Dioctyl sodium sulphosuccinate increases net ultrafiltration in peritoneal dialysis

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Abstract

Background. The surface-active substance dioctyl sodium sulphosuccinate (DSS) has been reported to increase the peritoneal clearances of urea and creatinine. This study investigated the effects of DSS on the fluid and solute transport characteristics of the peritoneum.

Design. A 4-h single-dwell experiment session of peritoneal dialysis using 25 ml of 3.86% glucose dialysis solution with an intraperitoneal volume maker was performed in 16 male Sprague–Dawley rats. In eight rats, 0.005% (50 p.p.m.) DSS was added to the dialysis fluid. No DSS was given to the other eight rats (control group). The transport of fluid, glucose, potassium, sodium, urea, phosphate and urate were analysed.

Results. There was a significant increase in the intraperitoneal volume in the DSS group. At 240 min, the drain volume in DSS group (33.0 ± 2.9 ml) was significantly higher compared to the control group (28.8 ± 2.1 ml, P < 0.01). This increase in the drain volume was mainly due to a decrease in peritoneal fluid absorption rate in the DSS group (0.040 ± 0.013 ml/min) as compared to the control group (0.054 ± 0.010 ml/min, P < 0.05). There was no significant difference in the diffusive permeability and sieving coefficient for the small solutes between these two groups. However, the clearances for urea and sodium were higher in the DSS group, mainly due to the increase in the dialysate volume.

Conclusion. Our results suggest that DSS significantly increases the net ultrafiltration of peritoneal dialysis. This effect, which was mainly due to a decrease in the fluid absorption rate, contributed to the increased clearances for urea and sodium. DSS did not alter the diffusive permeability and sieving coefficient for the small solutes.

Key words: dioctyl sodium sulphosuccinate; lymphatic absorption; peritoneal dialysis; ultrafiltration

Introduction

The increased use of peritoneal dialysis has led to a growing interest in the long-term viability of CAPD and its ability to deliver an adequate amount of dialysis [1,2]. Ultrafiltration capacity failure is not uncommon in long-term peritoneal dialysis patients. Heimbürger et al. [3] found that the cumulative risk of ultrafiltration capacity loss increased with time on CAPD and was 2.6% after 1 year and 30.9% after 6 years on CAPD. Insufficient ultrafiltration coupled with a negligible residual renal function may result in a fluid overload state [4].

Improvement of peritoneal dialysis efficiency has been tried by using several pharmacological agents, such as vasoactive and surface-active substances [5–7]. One surface-active substance, dioctyl sodium sulphosuccinate (DSS), which has been commonly used as an anticonstipant, has been shown to increase the clearances of urea and creatinine of the peritoneal membrane [8]. The aim of the present study was to make a detailed analysis of the effect of DSS on the peritoneal fluid and solutes transport characteristics in rats.

Subjects and methods

Sixteen male Sprague–Dawley rats with an average body weight of 300 g were randomly divided into two groups. Each rat was anaesthetized with a single intraperitoneal injection of 50 mg/kg pentobarbitone sodium. The fur over the abdominal wall was closely shaved. The animal was laid in a supine position and was kept at 37°C with a heating pad (CMA/Microdialysis, Sweden). Isotonic saline, 2 ml/h, was injected subcutaneously to prevent hypovolaemia. A multiholed silastic catheter (0.8 mm internal diameter, Cole Palmer, Chicago, IL, USA) was inserted percutaneously below the xiphoid process, placed in the left lower quadrant of the abdomen, and secured with a purse-string stitch. The catheter was used for dialysis fluid infusion and sampling. Each animal was infused intraperitoneally 25 ml of Dianeal® 3.86% glucose dialysis fluid with 0.005% (50 p.p.m.) DSS (DSS group) or without DSS (control group). The dialysis fluids (with or without DSS) contained 18.5 KBq 131I-human
serum albumin (RISA) (Institutt for Energiteknik, Kjeller, Norway). A priming dose of 0.4 g/l of human serum albumin was added in the dialysis solutions to minimize the adhesion of tagged albumin to the surface of the catheter. Solutions were prewarmed to 37 °C before being instilled intraperitoneally via a three-way valve (Viggo, Connecta, Helsingborg, Sweden) connected to the end of a 0.8 mm catheter over a period of about 1 min, and allowed to remain in the peritoneal cavity for 4 h. Dialysate samples (0.35 ml) were taken at 0, 3, 15, 30, 60, 90, 120, 180 and 240 min post-infusion. Prior to each sampling, 1 ml of the dialysate was flushed back and forth five times through the catheter. Blood samples were drawn at 0, 120 and 240 min from the tail artery. After 240 min, the peritoneal cavity was opened and the dialysate was collected using syringe and preweighed gauze tissues and the volume was recorded. The experimental study was approved by the Animal Ethical Committee of the Karolinska Institute at Huddinge Hospital.

Dialysate samples (0.1 ml) and blood samples (0.1 ml of plasma) were analysed for RISA activity on a gamma counter (Packard Instrument Company, IL, USA) for 10 min each. Dialysate and plasma concentrations of urea (urease-glutamate dehydrogenase method), sodium, potassium (ion selective electrode method), phosphate (UV–molybdate method), urate (uricase–peroxidase method) and glucose concentration (hexokinase method) were determined using a Hitachi 919 autoanalyser (Boehringer-Mannheim GmbH, Mannheim, Germany). Intraperitoneal dialysate volume was estimated from the dilution of RISA with corrections made for the elimination of RISA from the peritoneal cavity and the sample volume [9]. The peritoneal fluid absorption rate as estimated by the coefficient of RISA elimination from the peritoneal cavity, K_{ET} (ml/min), the transcapillary ultrafiltration rate, the diffusive mass transport coefficient, K_{BD} (ml/min), and the sieving coefficient, S, for urea, potassium, sodium, phosphate and urate were calculated using the modified Babb–Randerson–Farrell (BRF) model as described previously [10]. However, to avoid the problem involved in the calculation of S for glucose, the K_{BD} for glucose was estimated during a period of dialysis isovolaemia [11,12]. The dialysate over plasma concentration ratios, D/P, for all the investigated solutes were calculated by dividing the dialysate concentrations of the investigated solutes at a certain time with the aqueous concentrations of the investigated solutes in plasma [13]. If no blood sample was taken at the same time as a dialysate sample then the blood concentration of the solute was linearly interpolated from the blood sample taken before and after this moment [14]. The D/D_{o} for glucose was calculated as the dialysate glucose concentration divided by the glucose concentration in the fresh dialysis solution. The clearance of each investigated solute was calculated as the total amount of the solute in the drained dialysate at 240 min minus the infused amount and divided by the mean blood concentration of the solute and the dwell time.

The direct lymphatic absorption of fluid from the peritoneal cavity was assessed as the clearance of RISA from the dialysate to the blood, K_{EB} (ml/min). K_{EB} was calculated from the rate of increase of RISA amount in blood divided by the average intraperitoneal RISA concentration [15]. The remaining part of fluid absorption to the peritoneal tissue interstitium and capillaries, K_{ET} (ml/min), was calculated as K_{ET} minus K_{EB}.

Two-way ANOVA with repeated measurements was applied to compare intraperitoneal volume and D/P ratios. Student’s t test for unpaired data were applied to compare

![Fig. 1. Intraperitoneal volume versus time. Control group (△); DSS group (○) (mean ± SD). *P<0.05; **P<0.01.](image)
Discussion

The present study showed that a small dose of DSS could increase the net ultrafiltration in peritoneal dialysis, resulting in increased clearances of urea and sodium. However, DSS had no significant effect on the peritoneal diffusive permeability of glucose, urea, sodium, potassium, urate, and phosphate.

DSS is an anionic surfactant and is widely employed in the pharmaceutical industry as an emulsifying, wetting and dispersing agent [16]. In the clinic, DSS is commonly used as a stool softener [17]. This is attributed to two identified mechanisms: (1) DSS works as a surface-active wetting agent, (2) it produces colon epithelial cell membrane changes resulting in fluid loss into the lumen of colon. The net result is a stool containing more water [18].

Our study showed that DSS significantly increased the net ultrafiltration mainly by decreasing the fluid from the peritoneal cavity; \( K_{ET} \), RISA elimination rate to peritoneal tissue. Control rate, \( K_{EB} \). In addition, DSS seemed to result in an initial group ( ), DSS group ( ), * \( P < 0.05 \); ** \( P < 0.01 \). increase in the transcapillary ultrafiltration rate (see Figure 1). As there was no difference in the dialysate glucose concentration, we found that the initial increase was due to sodium ( \( P < 0.05 \) ). There were no significant differences in the clearances of potassium, phosphate, and urate between these two groups.

Table 1. Diffusional mass transport coefficients, \( K_{BD} \) (ml/min), for glucose, urea, sodium, potassium, phosphate and urate (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Glucose</th>
<th>Urea</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Phosphate</th>
<th>Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8</td>
<td>0.34 ± 0.09</td>
<td>0.26 ± 0.16</td>
<td>0.23 ± 0.14</td>
<td>0.13 ± 0.11</td>
<td>0.08 ± 0.03</td>
</tr>
<tr>
<td>DSS</td>
<td>8</td>
<td>0.32 ± 0.11</td>
<td>0.28 ± 0.12</td>
<td>0.23 ± 0.14</td>
<td>0.12 ± 0.07</td>
<td>0.06 ± 0.03</td>
</tr>
</tbody>
</table>

No significant differences were found between the two groups.

Table 2. Sieving coefficients, \( S \), for glucose, urea, sodium, potassium, phosphate and urate (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Glucose</th>
<th>Urea</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Phosphate</th>
<th>Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>NA</td>
<td>0.73 ± 0.66</td>
<td>0.68 ± 0.11</td>
<td>1.21 ± 0.51</td>
<td>0.26 ± 0.31</td>
<td>0.03 ± 0.18</td>
</tr>
<tr>
<td>DSS</td>
<td>NA</td>
<td>0.93 ± 0.51</td>
<td>0.56 ± 0.45</td>
<td>1.01 ± 0.33</td>
<td>0.48 ± 0.21</td>
<td>0.07 ± 0.20</td>
</tr>
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NA, not analysed because of the low sensitivity of this parameter for glucose. No significant differences were found between the two groups.

Table 3. Peritoneal clearances, ml/min, for urea, sodium, potassium, phosphate, and urate (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Urea clear ance (ml/min)</th>
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<tbody>
<tr>
<td></td>
<td>Urea</td>
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<tr>
<td>Control</td>
<td>8</td>
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<tr>
<td>DSS</td>
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* \( P < 0.05 \) compared with the control group.
conductance was not clear. The clearance of RISA from dialysate to blood has previously been used as a marker of the direct lymphatic flow from the peritoneal cavity to plasma [15,20]. In our study, the clearance of RISA from dialysate to blood (K_{ER}) was significantly lower in DSS group compared to the control group, suggesting that this decreased absorption rate was, at least partially, due to a decrease in the lymphatic absorption rate (Figure 2). The effect of DSS on fluid transport is similar to the effect of phosphatidylcholine, another surfactant, which may also increase the net ultrafiltration but not solute transport per se [21,22]. However, the mechanisms of these changes is not clear.

Penzotti and Mattocks [23] found that peritoneal transport of labelled urea and creatinine could be accelerated in rabbits by adding a small amount of DSS. Dunham et al. [8] verified a dose-dependent rise in creatinine and urea clearance when DSS was given intraperitoneally to rabbits. The effect persisted for several exchanges in 5 h. In our study an increase of urea and sodium clearances with DSS was observed and was resulted from increased dialysate volume, whereas solute transport parameters, K_{BD}, S and D/P ratios did not change. It is important to note that the study designs in our work and Dunham’s study were quite different. In Dunham’s study, continual dialysis was used for 15 exchanges in the same rabbit and the dwell time for each exchange was only 19 min. Although it was stated that no significant changes were found in the drainage volume following DSS administration in Dunham’s study, it is important to note that the statistical evaluation was based on the comparison between the mean value of four exchanges (exchanges 1–4) before DSS administration and the mean value of 11 exchanges (exchanges 5–15) after DSS administration in the same rabbits [8]. It is possible continuous cycling will change peritoneal solute and fluid transport, perhaps by more efficient stirring of the dialysate, resulting in increased peritoneal transport as well as decreased drainage volume [24].

The finding that the K_{BD} for urea was lower compared to K_{BD} for glucose in the present study may be a species-related phenomenon, as glucose absorption is much higher in rat than in human [25]. We also had K_{BD} for sodium higher than for potassium in clinical studies if they were estimated with the peritoneal absorption taken into account and for 3.86% solution [26]. It may also be partially a consequence of the variability of the transport coefficients during the dwell study [27] and the estimation using the BRF model, which estimates the K_{BD} and S simultaneously with the assumption that they are constant for the whole dwell period [10]. This problem of the apparent values of the transport coefficients is especially complicated for potassium because of possibly substantial release of potassium from cells during the initial part of the exchange [11]. The unphysiological S value for potassium (i.e. S > 1) is a well-known phenomenon in peritoneal transport evaluation [11]. It may be a result of local release and other factors not included in the BRF model [11,28].

The low dose of DSS used in the present study is not toxic to humans [17]. However, higher doses of DSS may increase the permeability of the intestinal epithelium to various drugs, inhibit transport of nutrients and water, and alter the activity of membrane bound enzymes [29,30]. In Dunham’s study, when a high dose of DSS (0.04%) was added to the dialysate, fibrinous material was noted in the dialysate effluents of two of the three rabbits [8], which was attributed to local peritoneal inflammation. The elimination of DSS is mainly through the bile [30]. Whether long-term use of DSS in peritoneal dialysis will cause the accumulation of this drug in the body or in the peritoneum is not clear.

In summary, our study suggests that DSS may significantly increase the net ultrafiltration of peritoneal dialysis, mainly by a decrease in fluid absorption, resulting in increased peritoneal clearances of urea and sodium. DSS does not seem to have a significant effect on the diffusive permeability of the peritoneum for small solutes such as glucose, urea, sodium, potassium, phosphate and urate.

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References


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