A Mathematical Model to Optimize the Drain Phase in Gravity-Based Peritoneal Dialysis Systems

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Use of patient-specific drain-phase parameters has previously been suggested to improve peritoneal dialysis (PD) adequacy. Improving management of the drain period may also help to minimize intraperitoneal volume (IPV).

A typical gravity-based drain profile consists of a relatively constant initial fast-flow period, followed by a transition period and a decaying slow-flow period. That profile was modeled using the equation

\[ V_D(t) = (V_{D0} - Q_{MAX} \cdot t) \cdot \Phi + (V_{D0} \cdot e^{-\alpha t}) \cdot (1 - \Phi), \]

where \( V_D(t) \) is the time-dependent dialysate volume; \( V_{D0} \), the dialysate volume at the start of the drain; \( Q_{MAX} \) the maximum drain flow rate; \( \alpha \), the exponential drain constant; and \( \Phi \), the unit step function with respect to the flow transition. We simulated the effects of the assumed patient-specific maximum drain flow \( Q_{MAX} \) and transition volume \( (\Psi) \), and the peritoneal volume percentage when transition occurs, for fixed device-specific drain parameters. Average patient transport parameters were assumed during 5-exchange therapy with 10 L of PD solution.

Changes in therapy performance strongly depended on the drain parameters. Comparing 400 mL/85% with 200 mL/65% \( (Q_{MAX}/(\Psi)) \), drain time (7.5 min vs. 13.5 min) and IPV (2769 mL vs. 2355 mL) increased when the initial drain flow was low and the transition quick. Ultrafiltration and solute clearances remained relatively similar. Such differences were augmented up to a drain time of 22 minutes and an IPV of more than 3 L when \( Q_{MAX} \) was 100 mL/min.

The ability to model individual drain conditions together with water and solute transport may help to prevent patient discomfort with gravity-based PD.

However, it is essential to note that practical difficulties such as displaced catheters and obstructed flow paths cause variability in drain characteristics even for the same patient, limiting the clinical applicability of this model.

Key words
Drain flow, breakpoint, kinetic model

Introduction

In peritoneal dialysis (PD), large fill volumes present a risk of increased intraperitoneal pressure, potentially leading to respiratory complications (1) and impaired ultrafiltration (UF) (2,3). Small fill volumes result in inadequate solute transport because the peritoneal membrane surface area in physical contact with dialysate decreases (4). At the end of an exchange, the time spent draining the peritoneal cavity is often longer and more variable than that needed to fill the cavity, and drain time therefore occupies a larger portion of the total dialysis time (5,6). In automated PD (APD), the fill and drain periods combined were shown to account for 35% – 55% of the total dialysis time (7), which inevitably results in loss of dialysis efficiency.

Studies that characterized the drain in either the supine or the sitting position revealed a common biphasic flow profile: a fast, relatively constant flow period, followed by a sudden transition to a slow-flow period (5,6). As a result, new therapy optimization methods such as “breakpoint” APD were devised. In “breakpoint” APD, the fast-to-slow flow transition point was determined for each patient so that the drain period could be stopped, thereby preventing lengthy drain times that contribute minimally to dialysis adequacy (6,8–10).

The attempts to optimize PD therapies have not yet been paralleled by the development of predictive kinetic models, despite numerous references concerning a need for them (1,5,6,11). Current models rely on simplified...
calculations to determine an “effective” dwell time, which is generally approximated as the sum of 50% of estimated fill time, estimated dwell time, and 50% of estimated drain time (11), or alternatively, the sum of estimated fill time and estimated dwell time, assuming negligible transport during the entire drain period (12). The drain time is generally calculated based on an exponentially decaying volume profile assumed to be identical across all exchanges. Inevitably, this assumption neglects the properties of complicated drain profiles.

Here, we present an improved mathematical description of the biphasic drain profile by incorporating patient- and device-specific drain parameters. Integrating these new drain equations with the three-pore model of peritoneal transport (13,14), we show that kinetic model predictions can be tailored for individual patients and their equipment—for example, bed height, catheter type, and so on. In addition, we show that the residual dialysate volumes at the end of each exchange can be estimated to alert physicians in advance and to prevent undesired problems of increased intraperitoneal volume (IPV) or overfill before therapy even starts.

Methods

Drain model and parameters
We investigated the effects of patient-specific parameters for a fixed set of device parameters. The chosen fixed values imply that a minimum of 85% of the fill volume has to be drained (for example, 0.85 × 2.0 L = 1.7 L) and a minimum drain flow rate of 75 mL/min has to be achieved before a given drain period ends. The patient-specific parameters were the maximum drain flow rate ($Q_{\text{MAX}}$) and the transition volume ($\Psi$), as illustrated in Figure 1. Three sets of values were studied as representative of fast (400 mL $Q_{\text{MAX}}$/85% $\Psi$—in short, 400/85%), moderate (200/75%), and poor drain (100/65%), using the equation

$$V_D(t) = (V_{D0} - Q_{\text{MAX}} \cdot t \cdot \Phi) + (V_{D0} \cdot e^{-\alpha t})(1 - \Phi),$$  

[1]

in which $V_{D0}$ is the peritoneal volume at the start of the drain, $\alpha$ is the exponential decay constant during the slow drain period, and $\Phi$ is the unit step function with respect to the flow transition. Figure 1 shows samples of modeled drain curves.

Integration of the drain model equations with the three-pore model
A modified three-pore model of peritoneal transport based on PD Adequest (15) was used to calculate water and solute transport across the peritoneal membrane. This model differed from PD Adequest 2.0 in allowing the flexibility to change the structure of the equations. For simplicity, the serum solute concentrations were assumed to be independent of time. Also, the three-pore model equations were solved numerically using the MATLAB software program (version 7.7.0.471: The Mathworks, Natick, MA, U.S.A.). A brief, informal verification of this model was previously reported (14).

The new drain model equations were integrated with the three-pore transport equations to calculate the drain time for a given set of patient, therapy, and

![Figure 1](image-url)
drain parameters. This approach allowed for simultaneous calculations of solute transport with UF (as a function of time) and of drain time with residual volume (as a function of exchange). Figure 2 describes the primary steps followed to perform these calculations.

**Patient data**

“Typical patient” parameters were derived from data submitted to Baxter Healthcare Renal Division by U.S. and Canadian centers participating in the TARGET [Treatment Adequacy Review for Gaining Enhanced Therapy (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.)] national adequacy initiative. The data were first grouped into the four peritoneal equilibration test (PET) categories (that is, high to low) according to 4-hour dialysate-to-plasma (D/P) creatinine ratios (16). Relevant kinetic transport parameters such as mass transfer area coefficients [MTACs (mL/min)] for solutes, the UF coefficient [LPA (mL min⁻¹ mmHg⁻¹)], and transport surface area [A0/dX (cm)] were estimated using PD Adequest 2.0 (15). As a last step, four “typical patients” were created, each representing a transport category. Table I shows the characteristics and relevant kinetic parameters for these typical patients.

**Results**

To demonstrate the benefits of the improved drain model, all simulations were performed for 9-hour, 5-exchange therapy with 2-L fill volumes of 2.27% glucose PD solution. This therapy regimen, with its multiple short exchanges, was chosen because it demonstrates the potential gains in solute and fluid removal and the risks of rising IPV when drain is poor.

The typical patients in the four PET groups were simulated individually. A starting residual volume of 150 mL was assumed for all patients. An initial assessment of the results indicated that the resulting residual volumes and drain times were similar for all patients. Hence, predictions relating to solute and fluid removal were averaged across the four patient groups. Table II summarizes the results. “Peak drain time” and “peak intraperitoneal volume” indicate the maximum values reached during the 5 exchanges and among the four PET groups. “Net UF,” “weekly urea Kt/V,” and “weekly creatinine clearance” are given as the sum of all exchanges and the average of all patients.

**Effect on drain time**

Figure 3 shows that $Q_{\text{MAX}}$ is more effective than $\Psi$ in determining the drain time. Fast drain flows (that is, 400 mL/min) produced shorter drain times than did slow drain flows (that is, 100 mL/min) with a maximum difference of 15.1 minutes (100/85% vs. 400/85%, $Q_{\text{MAX}}/\Psi$) regardless of the duration of the maximum drain flow (that is, the value of $\Psi$). Consequently, the effect of $\Psi$ was less, with a difference of up to only 1.8 minutes (200/65% vs. 200/85%). In addition, simulations indicated that the effect of $\Psi$ was more pronounced when the flow rate was high: 1.6 minutes (400/65% – 400/85%) compared with 0.5 minutes (100/65% – 100/85%). However, these differences in drain time relating to $\Psi$ are probably not clinically significant.

**Effect on net UF and weekly urea Kt/V**

The effects of $Q_{\text{MAX}}$ and $\Psi$ were assessed separately by fixing one and varying the other. Figure 4(A) shows increasing values of UF and weekly urea Kt/V corresponding to shorter drain periods for $Q_{\text{MAX}}$ (100, 200, 400 mL) and a $\Psi$ of 75%. A reduction of 14 minutes in drain time per exchange—that is, a total of 70 minutes’ drain time (14 min × 5 exchanges) converted to dwell time—resulted in approximately 14% more UF and 9% more weekly urea Kt/V (400/75% vs. 100/75%). As shown in Figure 4(B), the gain in adequacy with a prolonged transition point (that is, greater $\Psi$) was less. As a result of 1.8 minutes’ reduction in drain time per exchange (100/85% vs. 100/65%), the UF increased by about 4%, and the Kt/V, by about 2%.
Optimizing the Drain Phase in Gravity-Based PD

Residual volume, infused volume, and UF are the contributing factors to the total peritoneal volume. During short exchanges, multiple incomplete drains may result in an accumulation of fluid volume (that is, increased IPV or overfill), causing patient discomfort and impaired fluid removal. Figure 5(A) demonstrates the possibility of a large peritoneal volume if the maximum drain flow is limited (that is, more than 3.2 L when \( Q_{\text{MAX}} = 100 \text{ mL/min} \)). As the drain flow rate improves (that is, to 200 mL/min and 400 mL/min), the peak peritoneal volume declines to as low as approximately 2.4 L. In addition, it is also evident that, if the drain flow is limited, the prolonged transition period (that is, large values of \( \Psi \)) ensures drainage of a substantial volume, preventing accumulation of peritoneal fluid. To be specific, the case of 100/65% resulted in 3243 mL of IPV,

### TABLE I
Kinetic parameters estimated by PD Adequest 2.0\(^a\) according to patient transport as determined by a peritoneal equilibration test

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value by transport category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( H )</td>
</tr>
<tr>
<td>D/P creatinine (at 4 h)</td>
<td>0.86</td>
</tr>
<tr>
<td>D/D( O ) glucose (at 4 h)</td>
<td>0.25</td>
</tr>
<tr>
<td>Glucose MTAC (mL/min)</td>
<td>16.34</td>
</tr>
<tr>
<td>Creatinine MTAC (mL/min)</td>
<td>19.15</td>
</tr>
<tr>
<td>LPA (mL min(^{-1}) mmHg(^{-1}))</td>
<td>0.0575</td>
</tr>
<tr>
<td>( A_0/dX ) (cm)</td>
<td>40,398</td>
</tr>
</tbody>
</table>

\( a \) Baxter Healthcare Corporation, McGaw Park, IL, U.S.A.  
\( H = \) high; \( HA = \) high average; \( LA = \) low average; \( L = \) low; \( D/P = \) dialysate-to-plasma ratio; \( D/D_0 = \) end-to-initial dialysate concentration; \( MTAC = \) mass transfer-area coefficient; \( LPA = \) ultrafiltration coefficient; \( A_0/dX = \) transport surface area.

### TABLE II
Overall summary of all considered cases

<table>
<thead>
<tr>
<th>( Q_{\text{MAX}} ) (( \Psi )) [mL/min (%)]</th>
<th>Peak drain time(^a) (min)</th>
<th>Peak IP volume(^a) (mL)</th>
<th>Net UF(^b) (mL)</th>
<th>Weekly urea Kt/V(^c)</th>
<th>Weekly CCr(^c) (L/1.73 m(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 (65)</td>
<td>22.1</td>
<td>3243</td>
<td>724</td>
<td>1.18</td>
<td>30.3</td>
</tr>
<tr>
<td>100 (75)</td>
<td>22.4</td>
<td>2849</td>
<td>744</td>
<td>1.19</td>
<td>30.5</td>
</tr>
<tr>
<td>100 (85)</td>
<td>22.6</td>
<td>2538</td>
<td>767</td>
<td>1.21</td>
<td>30.7</td>
</tr>
<tr>
<td>200 (65)</td>
<td>13.5</td>
<td>2769</td>
<td>800</td>
<td>1.25</td>
<td>32.4</td>
</tr>
<tr>
<td>200 (75)</td>
<td>12.5</td>
<td>2673</td>
<td>819</td>
<td>1.27</td>
<td>32.8</td>
</tr>
<tr>
<td>200 (85)</td>
<td>11.7</td>
<td>2524</td>
<td>841</td>
<td>1.29</td>
<td>33.5</td>
</tr>
<tr>
<td>400 (65)</td>
<td>9.1</td>
<td>2429</td>
<td>847</td>
<td>1.30</td>
<td>33.6</td>
</tr>
<tr>
<td>400 (75)</td>
<td>8.4</td>
<td>2393</td>
<td>856</td>
<td>1.31</td>
<td>33.9</td>
</tr>
<tr>
<td>400 (85)</td>
<td>7.5</td>
<td>2355</td>
<td>856</td>
<td>1.31</td>
<td>33.9</td>
</tr>
</tbody>
</table>

\( a \) The maximum value reached considering all patient groups and exchanges.  
\( b \) The average (of four patient groups) total (of all exchanges) ultrafiltration.  
\( c \) The average value over all patient groups.  
\( Q_{\text{MAX}} = \) maximum drain flow; \( IP = \) intraperitoneal; \( UF = \) ultrafiltration; \( CCr = \) creatinine clearance.

**Effect on peritoneal volume**

Residual volume, infused volume, and UF are the contributing factors to the total peritoneal volume. During short exchanges, multiple incomplete drains may result in an accumulation of fluid volume (that is, increased IPV or overfill), causing patient discomfort and impaired fluid removal. Figure 5(A) demonstrates the possibility of a large peritoneal volume if the maximum drain flow is limited (that is, more than 3.2 L when \( Q_{\text{MAX}} = 100 \text{ mL/min} \)). As the drain flow rate improves (that is, to 200 mL/min and 400 mL/min), the peak peritoneal volume declines to as low as approximately 2.4 L. In addition, it is also evident that, if the drain flow is limited, the prolonged transition period (that is, large values of \( \Psi \)) ensures drainage of a substantial volume, preventing accumulation of peritoneal fluid. To be specific, the case of 100/65% resulted in 3243 mL of IPV,
and that of 100/85%, 2538 mL. By contrast, if the drain flow rate is fast, then the transition point is less critical.

Similarly, Figure 5(B) shows estimated residual volume at the beginning of each of the 5 simulated exchanges. A volume of 150 mL was assumed at the start of the first exchange. In later exchanges, the residual volume accumulates more or less depending on the maximum drain flow rate. At the slowest maximum drain flow of 100 mL/min, the residual volume quickly rises to about 620 mL at the end of exchange 3 and stays relatively constant thereafter in exchanges 4 and 5.

Discussion
The kinetics of peritoneal transport during the drain period are complex and still open to continued research for improving efficiency and patient comfort. The concept of “breakpoint APD” recently offered by the Serena cycler (Gambro Lundia AB, Lund, Sweden) and in related studies (9,10) are the latest efforts to optimize drain time on a patient-by-patient basis. Such device improvements have not been accompanied by improvements in the kinetic models. Current models largely ignore clinically observed drain characteristics and do not offer time-dependent residual volume predictions. The new model presented here aims to bridge that gap by adapting a more realistic description of drain period and providing predictions of drain time and maximum IPV.

The results presented here are consistent with previous clinical measurements that studied the effect of shortened drain times on small-solute clearances. Brandes et al. studied 38 patients and suggested that urea clearances increased by up to 10% by a shortening of the drain time to include only the fast-drain period (5). Durand reported unpublished data from a crossover randomized trial with 12 patients undergoing either breakpoint APD or continuous cycling PD. With breakpoint APD, drain times were reported to decrease by 55% on average, resulting in urea clearances that increased by about 8% (8). The present drain model predicts a 63% reduction in drain time between the 400/75% and 100/75% cases, resulting in a 9% increase in weekly urea Kt/V.

A risk of short drain periods is the accumulation of residual volume over multiple exchanges, leading to large IPVs and increased intraperitoneal pressure. Unfortunately, available cycler systems do not have the capability to continuously monitor peritoneal volume or pressure, potentially causing patient discomfort and impaired UF. The present drain model may be useful in predicting and preventing such instances, as shown in Figure 5(B), which clearly demonstrated the benefit of fast drain flow: the residual volume increased only minimally through the 5 exchanges when $Q_{\text{MAX}}$ was 400 mL/min. The present analysis reaffirms the importance of fast drain flows previously recognized by Amici and Tomaseth, who suggested modifications of disposable systems, namely catheter lumen size, to maximize drain flows (6).

A major limitation of the present drain model is its dependence on parameters ($Q_{\text{MAX}}$ and $\Psi$) that are highly variable. Mechanical problems such as displaced catheters and obstructed flow paths cause variability in drain characteristics even for the same patient, limiting
the clinical applicability of the model. Upon measuring the transition volume in 7 patients, Brandes et al. (5) determined that the coefficient of variation ranges between 7% and 78% (mean: 42%). In another study with 10 patients, the intra-individual coefficient of variation was 7% for $Q_{\text{MAX}}$ and 19% for transition volume (6).

Furthermore, estimations of drain time and residual volume are also directly related to device-specific parameters that were not the focus of this study. To that end, our model can be used as a valuable tool to conduct extended studies that include various device drain parameters. To that end, our model can be used as a valuable tool to conduct extended studies that include various device drain parameters. Finally, although gravity-based systems are the candidates intended to benefit from the use of this kinetic model, pump-driven cycler systems may also benefit as long as the resulting drain profiles are similar to those described here.

Conclusions
We presented a new drain model capable of performing customized simulations for individual PD patients. New drain equations describing biphasic drain profiles were integrated with modified three-pore model equations to provide predictions that parallel breakpoint APD. Good agreement in solute clearances between the model results and previously reported clinical measurements was observed. Estimation of residual volumes over multiple exchanges was also presented as a new feature to alert clinicians in advance of the potential for problems of increased IPV or overfill.

References
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