COMPUTATIONAL MODEL OF FLUID AND SOLUTES TRANSPORT IN HEMODIALYSIS PATIENTS WITH ACTIVE TRANSPORT OF SODIUM AND POTASSIUM ACROSS THE CELLULAR MEMBRANE

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Introduction

During hemodialysis (HD), the removal of water and substances from the vascular compartment by the dialyzer initiates a complex chain of exchanges of fluid and solutes between vascular, interstitial and intracellular spaces all over the body. From the equilibrium between these exchanges is determined how much is removed and from where. Understanding these processes is the key to develop therapies more efficacious and more tolerable by the patient; allowing clinicians to select the HD settings that promote the desired transport dynamics inside the body.

This study proposes a mathematical model of the transport of water, proteins, sodium, potassium, and urea during HD. The model was validated against clinical data from standard HD sessions.

Methods

- The model has three-compartments for water, and two-compartments for solutes, as shown in Figure 1. Proteins (TP) are move between interstitial and vascular compartment, and do not cross the cell membrane. Small solutes (Na, K, urea) have similar concentration in interstitial fluid and plasma, and thus are grouped into the extracellular compartment. The transport equations used are based on the principle of conservation of mass. Small solute transport across the cell membrane is passive-diffusive, with an active component (ATPase pump) for Na and K. Protein transport across the capillary wall is described with a 3-pore model: homogenously distributed large (LP), small (SP), and ultrasmall (UP) pores across which convection and diffusion take place.
- Transcellular water transport was described assuming that water shifted fast enough to keep intra- and extra-cellular total osmolarities equal, every instant. Transcapillary water transport was governed by the Starling equation, while lymphatic flow depended linearly on interstitial hydraulic pressure.
- For each patient, the data were used to estimate the following parameters: large pores fraction (α_{LP}), filtration coefficient (Lp), maximum ATPase pump rate (Jp_{max}). Table 1 reports the values of the fixed parameters in the model.

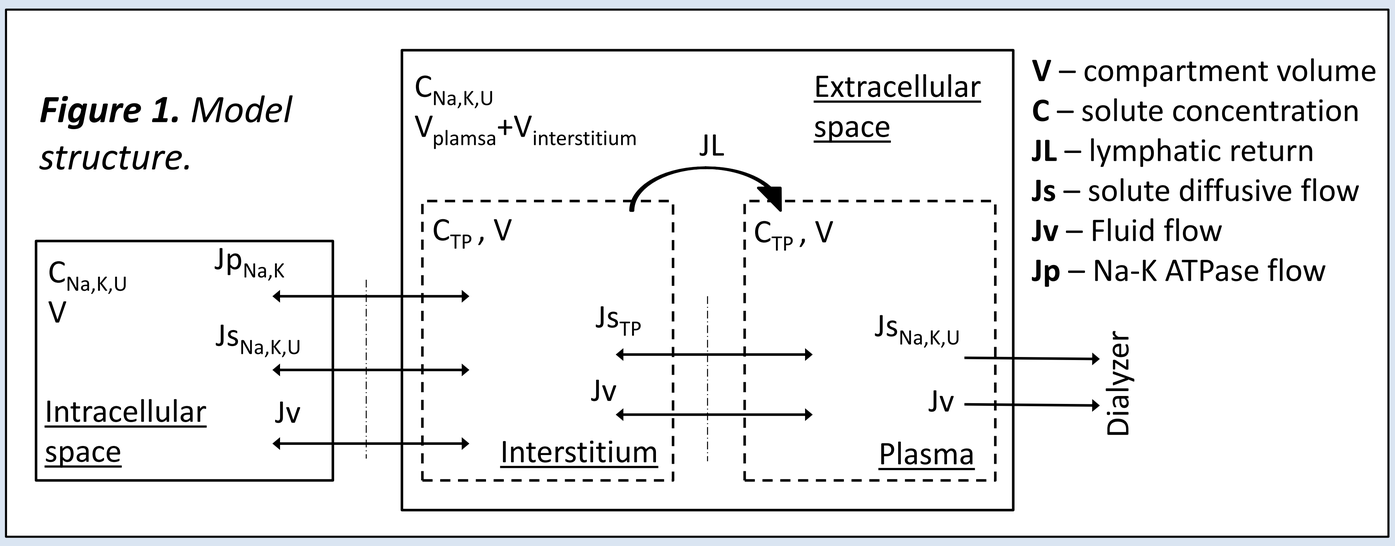

Figure 1. *Model structure.*

α_{SP}	0.6
LP radius (Å)	250
SP radius (Å)	45
UP radius (Å)	2
Protein radius (Å)	35.5
Urea permeability (mL/min)	770

Table 1. *Fixed parameters of the model.*

Results

The results refer to data from a sample of 20 patients. Some of the simulated profiles compared to the clinical data, see Figure 2. Table 2 and Table 3 report the values of the estimated parameters, and of the solute transport parameters calculated by the model, respectively. Figure 3 shows the changes in the transport rate of small solutes across the cellular membrane during the course of the HD session.

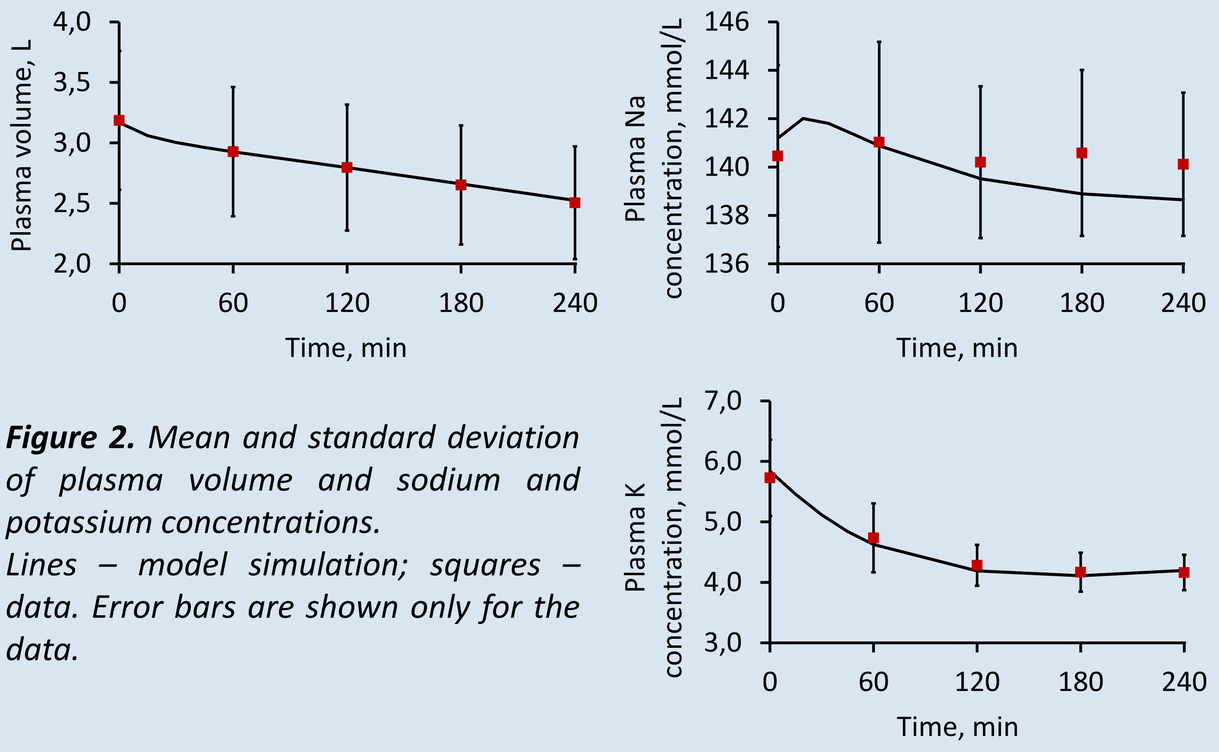

Figure 2. *Mean and standard deviation of plasma volume and sodium and potassium concentrations.*
Lines – model simulation; squares – data. Error bars are shown only for the data.

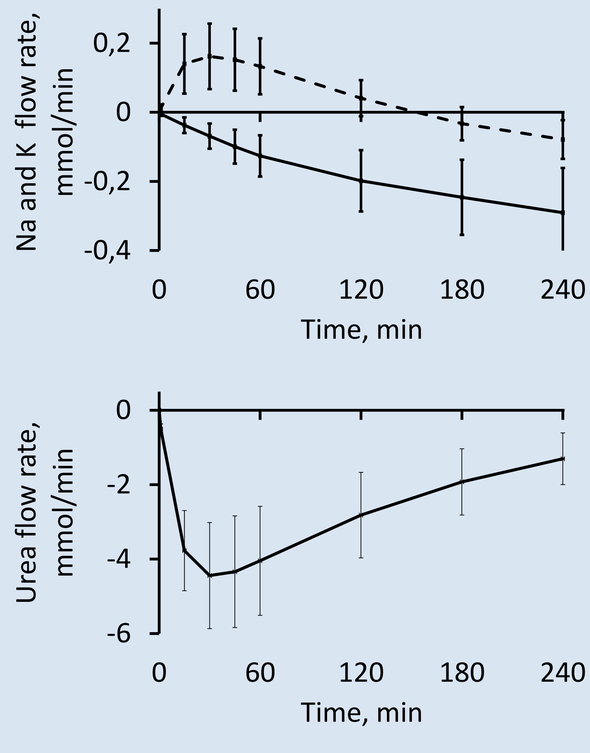

Figure 3. *Small solute flows across the cell membrane. Positive flows are directed towards the intracellular space. Top: sodium (dashed line), potassium (continuous line). Bottom: urea.*

Potassium and urea were removed from the intracellular space during the whole HD, while Na was transported to the cells during the first 2.5 h of treatment, resulting in a net accumulation of Na in the cells.

Table 2. *Mean and standard deviation of the estimated parameters of the model.*

α_{LP}	0.056 ± 0.016
Lp (mL/min/mmHg)	10.8 ± 5.3
Jp_{max} (mmol/min)	6.0 ± 4.4

Table 3. *Calculated whole-body transport parameters for proteins (PS_{TP}, across the capillary wall) and small solutes (w_{Na} and w_K, across the cell membrane). The coefficients for Na and K were estimated imposing the equilibrium between diffusive and active flows. Urea permeability was taken from literature.*

PS_{TP} (mL/min)	2.0 ± 1.5
w_{Na} (mL/min)	56.0 ± 40.4
w_K (mL/min)	28.3 ± 21.7

Conclusions

The model was able to describe the clinical data with good accuracy in most of the patients, with a small average relative error (4.8 ± 3.3 % of the data value). The estimated value of α_{LP} and LpS is in line with findings in similar studies. The estimation of Jp_{max} was characterized by higher scattering of the values; the scarcity of mathematical models proposed for HD which explicitly represent active transport of Na and K makes it difficult to draw comparisons. The model has the merit of being able to reproduce accurately individual patient data with the estimation of very few parameters.

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