Peritoneal Transport Characteristics with Glucose Polymer–Based Dialysis Fluid in Children

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Abstract. Scarce data are available on the use of glucose polymer–based dialysate in children. The effects of glucose polymer–based dialysate on peritoneal fluid kinetics and solute transport were studied in pediatric patients who were on chronic peritoneal dialysis, and a comparison was made with previously published results in adult patients. In nine children, two peritoneal equilibration tests were performed using 3.86% glucose and 7.5% icodextrin as a test solution. Dextran 70 was added as a volume marker to calculate fluid kinetics. Serum and dialysate samples were taken for determination of urea, creatinine, and sodium. After calculation of the initial transcapillary ultrafiltration (TCUF) rate, it was possible to calculate the contribution of aquaporin-mediated (AQP-mediated) water transport to ultrafiltration for icodextrin and 3.86% glucose and the part of LpS (the product of the peritoneal surface area and the hydraulic permeability) caused by AQP. In children, the transport parameters were similar for the two solutions, except for TCUF, which was lower for icodextrin (0.9 ml/min per 1.73 m²) as compared with 3.86% glucose (4 ml/min per 1.73 m²). Transport parameters were similar in children and adults for glucose, but with icodextrin, TCUF and marker clearance were significantly lower in children. AQP-mediated water flow was 83 versus 50% with glucose (child versus adult; P < 0.01) and 18 versus 7% with icodextrin (P < 0.01). This data indicate that transport parameters in children using icodextrin are similar to glucose except for TCUF. Differences are explained by the absence of crystalloid osmosis and that TCUF was determined after a 4-h dwell. Comparison of transport parameters and peritoneal membrane characteristics between children and adults reveal that there seem to be differences in the amount and functionality of AQP. However, there are no differences in clinical efficacy of this transport pathway because the absolute flow through the AQP is identical in both groups using 3.86% glucose.

Icodextrin contains glucose polymers as osmotic agent instead of glucose in the conventional peritoneal dialysis (PD) solutions. The effectiveness of icodextrin as a colloid osmotic agent has been very well established in adult patients (1–4). The solution is especially indicated in situations in which a high exposure to glucose should be avoided, such as in patients with exchanges with a long dwell time and in patients with ultrafiltration failure (5).

Until now, very little has been published about the use of glucose polymer–based dialysate in children. It was demonstrated that 7.5% icodextrin is capable of inducing sustained net ultrafiltration during long-term dwell in children and that the metabolism of icodextrin is similar compared with adults (6). The aim of the present study was to compare a 7.5% icodextrin-based dialysis solution with a 3.86% glucose solution with regard to peritoneal fluid kinetics and solute transport in a pediatric PD population. In addition, the results obtained in children were compared with results obtained in adult patients, which were previously published (5). A brief summary of the study in adult patients is given in the Materials and Methods section.

Materials and Methods

Pediatric Study

The patient group consisted of four girls and five boys, with a median age of 4.9 yr (range 1.6 to 10.9). The mean duration of nightly intermittent PD treatment was 26.2 mo (range 5.6 to 122.3). In each patient, two peritoneal equilibration tests were performed, using a different test solution for each peritoneal equilibration test. The solutions used were a 7.5% icodextrin solution (Extraneal; Baxter B.V., Utrecht, The Netherlands) and a 3.86% glucose solution (Dianeal; Baxter B.V.). All peritoneal equilibration tests were performed as described previously by Reddingius et al. (7). An intraperitoneal volume of 1200 ml/m² body surface area (BSA) was used in all tests. Dextran 70 (Macrodex NPBI; Emmercompascuum, The Netherlands) was added to the dialysate as a volume marker to calculate fluid kinetics. A serum sample was taken at the start of the study. Dialysis fluid was sampled before inflow; after 5, 30, 60, 120, and 180 min, and at the end of the test at 240 min. These samples were used for
measurement of dextran, glucose, creatinine, urea, and sodium. All peritoneal equilibration tests were performed at least 2 mo after any peritonitis episode. None of the patients had ultrafiltration failure.

Calculations

For the calculations, the principles of Nolph et al. (8) were applied, adapted by Krediet et al. (9). Transport parameters were calculated according to previously described formulas (7). In brief, transcapillary ultrafiltration (TCUF) was calculated from the dilution of the volume marker by subtracting the initial theoretical intraperitoneal volume (IPV) from the theoretical IPV. The theoretical IPV is the IPV in the absence of marker clearance and sampling, in which marker clearance equals the disappearance of fluid from the peritoneal cavity. The initial TCUF for the glucose solution and the icodextrin solution, meaning the TCUF during the first minute of a dwell (TCUF0–1min), were calculated according to the Lineweaver-Burk plot for the glucose-based solution and by linear regression for the icodextrin-based one (9). The TCUF rate (TCUFR) was obtained by dividing TCUF by the dwell time.

The change in IPV (Δ/IPV) was obtained by calculating the dilution of the volume marker after correction for incomplete recovery. The net ultrafiltration rate was obtained by dividing Δ/IPV by the dwell time. Marker clearance was defined as the difference between the amount of dextran instilled and the total amount recovered, divided by the product of dwell time and the mean dextran concentration. Marker clearance rate was calculated by dividing marker clearance by the dwell time. It was assumed that marker clearance is a linear process. The mass transfer area coefficient (MTAC) is the maximal theoretical diffusive clearance of a solute at time 0, before transport has actually started. The MTAC of urea and creatinine were calculated according to the Waniewski model (10), in which a correction for plasma water concentrations was used (5). The dialysate/plasma ratio of sodium was used to analyze the sieving of sodium during the first hour of the dwell for the 3.86% glucose and the 7.5% icodextrin peritoneal equilibration test.

Glucose induces ultrafiltration by increasing the crystalloid osmotic pressure in the peritoneal cavity, which induces fluid transport across the small interendothelial pores and also through the ultrasmall transcellular pores (aquaporins [AQP]). The effect of glucose on the large pores can be neglected because of their very small number and large pore size. The colloid osmotic pressure induced by icodextrin almost exclusively exerts its effect across the small pores. This suggests that the ultrafiltration coefficient (UFC) of the transcellular pores (UFCaqp) can be calculated from the difference between the total UFC (UFCtot) of the peritoneum, as calculated with 3.86% glucose, and the UFC of the small pores (UFCsp), as calculated with icodextrin: UFCaqp = UFCtot - UFCsp.

The UFC was calculated as described previously by Ho-Dac-Pannekeet et al. (5). A description of the calculations is given in Appendix A. The UFC is the product of the hydraulic permeability of the peritoneum (Lp) and the surface area (S). After calculation of the contribution of the transcellular pores to UFCtot, it is possible to calculate the fractional transcellular UFC, meaning the part of LpS that is caused by AQP. Subsequently, it is possible to calculate the fractional osmotic force exerted across the AQP. Calculations of the fractional transcellular UFC and the fractional osmotic force across AQP were performed using the formulas described by Krediet et al. (11). A description of the calculations is given in Appendix B. Calculations of the fractional transcellular UFC and the fractional osmotic force across AQP were also performed for the adult patient group.

Statistical Analyses

Results are given as mean and median values, SD, and ranges. For comparison of the results of the two solutions within the pediatric group, a paired t test was performed. Differences between children and adults were tested with the Mann-Whitney nonparametric rank test. Correlations were tested using the Spearman rank correlation analysis.

Study in Adult Patients

Ho-Dac-Pannekeet et al. (5) previously published a study about peritoneal transport characteristics with icodextrin performed in adults. Results obtained in this study were used (with permission of Ho-Dac-Pannekeet et al.) to make a comparison with the results of our study, which was performed in children. The patient group of Ho-Dac-Pannekeet et al. consisted of 10 stable patients, with a median age of 48 yr (range 23 to 64). The mean duration of continuous ambulatory PD treatment was 28 mo (range 3 to 92). In each patient, three peritoneal equilibration tests were performed, using a different test solution for each peritoneal equilibration test. The three test solutions consisted of 1.36% glucose, 3.86% glucose, and 7.5% icodextrin. The peritoneal equilibration test was standardized in the same way as in the pediatric study. Dialysate samples were taken at 10, 20, 30, 60, 120, 180, and 240 min. Blood samples were drawn at the beginning and at the end of the period. In the glucose dwells, dextran 70 was added as a volume marker, whereas in the icodextrin dwell, dextrin itself was used for that purpose. Calculations of transport parameters were made on the basis of the same principles as those used in the pediatric study. Calculations of the fractional transcellular UFC and the fractional osmotic force across AQP were not part of the adult study.

Results

The medians and ranges of fluid and solute transport parameters of children and adults obtained with 3.86% glucose and 7.5% icodextrin are given in Table 1. All data are expressed per 1.73 m² BSA.

Fluid Transport

The TCUFR with icodextrin was significantly lower compared with the TCUFR obtained with glucose 3.86% in our study group (P < 0.001). The marker clearance rate and net ultrafiltration rate were similar for the two solutions. Fluid profiles for 3.86% glucose and 7.5% icodextrin are given in Figure 1.

Transport parameters for fluid transport using 3.86% glucose were similar for children and adults. For 7.5% icodextrin, the TCUFR in children was significantly lower than in adults (P < 0.01). Also, the marker clearance rate was significantly lower (P < 0.02). The net ultrafiltration rate, however, was not significantly different from adult patients (P = 0.27). Consequently, the Δ/IPV was also similar for children and adults (P = 0.36).

Solute Transport

The transport of the low molecular weight solutes creatinine and urea in children was similar for both solutions. A correlation was found between net ultrafiltration rate and MTACcreat
(r = 0.69, P < 0.04) in the icodextrin dwell, which was not found in the glucose dwell. No relation was found between MTACcreat and age or time on PD.

No significant differences were found between children and adults. A marked dip in dialysate/plasma ratio of sodium was found in the initial phase of the 3.86% glucose dwell, which was absent in the dwell with the icodextrin solution (Figure 2).

**Contribution of the AQP to the Peritoneal UFC**

The mean UFCtot calculated with 3.86% glucose solutions was 0.12 ± 0.002 ml/min per mmHg. The AQP contributed 83.4 ± 6.4% to this value. In the adult patient group, the AQP contributed 50.5 ± 12% to a mean total UFC of 0.18 ± 0.04 ml/min per mmHg (P < 0.001). The mean UFCapp in children was 0.10 ± 0.02 ml/min per mmHg and in adults was 0.12 ± 0.10 ml/min per mmHg (P = 0.64).

In both children and adults, there was no significant correlation between the UFCapp and duration of PD treatment (children, r = 0.58, NS; adults, r = −0.56, NS) or age (children, r = −0.12, NS; adults, r = 0.19, NS).

The mean fractional transcellular UFC calculated using 3.86% glucose was 0.15 ± 0.06 ml/min per mmHg in children and 0.05 ± 0.04 ml/min per mmHg in adults (P < 0.001), which suggests that the AQP are responsible for, respectively, 15 and 5% of the LpS. The fractional transcellular UFC in children showed a significant negative correlation with the duration of PD treatment (r = −0.67, P < 0.05) but showed no correlation with age (r = 0.13, NS). In adults, there was no significant correlation with duration of treatment or age. The mean fractional osmotic force exerted across AQP using 7.5% icodextrin was 0.18 ± 0.07 ml/min per mmHg in children and 0.07 ± 0.06 ml/min per mmHg in adults (P < 0.001), suggesting that, respectively, 18 and 7% of the water flow occurs through the AQP during a dwell with icodextrin.

**Discussion**

During the past 10 to 15 years, there has been a growing recognition of the need for the development of dialysis solutions, which are more biocompatible than the standard commercially available glucose-based solutions. Icodextrin is

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**Table 1. Comparison of fluid and solute transport parameters in children and adults during a 4-hour dwell with 3.86% glucose and 7.5% icodextrin**

<table>
<thead>
<tr>
<th></th>
<th>3.86% Glucose</th>
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<th>7.5% Icodextrin</th>
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<td></td>
<td>Median</td>
<td>Range</td>
<td>Median</td>
<td>Range</td>
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<td>MTACurea (ml/min per 1.73 m²)</td>
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<td>14.1</td>
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<td>MCR (ml/min per 1.73 m²)</td>
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<td>0–2.0</td>
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<tr>
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<td>0.61</td>
<td>0.41–0.63</td>
<td>0.61</td>
<td>0.41–0.63</td>
</tr>
</tbody>
</table>

a Adult data are obtained from a previously published study (5). MTACurea, mass transfer area coefficient of urea; MTACcreat, mass transfer area coefficient of creatinine; TCUFR, transcapillary ultrafiltration rate; MCR, marker clearance rate; NUFR, net ultrafiltration rate; Δ-IPV, intraperitoneal volume; D/P creatinine, dialysate/plasma ratio creatinine. Statistical analysis was performed with Mann-Whitney nonparametric test.

b P < 0.01 3.86% glucose versus icodextrin.

c P < 0.01 children versus adults.
d P = 0.02 children versus adults.
mainly characterized by the absence of glucose. Instead, long-chain glucose polymers that are responsible for ultrafiltration are present. Ultrafiltration occurs according to the principle of colloid osmosis. The absorption of glucose polymers is limited, which gives rise to a prolonged persistence of the colloid osmotic gradient. The use of icodextrin has been studied extensively in adult patients. It has been shown that the daily use of icodextrin is safe, is generally well tolerated, and can replace the daily overnight use of hyperosmotic glucose solutions (2,3). Posthuma et al. (12) demonstrated that icodextrin could also be very well used in an automated PD regimen to enhance ultrafiltration during the long daytime dwell. The use of icodextrin is associated with a significant increase in serum concentrations of icodextrin metabolites, which, however, has not been associated with clinical adverse events (3,12).

Until now, very little has been published about the use of glucose polymer–based dialysate in children. In a previous study, it was demonstrated that the addition of a daytime icodextrin dwell to a nightly intermittent PD regimen in children results in an increase of both ultrafiltration and adequacy of dialysis and that the metabolism of icodextrin occurs at a similar rate compared with that in adults (6). However, there are no data available with respect to the effect of icodextrin on the peritoneal fluid kinetics and solute transport. The present study describes the behavior of icodextrin in the peritoneal equilibration test in children and compares the results with previously published data obtained in adults (5).

The values of fluid transport parameters with 3.86% glucose found in the present study were within the ranges of those found in a previous study performed in pediatric patients (13). The TCUF with icodextrin was different from that obtained with 3.86% glucose. This can be explained by the fact that ultrafiltration was measured after a 4-h dwell time; 3.86% glucose gives rise to a rapid ultrafiltration in the beginning of the dwell, which diminishes in time because of dissipation of the osmotic gradient, whereas icodextrin gives rise to a slow but sustained ultrafiltration during a prolonged period because of the limited absorption of the glucose polymers (14).

Icodextrin in Children

Fluid kinetics for 3.86% glucose are similar in children and adults. This is in accordance with a previous study that showed that fluid kinetics in different age groups are comparable if corrected for BSA (13,15). On the basis of these observations, it is expected that fluid kinetics for icodextrin are also similar between the different patient groups. Results previously published by Boer et al. (6) already showed that net ultrafiltration obtained with icodextrin is similar for children and adults after a long-term dwell. However, our results are not fully in accordance with the expectations. Net ultrafiltration is similar for both groups, but TCUF and marker clearance are significantly lower in children. Rippe et al. (16) demonstrated an advantage of using icodextrin in patients with an increased effective vascular area, because icodextrin will produce an increased
ultrafiltration rate when the vascular surface area is increased. The difference in transport parameters using icodextrin between adults and children thus may be explained by a difference in effective vascular surface area. Although a statistical difference in treatment period is not present, there seems to be an overrepresentation of long-term dialysis in the adult patient group. Long-term dialysis is associated with neoangiogenesis in the peritoneum (17–19), which can explain an increase in the effective peritoneal surface area. However, there was no significant difference in MTAC<sub>crea</sub>, which indicates that there is no difference in the effective peritoneal surface area. Because of the small sample of patients, we also have to realize that statistical comparison is easily bothered by chance observations. On the basis of these results, it therefore is not possible to give an explanation for the differences seen in marker clearance and TCUF. As the net ultrafiltration is similar for children and adults, it is most likely that in clinical practice, there are no differences to be expected.

### Osmotic Effect of Icodextrin on the Peritoneal Membrane

On the basis of the three-pore model of peritoneal transport suggested by Rippe et al. (20,21), the AQP play a minor role in TCUF when using icodextrin but a major role in TCUF when using 3.86% glucose. This is demonstrated by the significant difference in contribution of AQP using 3.86% glucose and icodextrin in both children and adults. This difference can be visualized by analyzing the difference in sodium sieving during the first hour of a dwell. As the water flow through the AQP will exceed the flow of water and small solutes through the small pores using 3.86% glucose, it will cause a fall in the sodium dialysate concentration. Using icodextrin, there will be no fall in sodium dialysate concentration. In the present study, this different role of the AQP is very well visualized. Using 3.86% glucose, the dialysate/plasma ratio of sodium decreased, whereas using icodextrin, the dialysate/plasma ratio did not change. The sodium dialysate/plasma curves are similar for children and adults, suggesting a similar role for AQP in both children and adults. The theory that transport through the small pores is of great importance for the action of 7.5% icodextrin is supported by the fact that in both children and adults, a relation was found between the MTAC<sub>crea</sub> and TCUF, whereas this relation was not found using 3.86% glucose. However, our calculated data show that a significant difference in the water flow through the AQP in both glucose- and glucose polymer–induced ultrafiltration is present between children and adults. This difference diminished as we calculated the absolute amount of the contribution of the AQP-mediated water flow to the UFC<sub>int</sub> (see below).

### Functional Characterization of the Peritoneal Membrane

The UFC is the product of the peritoneal surface area (S) and its hydraulic permeability (L<sub>p</sub>). In children, 15% of the L<sub>p</sub>S is determined by AQP versus 5% in adults. This suggests that the children in our study group have a 3 times higher amount of functional AQP as compared with the individuals in the adult study group. Lai et al. (22) demonstrated that transcription and biosynthesis of AQP-1 in human peritoneal mesothelial cells is significantly increased upon exposure to glucose in vitro. This upregulation of AQP-1 upon exposure to glucose is time and dose dependent. They also demonstrated an absence of AQP-1 in peritoneal lining denuded of mesothelial cells and speculated that long-term PD might lead to decreased expression of AQP-1 on the peritoneal lining because of denudation of mesothelium. The negative correlation between the fractional transcellular UFC and treatment period in children indeed suggests a decreased expression of AQP in long-term PD. The absence of a relation between fractional transcellular UFC and age suggests that the differences observed in AQP function are not related to age groups but are determined by other factors as duration of treatment and glucose exposure. It is also important to realize that the age range of the pediatric patients was small, as was the number of our observations. The current method makes it impossible to compare the (cumulative) glucose exposure between both study groups. A recent study showed that AQP can be inactivated while they remain on the cell surface (23). This suggests that inactivation of AQP can be accomplished through means other than degradation of the water channels. It is not yet clear which mechanism is responsible for the inhibition of the AQP, but this might be an explanation for the differences found between children and adults. It also should be considered that the differences in the amount of functional AQP are the result of a lower small pore area in children. As the children are smaller, they do have lower actual small pore areas. However, by adjusting both the dwell volume and the transport parameters to the BSA, such differences between adults and children are no longer expected. This is confirmed by the fact that the MTAC for small solutes are the same in children and adults, which means that the functional size of the small pore area will not be essentially different.

Next to the observation of differences in the amount of functional AQP, the AQP system seems also more efficient in the pediatric study group, because 83% of glucose-induced ultrafiltration takes place through these AQP compared with 50% in adult patients. The effectiveness of the system can be explained by the fact that L<sub>p</sub>S is a physical quantity that is defined on the basis of hydrostatic pressure (expressed as ml/min per mmHg). The resistance caused by the ultrasmall AQP is much larger than the resistance caused by the small pores. The reason that such a great part of the ultrafiltration occurs through the AQP is because PD is based on a crystalloid osmotic pressure instead of a hydrostatic pressure.

Further calculations show that the total amount of water, transported through the AQP during a glucose dwell (UFC<sub>aqp</sub>), is the same for children and adults. This suggests—although it seems that there are differences in the AQP between both study groups—that the effect of the 3.86% glucose solution on the AQP is exactly the same.

It can be concluded that fluid and solute parameters are similar for glucose polymer–based dialysate and 3.86% glucose in children, except for the TCUF. This can be explained by the absence of crystalloid osmosis and that TCUF was measured after a 4-h dwell.
Comparison of transport parameters and peritoneal membrane characteristics reveals that there seem to be differences between the peritoneal transport pathways in children and adults, but these differences do not interfere with the clinical efficacy of the AQP because the absolute water flow through the AQP is identical in both groups using 3.86% glucose. Further studies are needed to explore the differences between children and adults in the amount and the functionality of the AQP and the small pores.

Appendix A

The UFC can be calculated from the following equation:

$$\text{TCUFR} = \text{UFC} \cdot \left[ \Delta P - \sigma \Delta \Pi + \sigma \Delta O \right]$$

(1)

in which TCUFR$_{0-1 \text{ min}}$ is the maximal TCUFR obtained during the first minute of an exchange, $\Delta P$ is the hydrostatic pressure gradient, $\Delta \Pi$ is the colloid osmotic pressure gradient, and $\Delta O$ is the crystalloid osmotic pressure gradient. $\Sigma$ is the reflection coefficient that can range from 1.0 (ideal semipermeable membrane) to 0 (no osmotic effect). It was assumed that $\Delta P$, during peritoneal equilibration tests, has a constant value of 9 mmHg, as the capillary pressure is ~17 mmHg (24) and the intraperitoneal pressure is 8 mmHg while resting (25). According to Van ‘t Hoff’s law, every mOsm/L exerts an osmotic pressure of 19.3 mmHg in the case of an ideal semipermeable membrane. This suggests that the osmotic pressure generated by an osmotic gradient is given by [osmolality · $\sigma$ · 19.3]. The reflection coefficient of albumin is generally considered to approach 1.0. The reflection coefficient of icodextrin was calculated using the relation between reflection coefficients of low molecular weight solutes (urea, urate, glucose, and creatinine) and albumin and their molecular weights. The molecular weight of icodextrin (16,800 Da) resulted in a value of 0.767 for the reflection coefficient. The capillary colloid osmotic pressure ($\Pi_c$) was assumed to be determined by the serum albumin concentration for 75% (26). To this value, 0.04 was added because of the Gibbs-Donnan equilibrium (26):

$$\Pi_c = \left[ \frac{\text{SA} \cdot 1000}{16,800} \right] \cdot 0.4 + 3 \cdot 0.767 \cdot 19.3 = 0.38 \text{ SA} + 7.72 \text{ mm Hg}$$

(2)

In this equation, SA represents serum albumin (g/L), 68,000 is the molecular weight of albumin, and the factor 1000 converts osmoles to mosmoles. The osmotic pressure within the peritoneal cavity ($\Pi_{pc}$), exerted by icodextrin, equals

$$\Pi_{pc} = \left[ \frac{\text{DIC} \cdot 1000}{16,800} \right] \cdot 0.767 \cdot 19.3 = 0.88 \text{DIC}$$

(3)

in which DIC is the dialysate icodextrin concentration in g/L, 16,800 is the molecular weight of icodextrin, and 0.767 is the reflection coefficient. Therefore, the TCUFR through the small pores (TCUFR$_{sp}$) during the initial phase of the exchange, before absorption of solutes has taken place, equals

$$\text{TCUFR}_{sp} = \text{UFC}_{qp} \cdot \Delta P - (\Pi_c - \Pi_{pc})$$

$$= \text{UFC}_{qp} \cdot \left[ 9 - 0.38 \text{SA} - 7.72 + 0.88 \text{DIC} \right]$$

$$= \text{UFC}_{qp} \cdot [1.28 + 0.88 \text{DIC} - 0.38 \text{SA}]$$

(4)

The TCUFR during the first minute of the dwell was considered to represent the initial TCUFR.

It suggests that the UFC of icodextrin (ID) can be written as

$$\text{UFC}_{ID} = \frac{\text{TCUFR}_{0-1 \text{ min}} (\text{ID})}{0.88 \text{DIC} - 0.38 \text{SA} + 1.28} \text{ (ml/min/mm Hg)}$$

(5)

For 3.86% glucose, a similar equation can be given:

$$\text{UFC}_{0.38 \text{SA}} = \frac{\text{TCUFR}_{0-1 \text{ min}} (3.86\% \text{ glucose})}{283 - 0.38 \text{SA} - 0.58 \text{Osm}} \text{ (ml/min/mm Hg)}$$

(6)

Appendix B

The UFC is the product of the hydraulic permeability of the peritoneum ($L_p$) and the surface area (S). It can be calculated from the initial TCUFR and the overall peritoneal pressure gradient according to Starling’s equation (see Appendix A):

$$\text{TCUFR}_{0-1 \text{ min}} = \frac{\text{UFC}_{tot} \cdot \Delta P - \Pi_c + \sigma \Delta O}{L_p \cdot S}$$

(7)

Subtraction of Eq. 5 from Eq. 8 gives the UFC of the AQP:

$$\text{UFC}_{aqp} = \frac{\text{TCUFR}_{0-1 \text{ min}} (3.86\% \text{ glucose})}{283 - 0.38 \text{SA} - 0.58 \text{Osm}} - \frac{\text{TCUFR}_{0-1 \text{ min}} (\text{ID})}{0.88 \text{DIC} - 0.38 \text{SA} + 1.28}$$

(8)

There are apparent differences for $L_pS$ values calculated using either icodextrin or glucose, whereas $L_pS$ is a membrane constant that is constant by definition. The most probable explanation is the heteroporosity of the peritoneum. The presence of AQP is especially important in this respect because they represent only a small proportion of the surface area but contribute largely to water flow induced by crystalloid osmosis.
the small contribution by AQP to total peritoneal LpS, a very large proportion of the osmotic force is exerted across this pathway. This is because the osmotic force is composed of the fractional UFC values (across small pores and AQP), each multiplied by the solute reflection coefficient across each pore system.

For glucose, the following calculation can be made, assuming a reflection coefficient of 1.0 across the AQP and 0.03 across the small pores.

The partial osmotic forces are as follows:

\[
\text{Aquaporins: } X \cdot L_pS \cdot 1.0 \quad (11)
\]

Small pores: \((1 - X) \cdot L_pS \cdot 0.03 = L_pS[0.03 - 0.03X] \quad (12)\]

in which \(X\) is the part of \(L_pS\) caused by AQP.

The fractional osmotic force across AQP now becomes

\[
\frac{X}{0.03 + 0.97X} = \text{UFC}_{\text{AQP}} \quad (13)
\]

in which UFC_{\text{AQP}} is the contribution of AQP to UFC_{\text{tot}} (see Appendix A, Eq. 9).

A similar calculation can be made for icodextrin, assuming a reflection coefficient of 1.0 across AQP and 0.767 across the small pores. The partial osmotic forces are as follows:

\[
\text{aquaporins: } Y \cdot L_pS \cdot 1.0 \quad (14)
\]

small pores: \((1 - Y) \cdot L_pS \cdot 0.767 = L_pS[0.767 - 0.767Y] \quad (15)\]

in which \(Y\) is the fractional osmotic force across AQP as calculated according to Eq. 13.

The fractional osmotic force across AQP now becomes

\[
\frac{Y}{0.767 + 0.233Y} \quad (16)
\]

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References

22. Lai KN, Li FK, Lan HY, Tang S, Tsang AWL, Chan DTM, Leung JC: Expression of aquaporin-1 in human peritoneal me-


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