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Parameter estimation in six numerical models of transperitoneal transport of potassium in patients undergoing peritoneal dialysis

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Summary. The mechanisms of transperitoneal potassium transport during peritoneal dialysis were evaluated by validation of different mathematical models. The models were designed to elucidate the presence or absence of diffusive, non-lymphatic convective and lymphatic convective solute transport. Experimental results were obtained from 26 non-diabetic patients undergoing peritoneal dialysis. The validation procedure demonstrated that models including both diffusive and non-lymphatic convective solute transport were superior to the other models. Lymphatic convective solute transport was not identifiable. Furthermore, it was demonstrated experimentally that the equilibrium distribution of potassium between plasma water and dialysate did not differ from a Donnan equilibrium, although the precondition of the Donnan equilibrium was not fulfilled, i.e. the volumes on each side of the membrane were not constant and dialysate was not an ultrafiltrate of plasma.

Key words: diffusion potential, diffusive mass transfer area coefficient, kinetic modelling, lymphatic convective solute transport, ultrafiltration sieving coefficient.

Introduction

A number of mathematical models of transperitoneal solute and water transport have been used to investigate the mechanisms of transport and to provide estimates of transport parameters. Early models described transperitoneal solute transport in terms of diffusion alone (Kallen, 1966; Miller *et al.*, 1966; Henderson & Nolph, 1969; Moncrief *et al.*, 1972; Bomar *et al.*, 1974; Goldsmidt *et al.*, 1974), whereas newer models included convective solute transport (Babb *et al.*, 1973; Bomar, 1975; Randerson & Farrell, 1980; Pyle, 1981; Garred *et al.*, 1983; Krediet *et al.*, 1986; Jaffrin *et al.*, 1987; Lindholm *et al.*,

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1987) or convective and lymphatic solute transport as well (Flessner *et al.*, 1984; Leypoldt *et al.*, 1988; Hallett *et al.*, 1989; Rippe & Stelin, 1989).

In uraemic patients the removal of potassium by dialysis is obviously important. The application of simple peritoneal mass transport models to transperitoneal potassium transport has failed to provide an exact description of the transport mechanism involved. Only a few publications have addressed the issue of transperitoneal potassium transport (Brown *et al.*, 1973; Rubin *et al.*, 1982; Waniewski *et al.*, 1991a, 1991b, 1992a, 1992b; Heimbürger *et al.*, 1992; Hutchison *et al.*, 1992). Unlike creatinine, urea and glucose, potassium carries an electric charge, and the movement of potassium across the peritoneal membrane is therefore influenced both by a chemical and by an electrical gradient. The driving forces will tend to establish an electrochemical equilibrium between plasma water and dialysis fluid. If the ionic diffusion takes place for a sufficient period of time, and if the volumes on each side of the membrane remain constant, dialysis fluid will ultimately become an ultrafiltrate in Donnan equilibrium with plasma.

The aim of the present study was to study the mechanism of transperitoneal potassium transport and to evaluate the magnitude and the nature of the equilibrium distribution of potassium between plasma water and dialysate. A family of six nested models was validated as suggested by Carson *et al.* (1983).

Subjects and methods

CLINICAL STUDIES

Patients. A total of 26 non-diabetic patients (16 men and 10 women) undergoing peritoneal dialysis therapy were included in the study. Fourteen of these patients had chronic renal failure of unknown aetiology, six had chronic glomerulonephritis, two had chronic pyelonephritis, two had polycystic kidney disease, one had obstructive nephropathy, and one had nephrosclerosis. Median age was 63 years (range 23–75 years), median daily urine output was 500 ml (range 0–2500 ml) and median body weight was 73 kg (range 41–90 kg). Twenty-three patients were treated with continuous ambulatory peritoneal dialysis (CAPD) and three with continuous cycling peritoneal dialysis (CCPD) for 0·5–78 months prior to the study.

Ethics. Written informed consent was obtained from all patients, and the study protocol was approved by the local medical ethics committee.

Dialysis procedure. Each patient participated in a 6-h dwell study as described in detail previously (Fugleberg *et al.*, 1994; Graff *et al.*, 1994). Two litres of pre-heated (37–38°C) dialysis fluid containing 22·7–23·0 g glucose l^{-1} (Dianeal, Baxter Healthcare Corporation, Castlebar, Ireland or Lockolys-Glucos, Fresenius AG, Bad Homburg, Germany) were used. Dialysate samples were collected at 0, 30 and 60 min, and at 30-min intervals thereafter up to 360 min. Blood samples were drawn at 0, 120, 240 and 360 min.

Dialysate volumes. These were measured using haemoglobin as a volume marker. Details of the volume measurements can be found in Fugleberg *et al.* (1994) and Graff *et al.* (1994).

ANALYTICAL METHODS

Potassium concentrations in serum and dialysate were measured by a SMAC 3 (Technicon, Tarrytown, NY, USA). The plasma potassium concentrations were calculated from the measured serum concentrations by subtraction of 0·37 mmol l^{-1} (Ladenson *et al.*, 1974). Dialysate haemoglobin concentrations were measured by the cyanmethaemoglobin method, after centrifugation of the dialysate.

MODEL FORMULATION

A family of six nested models was formulated. Model 1 was purely diffusive, i.e. non-lymphatic convective transport and lymphatic convective transport were ignored. Model 2 included diffusive transport, non-lymphatic convective transport (constant ultrafiltration sieving coefficient=1), and lymphatic convective transport. Model 3 included diffusive and non-lymphatic convective transport (fitted ultrafiltration sieving coefficient) without lymphatic convective transport. Model 4 included diffusive and lymphatic convective transport without non-lymphatic convective transport. Model 5 included diffusive transport and non-lymphatic convective transport (constant ultrafiltration sieving coefficient=1) without lymphatic convective transport. Model 6 (the global model) included all three mechanisms of transport: diffusion, non-lymphatic convective transport (fitted ultrafiltration sieving coefficient) and lymphatic convective transport.

The six models were based on the following assumptions:

(1) The peritoneal membrane was a barrier separating a well-mixed dialysate compartment of variable volume and composition from the well-mixed peritoneal capillary plasma water. Any deviation from the one-compartment assumption (i.e. one plasma water compartment) was ignored.
(2) Measured net changes of peritoneal volume (dVol/dt) could be partitioned into:
    (i) water transport characterized by concomitant potassium transport subject to molecular sieving, hereafter referred to as ultrafiltration; and
    (ii) water transport characterized by concomitant potassium transport not subject to molecular sieving, hereafter referred to as lymphatic flow.

Thus water transport was defined in terms of the resulting potassium transport, and the definition of lymphatic flow included a number of water transport mechanisms, e.g. dialysate sampling, direct lymphatic entry, interstitial lymphatic entry, and direct blood entry (Shockley & Ofsthun, 1992).

Net volume change was determined experimentally. No attempt was made to investigate the mechanisms of water transport.

(3) The solute (potassium) moved passively across the peritoneum by one, two or three of the following transport mechanisms:
   (i) *diffusive transport*, defined as a process whose transport rate was proportional to the electrochemical gradient between dialysate and plasma.
   (ii) *non-lymphatic convective transport*, defined as a process whose transport rate was proportional to the ultrafiltration rate and the average intramembrane solute concentration.
   (iii) *lymphatic convective transport*, defined as a solute size independent process whose transport rate was proportional to the solute concentration of the plasma water or the dialysate, depending on the direction of flow.

(4) The transport parameters (diffusive mass transfer area coefficient, ultrafiltration sieving coefficient and lymphatic flow rate) were constant during the experiment.

(5) Haemoglobin disappearance rate from the peritoneal cavity was proportional to the intraperitoneal mass of haemoglobin.

(6) Mechanisms of potassium transport were identical in all patients, whereas the magnitude of the individual transport parameters varied between individuals.

A detailed discussion of these assumptions has been published previously (Fugleberg *et al.*, 1994).

CALCULATIONS

Parameter estimation. The six models were mathematically formulated in two differential equations:

(i) $$dVol/dt = QU - QL$$

Equation (i) states that net volume change per unit time is the difference between ultrafiltration rate and lymphatic flow rate.

(ii) $$dM/dt = MTAC*(fct*Cpw - CD) + SiCo*QU*MC - QL*CL$$

Equation (ii) partitions net solute transport per unit time into diffusive transport, non-lymphatic convective transport and a remainder term (lymphatic convective transport). The first term of the right-hand side of equation (ii) describes diffusive transport as the product of a clearance (MTAC) and the electrochemical gradient. The electrochemical gradient is defined as the difference between fct*Cpw and CD, where fct is the best- fit equilibrium distribution ratio for potassium (CD/Cpw), Cpw is the peripheral vein plasma water potassium concentration, and CD is the dialysate concentration of potassium. The second term describes non-lymphatic convective transport

as the product of the ultrafiltration sieving coefficient (SiCo), the ultrafiltration rate (QU) and the average intramembrane potassium concentration (MC). The third term describes the remainder transport rate (lymphatic convective transport) as the product of the lymphatic flow rate (QL) and the potassium concentration (CL). CL=Cpw or CD, depending on the direction of the lymphatic flow.

In each model M(t=0), MTAC and fct were searched for in the set of real numbers, whereas SiCo and QL were searched for in the set of real numbers or kept constant as indicated in Table 1. The search for the best-fit values of M(t=0), MTAC, fct and SiCo was not restricted to positive values, since unphysiological estimates effectively invalidate the model(s) in question.

Dialysate volume calculation. The dialysate volumes were calculated as described previously (Fugleberg *et al.*, 1994; Graff *et al.*, 1994).

Ultrafiltration rate. This was calculated from the estimated dialysate volumes and the lymphatic flow rate, as described previously (Fugleberg *et al.*, 1994; Graff *et al.*, 1994).

Average intramembrane solute concentration (MC). MC was calculated as described by Villaroel *et al.* (1977).

$$MC=Cpw-f^{*}(Cpw-CD);$$

$$f=(1/\beta)-1/(\exp(\beta)-1);$$

$$\beta=\text{Péclet number}=QU^{*}SiCo/MTAC.$$

Calculation of dialysate solute concentration-time curve from M(t=0), MTAC, fct, SiCo and QL. The relationship between time (t, min, independent variable) and dialysate solute concentration (CD, mmol l^{-1}, dependent variable) for given values of M(t=0), MTAC, fct, SiCo and QL was calculated by numerical integration (fourth order Runge-Kutta's method). Details can be found in Fugleberg *et al.* (1994) and Graff *et al.* (1994). When values of Cpw were not available, concentrations were estimated by linear interpolation.

Curve-fitting procedure. For each set (n=13) of paired observations (t, CD) the vector (M(t=0), MTAC, fct, SiCo, QL) and the resulting solute concentration-time curve giving the smallest sum of squared residuals was found by the Simplex method (Nelder & Mead, 1965). For details see Fugleberg *et al.* (1994) and Graff *et al.* (1994).

The Akaike criterion (AIC) (Akaike, 1974). This made it possible to compare the goodness of fit of two or more models with an unequal number of estimated parameters on the basis of the calculated sum of squared residuals. The number of estimated parameters was three in models 1 and 5, four in models 2, 3 and 4, and five in model 6. For each patient, models 1 to 6 were given ranks from 1 (lowest AIC) to 6 (highest AIC). The median rank was calculated for each model.

The F-test (Draper & Smith, 1981; Bates & Watts, 1988). This is an alternative method used to compare goodness of fit in two competing models with an unequal number of estimated parameters. Details can be found in Fugleberg *et al.*, 1994).

STATISTICAL ANALYSIS

Since the parameter estimates were skewed, the results were presented as medians (95% confidence interval). Differences in goodness of fit (AIC and *F*-test) between two models were analysed using the sign test. Residual errors were tested for randomness by the runs test. The level of significance was 0·05.

Results

The peripheral vein plasma water potassium concentrations (Cpw), measured at 0, 120, 240 and 360 min, demonstrated a statistically significant difference in location (Friedmann's test corrected for ties), $n=26$, $K=4$, $p=0{\cdot}03$).

Median transport parameter estimates (95% confidence interval), the median ranks of AIC and the number of runs from the analysis of residual errors are shown in Table 1. Figure 1 shows the mean peritoneal volume vs. time, and Fig. 2 depicts mean volume change rate vs. time. Figure 3 shows mean dialysate and mean peripheral vein plasma water potassium concentrations vs. time.

Table 1. Median (95% confidence interval) of the transport parameter estimates (constants in bold face text) and median ranks (95% confidence interval) of the Akaike information criterion of models 1 to 6

	MTAC (ml min^{-1})	SiCo	QL (ml min^{-1})	AIC	fct	*R*
1	34·6 (27·2–38·5)	**0**	**SR**	5 (4–5)	0·91 (0·88–0·95)	3
2	4·4 (1·9–18·9)	**1**	2·4 (−8·6–19·4)	3 (2–3)	0·87 (0·03–0·94)	4
3	19·5 (15·0–25·6)	0·96 (0·81–1·49)	**SR**	2 (2–3)	0·96 (0·94–1·00)	7
4	32·2 (25·5–35·1)	**0**	2·9 (2·3–4·7)	6 (6–6)	1·00 (0·98–1·01)	3
5	24·7 (19·5–26·1)	**1**	**SR**	3 (1–4)	0·95 (0·92–0·97)	6
6	11·6 (4·1–19·2)	1·07 (0·94–1·18)	0·7 (−3·2–4·1)	3 (2–4)	0·93 (0·18–1·01)	7

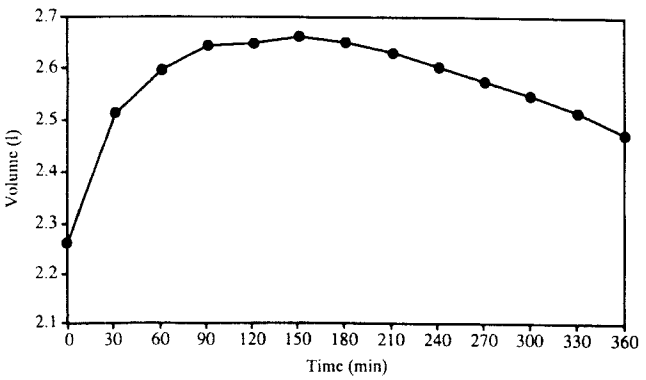

Fig. 1. Mean peritoneal volume vs. time.

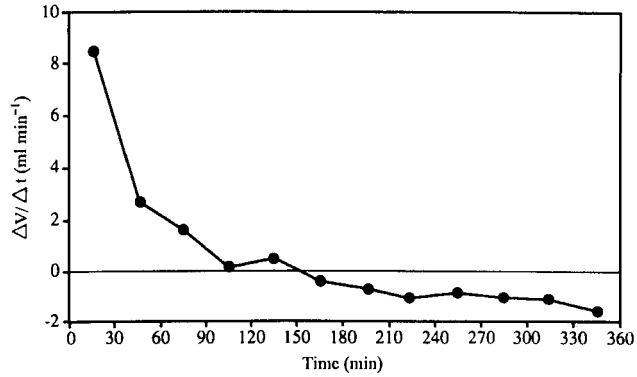

Fig. 2. Mean volume change rate vs. time.

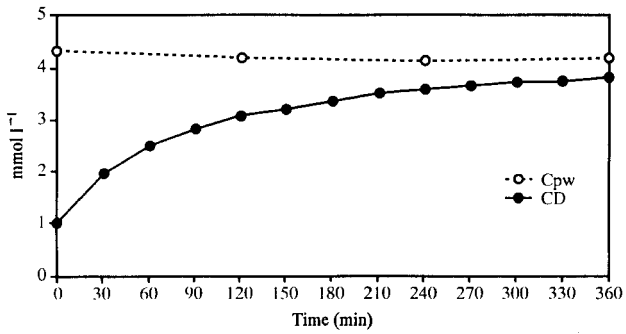

Fig. 3. Mean dialysate (CD) and mean plasma water (Cpw) potassium concentration vs. time.

THEORETICAL IDENTIFIABILITY

The global model (model 6) is a linear equation in five unknowns. All parameters (M(t=0), MTAC, fct, SiCo and QL) are theoretically identifiable if the dialysate volume-time profile and five or more experimental points (time, dialysate potassium concentrations) are provided.

GOODNESS OF FIT

When models 3 and 5 were compared using the Akaike information criterion, model 3 was preferred for 15 patients, and model 5 for 11 patients (P=0·56, sign test). When models 3 and 5 were compared using the F-test, model 3 was preferred for 8 patients, and model 5 for 18 patients (P=0·08, sign test). When models 3 and 6 were compared using the Akaike information criterion, model 3 was preferred for 20 patients, and model 6 for 6 patients (P=0·009, sign test). When models 3 and 6 were compared using the F-test, model 3 was preferred for all 26 patients (P<0·0001, sign test). When models 5 and 6 were compared using the Akaike information criterion, model 5 was preferred for 13 patients, and model 6 for 13 patients (P=1, sign test). When models 5 and 6 were compared using the F-test model 5 was preferred for 21 patients, and model 6 for 5 patients (P=0·003, sign test).

Table 2. Overall validation of models 1 to 6

Model	1	2	3	4	5	6
Theoretical identifiability	Yes	Yes	Yes	Yes	Yes	Yes
Preferred by the AIC values			Yes		Yes	No
Preferred by the *F*-test			Yes		Yes	No
Random residual errors	No	No	Yes	No	Yes	Yes
Parameter plausibility	Yes	Yes	Yes	Yes	Yes	Yes
Overall validation	No	No	Yes	No	Yes	No

RESIDUAL ERRORS

The expected number of runs for $n=13$ was 7·5 (approximate 95% confidence interval: 5–10). The runs test demonstrated that the residual errors of models 3, 5 and 6 were randomly distributed, whereas the residual errors of the other models were non-random.

PARAMETER PLAUSIBILITY

In all models, no unphysiological parameter estimates were found.

OVERALL MODEL VALIDATION

Overall model validation includes theoretical identifiability, goodness of fit, analysis of residual errors and the assessment of parameter plausibility. The results of the overall model validation are given in Table 2.

Discussion

In the present study we used the criteria of model validation, as suggested by Carson *et al.* (1983), in order to investigate whether the best model of transperitoneal potassium transport during a hypertonic exchange is purely diffusive, or whether non-lymphatic convective and/or lymphatic convective transport mechanisms are identifiable as well. For this purpose, six nested models were formulated and tested for theoretical identifiability, goodness of fit, random residual errors and plausibility of parameter estimates. The principles of model validation have been explained elsewhere (Fugleberg *et al.*, 1994). A test for practical identifiability was not performed as the data were skewed.

All models were theoretically identifiable. Models 1, 2 and 4 were rejected on the basis of non-randomly distributed residual errors. It was not possible to invalidate any model on the basis of unphysiological parameter estimates. Among the remaining three models (3, 5 and 6) the model with the best fit is generally considered to be superior. Goodness of fit describes in quantitative terms the agreement between raw data and model prediction—in this case measured and calculated dialysate potassium concentrations. When models with an equal number of estimated parameters are compared,

goodness of fit can be estimated solely from the sum of squared residuals. When two or more models with a different number of estimated parameters are compared, a comparison of the sums of squared residuals is not appropriate, since the addition of parameters to a model always lowers the sum of squared residuals. Therefore, the improvement in fit obtained by adding parameters to any given model should not be evaluated from the uncorrected sum of squared residuals: the sums of squared residuals should be corrected for the difference in the number of parameters. The Akaike criterion (Akaike, 1974) and the *F*-test criteria (Draper & Smith, 1981; Bates & Watts, 1988) are available for this purpose. Model 6 was rejected on the basis of a comparison of goodness of fit (model 3 vs. 6 and model 5 vs. 6). Neither AIC nor the *F*-test criteria demonstrated any difference in goodness of fit between models 3 and 5. However, there were only small differences between models 3 and 5. Thus, both models only included diffusion and non-lymphatic convection, ignoring lymphatic convection, but the ultrafiltration sieving coefficient of model 3 was fitted, whereas that of model 5 was constant and equal to one. The fitted estimate in model 3 was found to be 0·96 (0·81–1·49), which was not statistically significantly different from one. Furthermore, the estimates of the fct of the two models were not significantly different either. Thus, from the overall model validation, it must be concluded that the models including diffusive and non-lymphatic convective transport mechanisms (models 3 and 5) were superior to the other four models.

The peritoneal capillary plasma potassium concentration was not available for direct measurement. Therefore, the concentrations were calculated from the peripheral vein serum potassium concentrations by subtraction of 0·37 mmol l^{-1} (Ladenson *et al.*, 1974). The difference between plasma and serum potassium concentrations, caused by potassium leaked from the thrombocytes during coagulation, was essential for accurate parameter calculations. The plasma concentrations were then adjusted for plasma proteins. No further adjustments were made. Thus any differences between the calculated peritoneal capillary plasma water potassium concentrations and the true concentrations available for transport, caused by haemolysis, stasis during drawing and protein binding (Fogh-Andersen *et al.*, 1984) were ignored.

The estimates of the diffusive mass transfer area coefficient for potassium (models 3 and 5) were found to be considerably higher than results reported previously (Waniewski *et al.*, 1991a, 1991b, 1992a, 1992b; Heimbürger *et al.*, 1992; Hutchison *et al.*, 1992). An explanation of this difference could be that these authors corrected the difference between plasma and serum potassium by a different method to that used by us. Thus, if a smaller value than 0·37 mmol l^{-1} was subtracted from the serum concentrations, the driving concentration difference of the diffusive term of equation (ii) would be larger and the estimated MTAC smaller.

The ultrafiltration sieving coefficient depends on the properties of both membrane and solute. The relative size of the solute molecule, its charge and the charge of the membrane, steric hindrance and solubility in the membrane all influence the ultrafiltration sieving coefficient. By definition, it can never become negative and should not

exceed one in the case of potassium as the dialysate side of the peritoneal membrane is positively charged. The estimated median ultrafiltration sieving coefficients for potassium (model 3) were found to be considerably larger than those reported previously (Brown *et al.*, 1973; Rubin *et al.*, 1982), but considerably smaller than those reported by Waniewski *et al.* (1991a, 1992a, 1992b). Since the estimated ultrafiltration sieving coefficient was very sensitive to errors in the calculated ultrafiltration rate, differences in measurement and calculation of the ultrafiltration rate might explain the differences between the ultrafiltration sieving coefficients in our study and those reported by Rubin *et al.* (1982). In the studies of Waniewski *et al.* (1991a, 1992a, 1992b), unphysiologically high ultrafiltration sieving coefficients were found with the Pyle-Popovich model (model 3). Their parametric data presentation might be partly responsible for this apparent overestimate. Since our parameter estimates were skewed, the results were presented as medians and not as means. However, if our results had been presented as mean values±SD, the ultrafiltration sieving coefficient in model 3 would be 1·18±0·73.

From a clinical point of view it seems reasonable that the ultrafiltration sieving coefficient of potassium is close to unity, since hyperkalemia—unlike hypernatraemia (Nolph *et al.*, 1969)—does not occur during dwells with hypertonic dialysis fluid.

In contrast to creatinine transport (Fugleberg *et al.*, 1994) a lymphatic convective potassium transport mechanism was not identifiable by the best-fit models, i.e. the inclusion of QL in the models did not significantly improve the goodness of fit and did not resolve the question of whether or not this transport mechanism did exist in the system under investigation. One reason why the amount of information contained within the data was inadequate to identify this transport mechanism could be that some of the transport mechanisms included in the collective term QL (e.g. direct lymphatic, interstitial lymphatic and direct blood entry [Shockley & Ofsthun, 1992] might be influenced by the positive charge of the investigated solute. Hence, the total amount of potassium transported by lymphatic convection becomes negligible compared to the amount transported by diffusion and non-lymphatic convection.

Unlike creatinine, urea and glucose, potassium carries an electric charge, and the movement of potassium across the peritoneal membrane is therefore influenced both by a chemical gradient and by an electrical gradient.

In calculations of the diffusive potassium transport, the plasma water potassium concentrations at equilibrium must be corrected for the actual electric potential difference. The importance of this correction has been shown by Waniewski *et al.* (1992a), who adjusted the plasma concentrations for electrolytes for the Donnan factor to obtain correct values of MTAC.

Dialysis fluid differs from plasma not only in having almost zero protein concentration, but also in having a different electrolyte composition. Thus at the beginning of the dwell the diffusion of ions gives rise to a diffusion potential difference. During the dwell, the electric potential difference gradually changes towards a Donnan potential. A true Donnan equilibrium is theoretically never achieved, because the volumes on each side

of the membrane are not constant, and because dialysate is not an ultrafiltrate of plasma, even after 6 h. However, after 6 h, the molality ratios are close to a Donnan ratio.

It is possible to calculate the diffusion potential (E_{diff}) between dialysate and plasma by the Henderson equation (Henderson, 1907). E_{diff} was calculated to be −1·09 mV for the initial situation, and the corresponding $c_{dialysate}\ K^+/m_{plasma}\ K^+$ ratio was calculated to be 0·941 (kg l^{-1}) by the Nernst equation. Similarly, the predicted Donnan potential is −1·2 mV (Fogh-Andersen *et al.*, 1993), and the Donnan ratio for potassium between dialysate and plasma ($c_{dialysate}\ K^+/m_{plasma}\ K^+$) is 0·937 (kg l^{-1}). Thus during the 6 h of study, the expected equilibrium distribution ratio for potassium is predicted to be 0·94, based on conventional physical chemistry.

In order to investigate the distribution of potassium between plasma and dialysate, we compared the best-fit equilibrium distribution of potassium between dialysis fluid and plasma water (fct=CD/Cpw, models 3 and 5; Table 1) with the theoretical equilibrium distribution predicted by physical chemistry. In models 3 and 5, no statistically significant difference was found between the experimentally determined values and the theoretical value. Thus our results demonstrate that the equilibrium distribution of potassium between plasma and dialysis fluid did not differ from a Donnan equilibrium, although the precondition of the Donnan equilibrium was not fulfilled, i.e. the volumes on each side of the membrane were not constant and dialysate was not an ultrafiltrate of plasma.

In conclusion, the best models of transperitoneal transport of potassium during a hypertonic exchange involve diffusive and non-lymphatic convective transport. These models are theoretically identifiable, give the best fit to the experimental values, demonstrate small and non-systematic residual errors and give physiologically acceptable parameter estimates consistent with physico-chemical theory. Furthermore, it is concluded that the distribution of potassium between plasma and dialysate does not differ from a Donnan equilibrium.

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Appendix: abbreviations in alphabetic order

AIC: Akaike information criterion;
β: β=Péclet number=QU*SiCo/MTAC (dimensionless);
CAPD: continuous ambulatory peritoneal dialysis;
CCPD: continuous cycling peritoneal dialysis;
CD: dialysate potassium concentration (mmol l^{-1});
CL: if QL≥0 then CL=CD, otherwise CL=Cpw;
Cpw: peripheral vein plasma water potassium concentration (mmol l^{-1}), (time-dependent); Cpw=U*plasma potassium concentration; U=1/(0·984−0·000718*Cprot; Cprot=plasma total protein concentration (g l^{-1}); plasma potassium concentration=serum potassium concentration−0·37 (mmol l^{-1});
dM/dt: transperitoneal potassium mass transport rate (mmol min^{-1});
dVol/dt: rate of peritoneal net volume change (l min^{-1});
exp(x): the base of the natural logarithm raised to the power of x;
f: f=(1/β)−1/(exp(β)−1) (dimensionless);
fct: the time-independent factor defined as the best-fit equilibrium distribution between CD and Cpw;
M: intraperitoneal potassium mass (mmol);
MC: average intramembrane potassium concentration (mmol l^{-1});
MTAC: diffusive potassium mass transfer area coefficient (l min^{-1});
QL: defined by the equation dVol/dt=QU−QL (l min^{-1}). The following sign convention was adopted: QL≥0 if the direction of flow was from the peritoneal cavity into the plasma, otherwise QL<0;
QU: ultrafiltration rate (l min^{-1}). The following sign convention was adopted: QU≥0 if the direction of ultrafiltration was from plasma into the peritoneal cavity, otherwise QU<0;
R: number of runs (analysis of residual errors, runs test);
SiCo: ultrafiltration sieving coefficient (dimensionless);
SR: sampling rate=0·00065 l min^{-1} (233 ml/360 min);
Vol: peritoneal volume (l).