ▥, From before to the end of dialysis; ■, first 45 min of dialysis; □, from 45 min to the end of dialysis

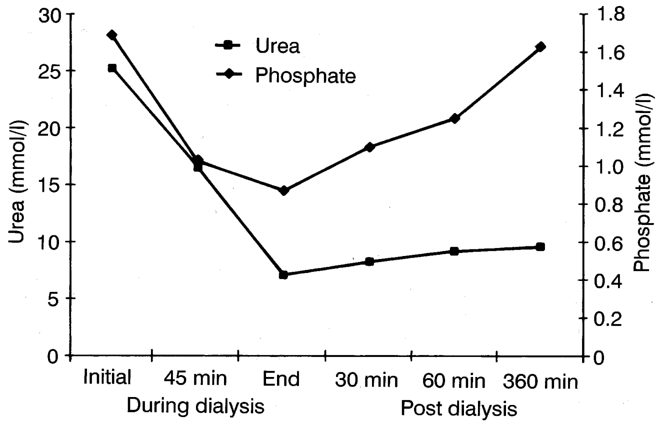

Fig. 2. Urea and serum phosphate levels over dialysis and post dialysis

midweek sessions per child), serum levels were followed up immunoradiometric assay to 360 min after dialysis. Calcium (total and ionized) and serum parathyroid hormone (PTH) levels (PTH, immunoradiometric assay, normal values 10–65 pg/ml) were also measured at the beginning and at the end of the dialysis session.

The reduction ratios (RR) were calculated as the percentage decrease in serum values over the different dialysis times (the entire session $_{i\text{-}e}$; initial period $_{i\text{-}45}$; last period $_{45\text{-}e}$) for urea (URR) and for phosphate (PRR):

$$URR_{i-e} = \frac{U_i - U_e}{U_i} \quad URR_{i-45} = \frac{U_i - U_{45}}{U_i} \quad URR_{45-e} = \frac{U_{45} - U_e}{U_{45}}$$

Post dialysis rebound was calculated as the percentage increase in serum values between the end of dialysis and at 30, 60 and 360 min post dialysis for urea (PDUR) and for phosphate (PDPR):

$$PDUR_{e-30} = \frac{U_{30} - U_e}{U_e} \quad PDUR_{e-60} = \frac{U_{60} - U_e}{U_e} \quad PDUR_{e-360} = \frac{U_{360} - U_e}{U_e}$$

All values are expressed as mean plus or minus standard error. Values were analyzed for the whole population as for each age group. Student's *t*-test was used for the analysis of the results. Correlations were evaluated by linear regression analysis. A *P* value less than 0.01 was considered to be significant. The purpose of the study was explained to the children and parents, and informed consent was obtained before the study.

Results

$URR_{i\text{-}e}$ (72%±9%) was significantly higher than $PRR_{i\text{-}e}$ (47%±12%) in the 140 analyzed sessions (Fig. 1). During the period from the beginning to the 45th min of the dialysis session, $URR_{i\text{-}45}$, (35%±10%) was in the same range as $PRR_{i\text{-}45}$ (49%±9%). In contrast, from the 45th min to the end of the dialysis session, $URR_{45\text{-}e}$ (57%±13%) was significantly higher than $PRR_{45\text{-}e}$ (11%±18%). Expressed as reduction rate no differences were noted between children aged groups 1–7 years and those 8–15 years, for urea or phosphate.

The serum phosphate levels decreased during the initial 45 min of dialysis from 1.69±0.48 mmol/l to 1.02±0.31 mmol/l (Fig. 2). Subsequently, from the 45th min to the end of the dialysis session, the serum phosphate levels decreased only slowly to a P_e of 0.87±0.21 mmol/l. In contrast, urea levels decreased evenly over the whole dialysis session: U_i 25.3±6 mmol/l, U_{45} 16.5±5 mmol/l, U_e 7.1±3 mmol/l (Fig. 2).

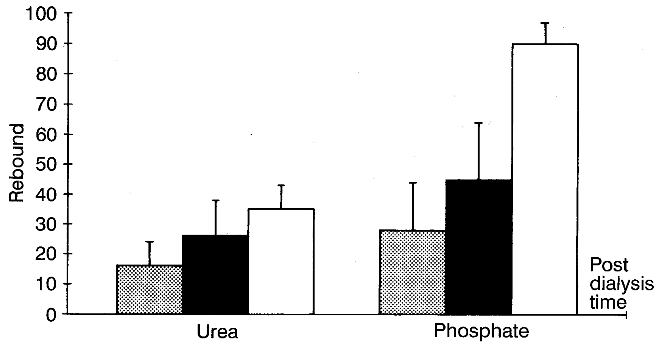

Fig. 3. Postdialytic rebound for urea and phosphate over the different postdialytic times (mean ±SD of *n* dialysis sessions). ▥, 30 min post dialysis/end (*n* = 140); ■, 60 min post dialysis/end (*n* = 24); □, 360 min post dialysis/end (*n* = 24)

PDUR was slower than PDPR (Fig. 3) at 30 min post dialysis. The serum urea levels (Fig. 2) were 8.3±3.1 mml/l at 30 min (*n*=140 sessions), 9.2±2.6 mmol/l at 60 min (*n*=24 sessions), and 9.6±2.4 mmol/l at 360 min (*n*=24 sessions). In contrast, at 30 min post dialysis the serum phosphate levels 1.10±0.24 mml/l (n=140 sessions) were already equal to the serum phosphate levels achieved after 45 min of dialysis 1.02±0.31 mmol/l. Moreover, serum levels at 60 min, 1.25±0.19 mml/l (n=24 sessions) and at 360 min 1.63±0.31 mml/l (n=24 sessions) increased post dialysis to the predialysis value. Five children had low basal PTH value, mean 31±15 pg/ml, range 17–47, while seven others had basal PTH values between 2 and 4 times the upper normal limit, mean 197±75 pg/ml, range 141–265. No differences in dialytic and postdialytic serum phosphate levels were noted according to the parathyroid status. Ionized calcium increased by 0.29±0.07 mmol/l and PTH was suppressed to 30 to 60% of the baseline value during dialysis.

A positive correlation was established between $URR_{i\text{-}45}$ and $PRR_{i\text{-}45}$: $y = 0.461x + 0.234$, $r = 0.497$, $P < 0.0001$. Conversely no relation was noted between $URR_{45\text{-}e}$ and $PRR_{45\text{-}e}$. The serum urea levels at 30 min post dialysis were positively correlated with the levels after 45th min of dialysis: $y = 1.271x + 6.232$, $r = 0.817$, $P < 0.0001$, as were the serum phosphate levels at the same post dialysis

(30 min) and dialysis (45th min) times: $y = 1.102x - 0.142$, $r = 0.63$, $P < 0.0001$.

Discussion

RR rates over the dialysis periods are widely used to assess adequacy of dialysis [7]. Serum urea levels show a rapid increase, termed rebound, after a dialysis session which is limited to a short period of time, usually less than 60 min [1, 8]. Only a very small amount of this rebound is caused by the post dialysis urea generation rate, at a basal interdialytic rate or at an accelerated rate induced by dialysis bioincompatibility [1, 8]. Most of the PDUR seems to be related to urea reequilibration between the body water pools [1]. Thus dialysis adequacy indexes, based on RR ratios should take into account this rebound phenomenom. The profiles of serum phosphate levels during and post dialysis [3, 4, 9] have received far less attention even in adults. Therefore, we have studied and compared urea and phosphate profiles during and after dialysis.

Our study of a large population of hemodialyzed children shows a decrease in serum phosphate levels during the initial dialysis period. This phosphate decrease, estimated by the RR rate is only slightly higher than the URR rate, over the same period of dialysis (Fig. 1). These results differ from other studies where phosphate levels decreased strikingly during the initial period of hemodialysis [3, 4], especially during high flux hemodialysis [9]. In fact, the initial RR rate seems directly related to the predialysis levels [6], which in our study were only slightly elevated. Thereafter, from the 45th min to the end of dialysis the serum urea and the phosphate levels show completely different profiles. Urea decreased continuously over the dialysis period, suggesting kinetics which best match a two-pool urea kinetics model [10, 11]. In contrast, after an initial decrease the serum phosphate levels either stabilized or increased slightly [6], despite persistent dialytic phosphate removal [5, 12]. Most of the PRR was achieved after 45 min of dialysis (Fig. 1) in our study. Moreover, PRR and URR only correlated during the initial dialysis period. This could be explained by a time-dependent influx from the intracellular compartment to the extracellular compartment being influenced by different factors for urea and phosphate [9, 13–15].

PDUR seems complete within 60 min dialysis, as suggested by other data in children [9]. Thereafter, the serum urea levels increase only slowly (Fig. 2). After dialysis, PDPR was higher than PDUR. Post dialysis the phosphate profile shows a striking increase, with no interruption in the rebound between the end of dialysis and 360 min post dialysis. At 30 min post dialysis, the serum phosphate values (1.10 ± 0.24, $n = 140$ dialysis sessions) were nearly the same as those after 45 min of dialysis (1.02 ± 0.31, $n = 140$ dialysis sessions). At 360 min post dialysis the serum phosphate values (1.63 ± 0.31, $n = 24$ dialysis sessions) reached the predialysis values (1.69 ± 0.48, $n = 140$ dialysis sessions). Even though the number of children studied at 360 min post dialysis is limited, these results are noteworthy. No relationship could be established between serum phosphate levels during or post dialysis and baseline PTH values used as a marker of low, normal, or high turnover bone disease, or the rate of PTH suppression during dialysis. The PDPR noted in our study cannot be fully explained by a clinical intracellular extracellular two-pool model [13]; however, a rapid and time-dependent influx of phosphate into the extracellular compartment could possibly explain the PDPR, influx resulting from phosphate production by biochemical reactions [5], from cellular wash out [12], or from a bone compartment outflow. The correlation established in our study for serum levels of urea and phosphate between 45 min into dialysis and 30 min post dialysis suggests that similar factors may explain the rebound and the RR during these periods for urea and phosphate.

In conclusion, the phosphate profile over dialysis and post dialysis periods demonstrates that serum phosphate levels in children, as in adults [9], are misleadings parameters of dialysis efficiency; in particular, the P_e should not be used for quantification of dialytic phosphate removal [5, 9].

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