KINETIC ASSESSMENT OF DIFFERENT HYPOTHESES ON FACTORS RESPONSIBLE FOR CHANGES IN PHOSPHATE CONCENTRATION IN PLASMA DURING HEMODIALYSIS

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OBJECTIVES

Phosphate concentration in plasma, in contrast to urea and creatinine, stabilizes after 1 – 2 hours and even increases before the end of 4-hour hemodialysis session. This phenomenon was attributed to the phosphate exchange with the fast compartment (related to bone phosphate) and exploited by pseudo-one compartment model of phosphate kinetics (Agar, CJASN 2011). Recently, experimental data revealed increased intracellular phosphate concentration during hemodialysis (Lemoine, JASN 2016) and it was proposed that this effect was responsible for the specific kinetics of phosphate in plasma. We constructed a mathematical model that incorporated two phosphate sources (fast bone compartment and intracellular) and compared its predictions with clinical data.

METHODS

The model comprised the compartments of free and protein bound phosphate in plasma and interstitium, the free intracellular phosphate and intracellular phosphate store (related perhaps to ATP, polyphosphate or glycophosphate), and fast compartment, **Figure 1**. The steep increase of the generation of phosphate to intracellular phosphate compartment from an intracellular store during hemodialysis and a similar decrease after the end of the dialysis session were assumed. The exchange of the phosphate with the fast compartment was described as in the pseudo-one compartment model. The predictions from the computer-based simulations were compared to the kinetics of plasma phosphate concentration during one week cycle of three hemodialysis sessions with 2-2-3 day breaks between the sessions (Debowska, NDT 2015). The patients were assumed to be in the metabolically stable state, i.e., the status of all compartments was the same at the beginning and end of the week cycle of dialysis. The model desribed also the kinetics of calcium, **Figure 1**.

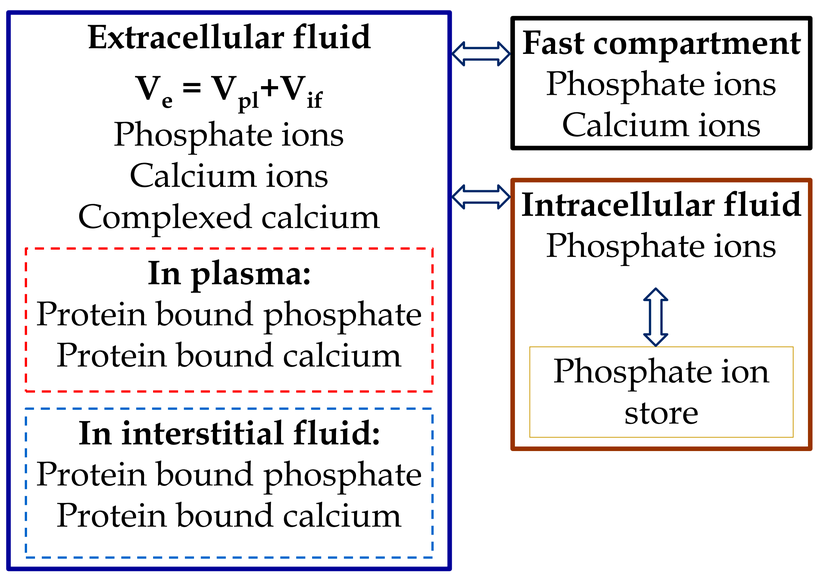

Figure 1. Model for phosphate and calcium kinetics.

RESULTS

- The three versions of the model: *Model F* without intracellular store, *Model IC* without fast compartment, and *Model F&IC* with both these compartments, were well adjusted by selection of the parameters to provide the qualitative description of measured profiles of phosphate in plasma during hemodialysis, see **Figure 2** for model F.
- Model IC predicted the fastest equilibration of plasma phosphate during dialysis and its slight increase at the end of the 4 h session, **Figure 3**.
- The intracellular phosphate increased during dialysis by about 10% in agreement with the experimental data; to obtain metabolic stability of the patient it was necessary to introduced very fast exchange of phosphate between the free intracellular phosphate and the intracellular phosphate store.
- Model F had the phosphate clearance from the fast compartment as in the pseudo-one compartment model.
- In Model IC&F, the permeability of the cellular membrane had to be decreased and the clearance from the fast compartment increased to adjust the model to the measured data.
- All three versions of the model predicted quick return of the phosphate level to its initial value after the end of dialysis session and Model IC predicted a slight rebound of plasma phosphate, **Figure 3**.

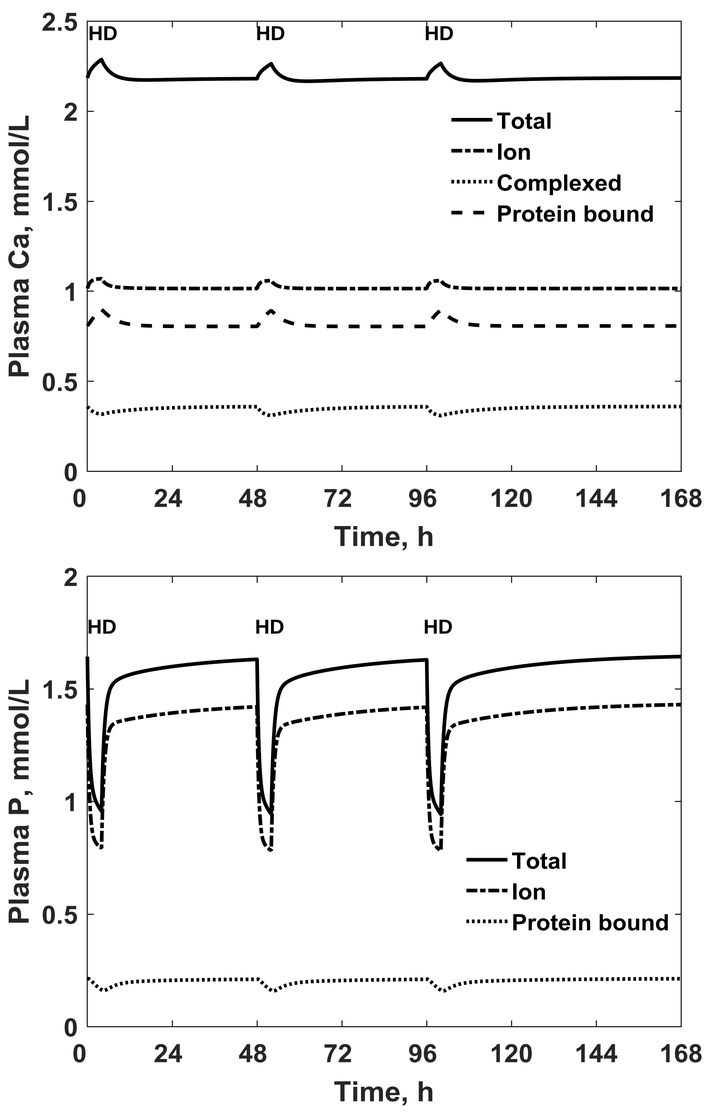

Figure 2. Concentration profiles of different forms of calcium (ionic, complexed with small ions, protein bound) and phosphate (ions and protein bound) in plasma during one week cycle of three hemodialysis sessions predicted by *Model F*.

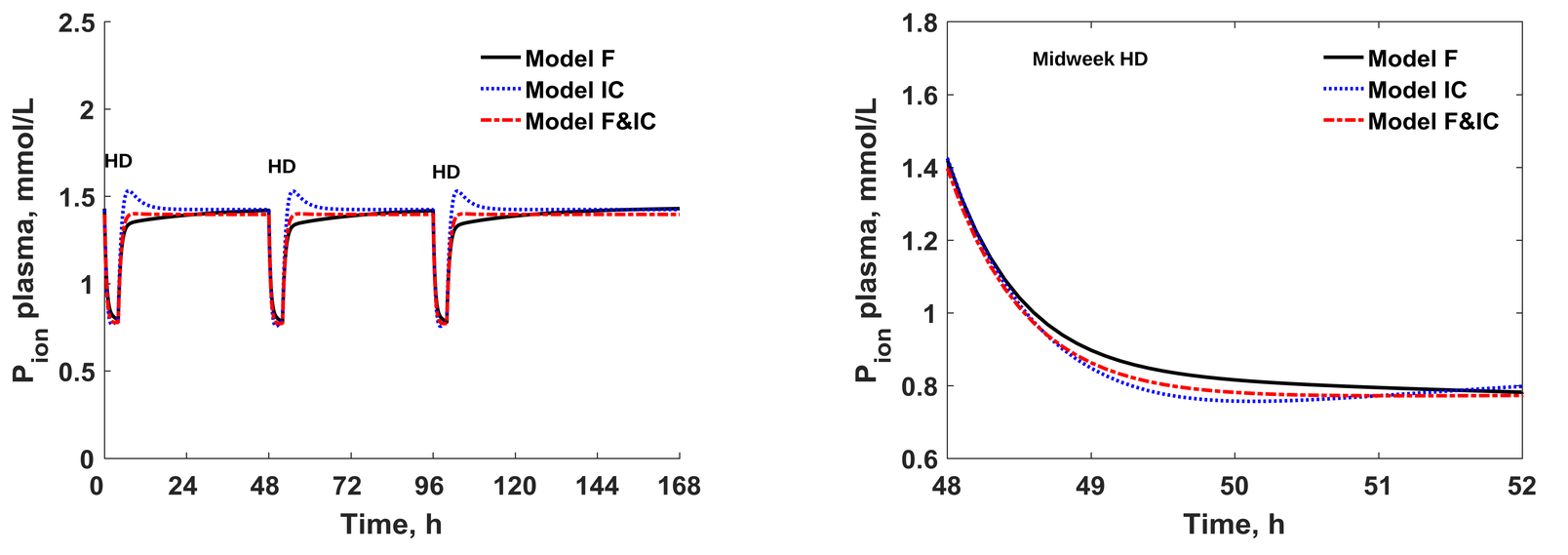

Figure 3. Concentration profiles of ion phosphate in plasma during one week cycle of three hemodialysis sessions (left panel), close up of phosphate profiles during the midweek dialysis session (right panel) predicted by *Models F* (black continuous line), *IC* (blue dotted line) and *F&IC* (red hatched line).

CONCLUSIONS

The hypotheses of the fast compartment and the intracellular store compartment were shown to be kinetically compatible with clinical data separately or in conjunction after adjusting of the model parameters. More physiological information about the exchange of phosphate with these compartments is necessary to evaluate their contribution to the phosphate kinetics during hemodialysis.

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