Day-to-day variability of fluid and solute transport in upright and recumbent positions during CAPD

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Abstract

Background. The effect of posture on peritoneal transport characteristics during CAPD is unpredictable because (1) although the capillary pressure is higher in the upright position, the intraperitoneal pressure is also elevated, and (2) the contact of dialysate with the subdiaphragmatic lymphatics is probably more extensive during recumbency.

Methods. In eight CAPD patients, six peritoneal permeability tests (4 h, glucose 2.27%, dextran 70 as volume marker) were performed within 2 weeks, while the body posture was either recumbent (3 tests) or upright (3 tests). In addition, intraperitoneal pressure measurements were done in the recumbent and upright positions.

Results. The intraperitoneal pressure, not corrected for the contribution of the hydrostatic column, was higher in upright position (12.6 ± 0.8 mmHg, mean ± SEM) than during recumbency (6.7 ± 0.8; P < 0.0005). Net ultrafiltration rate was lower when upright: 0.96 ± 0.09 ml/min/1.73 m², compared to 1.14 ± 0.12 in the supine position (P < 0.05). This was achieved because the effective lymphatic absorption rate was marginally higher and the transcapillary ultrafiltration rate was slightly lower in the upright position. The mass transfer area coefficient of creatinine, representing effective peritoneal surface area, decreased from 10.7 ± 1.3 ml/min/1.73 m² (recumbent) to 9.9 ± 1.4 (upright; P = 0.08) in the upright position. The clearances of five serum proteins decreased more the higher the molecular weight. As a consequence, the restriction coefficient was 2.07 ± 0.09 (recumbent) vs 2.23 ± 0.08 (upright; P = 0.06). Hence the intrinsic permeability to macromolecules was higher during recumbency. The intraperitoneal pressure was correlated with the net ultrafiltration rate (r = -0.71, P = 0.05) only during recumbency. In upright position relations were found between the effective lymphatic absorption rate and the mass transfer area coefficients of low molecular solutes. The coefficients of variation of fluid and solute parameters were not different between both positions.

Conclusions. It is concluded that the decrease in net ultrafiltration rate in the upright position is only small and probably caused by counteracting effects of a higher intra-abdominal pressure and the effect of gravity. The upright position also led to only small decreases in solute transport parameters.

Key words: CAPD; transport kinetics; body posture; variability

Introduction

Peritoneal fluid and solute transport in CAPD patients is partly dependent on characteristics of the dialysate, for instance the dialysate volume, its osmolarity and the type of osmotic agent that is used [1–4]. The role of body posture on peritoneal fluid and solute transport is not well known. It has been reported that urea and creatinine clearances and the net ultrafiltration were higher in the lying than in the sitting position [5,6]. In contrast, Otero et al. [7] were not able to find an effect of postural changes on the dialysate/plasma ratio of creatinine and on the ultrafiltration rate during 4-h exchanges. These reports are not only conflicting, but also difficult to interpret, because kinetic studies were not done.

The effective surface area and intrinsic permeability are the characteristics of the peritoneal membrane that determine solute transport rates [8]. The effective peritoneal surface area is dependent on the contact between dialysate and mesothelial cells and on the number of perfused peritoneal capillaries. The latter may vary during several conditions. This has a direct effect on the number of pores available for transport. We found that changes in the mass transfer area coefficients of low-molecular-weight solutes, like creatinine, are caused by changes in the effective peritoneal surface area [9]. Therefore the mass transfer area coefficient...
of creatinine can be used as a functional representation of the effective surface area. The intrinsic permeability of the peritoneum can be characterized by the restriction coefficient to macromolecules [9–11].

Net ultrafiltration during CAPD is the difference between transcapillary ultrafiltration and lymphatic absorption from the peritoneal cavity [12]. These parameters can be calculated using intraperitoneally administered macromolecules, such as dextran 70 [9,13,14]. With this method we found in a previous study that an increase in the intraperitoneal pressure, obtained by external abdominal compression in the recumbent position, led to a higher effective lymphatic absorption and a decreased transcapillary ultrafiltration [15]. Also the transport of low-molecular-weight solutes and of serum proteins was reduced during high intraperitoneal pressure. The intraperitoneal pressure is higher in the upright than in the supine position during CAPD [16,17], but the contact between the dialysate and the peritoneal tissues lining the subdiaphragmatic lymphatics may be more extensive during recumbency. Therefore the effect of posture on solute and fluid kinetics is unpredictable.

The day-to-day variability of protein transport during CAPD in the supine position is caused by changes in the effective peritoneal surface area and in the intrinsic permeability of the peritoneal membrane [10]. Coefficients of variation ranging from 15 to 20% for the mass transfer area coefficients of low-molecular-weight solutes have been reported (position not standardized) [18–20] and are most likely due to changes in the number of perfused peritoneal capillaries. The day-to-day variability of peritoneal fluid transport is unpredictable.

The aim of the present study was to examine the effect of body posture (1) on peritoneal fluid and solute kinetics and (2) on the day-to-day variability. In addition, intraperitoneal pressure measurements were done in the upright and the recumbent position.

Subjects and methods

Patients

Six peritoneal permeability tests were done in eight stable CAPD patients within 2 weeks. Detailed clinical characteristics of the patients are given in Table 1. All used commercially available dialysate (Dianeal®, Baxter BV, Utrecht, The Netherlands). None of the patients had peritonitis at the time of the study or in the 4 preceding weeks. Informed consent was obtained from all patients after an explanation of the aim of the study. The protocol was approved by the Committee for Medical Ethics of the University Hospital of Amsterdam.

Study protocol

The peritoneal permeability tests had a dwell time of 4 h each and were performed during the morning hours using 2 litres glucose 2.27% (Dianeal® 2.27%, Baxter BV, Utrecht), while the patients were either in the upright (sitting or standing) or in the recumbent position. The position with which the first test was started, was randomized and alternated during the subsequent days. Three permeability tests were done during 3 consecutive days in the first week, followed by three tests during 3 consecutive days in the second week. The mean interval between the third and the fourth test was 4 days (range 1–11). The first examination was performed in the hospital, and the remaining five tests were done at home. The investigator was always present at the start of each test. During the first examination the patient was instructed on how to perform the rinsing procedure properly at the end of the dwell period (see below). Dextran 70 (Macrodex®, NPBI, Emmercompascuum, Amsterdam, The Netherlands) 1 g/l was added to all test bags as a macromolecular marker [13,14].

The test solution was instilled immediately after drainage of the night effluent. A volume of 10 ml dialysate was taken at 10 and 240 min after completion of inflow of the test solution. These samples were collected after a temporal drainage of 100–200 ml. The dialysate sample at 10 min was drawn by the investigator in all cases. Thereafter, the patient went to bed when the experiment was in the recumbent position, or continued his/her daily activities when the test was in the upright position. After drainage of the test solution at 240 min, the peritoneal cavity was rinsed once with 2 litres glucose 2.27%. The rinsing solution was drained by gravity immediately after completion of inflow. To ensure maximal drainage during all experiments the patients were instructed to stand up a few times when spontaneous fluid flow had stopped. Samples were taken from the rinsing bag for the calculation of the residual volume. Prior to each experiment a blood sample was taken. Furthermore, 20 ml of dextran 1 (Promiten®, NPBI, Emmercompascuum) was given intravenously on the 1st and the 4th examination to prevent possible

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Renal disease</th>
<th>Months on CAPD</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BSA (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>66</td>
<td>DN</td>
<td>58</td>
<td>162</td>
<td>60</td>
<td>1.64</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>43</td>
<td>RVD</td>
<td>16</td>
<td>178</td>
<td>63</td>
<td>1.81</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>38</td>
<td>CrN</td>
<td>35</td>
<td>167</td>
<td>64</td>
<td>1.73</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>59</td>
<td>CGN</td>
<td>11</td>
<td>178</td>
<td>54</td>
<td>2.04</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>57</td>
<td>DN</td>
<td>15</td>
<td>168</td>
<td>77</td>
<td>1.87</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>69</td>
<td>RVD</td>
<td>29</td>
<td>172</td>
<td>74</td>
<td>1.88</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>50</td>
<td>RVD</td>
<td>65</td>
<td>178</td>
<td>68</td>
<td>1.85</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>62</td>
<td>RVD</td>
<td>5</td>
<td>173</td>
<td>68</td>
<td>1.80</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>2F/6M</td>
<td>56 ± 4</td>
<td></td>
<td>29 ± 8</td>
<td>172 ± 2</td>
<td>70 ± 3</td>
<td>1.83 ± 0.04</td>
</tr>
</tbody>
</table>

BSA, body surface area; CGN, chronic glomerular nephritis; CrN, chronic interstitial nephritis; DN, diabetic nephropathy; RVD, renal vascular disease.
anaphylaxis to dextran 70 [21]. Following the six peritoneal permeability tests, the intraperitoneal pressure in all patients was measured as described previously [15]. Briefly, a Hewlett-Packard quartz pressure transducer (Model 1290A) was connected to the peritoneal dialysis system with a three-way stopcock. The zero-point reference level was defined in the midaxillary line in the recumbent position and at half of the distance from the xiphoid process to the symphysis pubis in the upright position (sitting and standing). Hence the intraperitoneal pressure determined this way is the result of (1) the pressure exerted by the interaction of the intraperitoneal volume and the compliance of the abdominal wall, and (2) the hydrostatic pressure determined by the length of the hydrostatic column. After the instillation of 2 litres 1.36% glucose dialysate, the intraperitoneal pressure was recorded continuously for 10 min periods on a Hewlett-Packard pressure recorder (Model 78205B) and on a stripchart recorder (Kratos Analytical, Austria) in the recumbent, the sitting, and the standing positions. The height of the intraperitoneal pressure was read every minute in order to obtain a mean intraperitoneal pressure for each position. The intraperitoneal pressure in the upright position was calculated as the mean of the intraperitoneal pressure in the sitting and the standing positions.

**Laboratory methods**

Urea, creatinine, and urate were measured by enzymatic methods (Boehringer Mannheim, Mannheim, Germany) in all dialysate and blood samples. The solute concentrations were determined by autoanalysers (Hitachi, H747, Boehringer Mannheim). The coefficients of variation for these solutes as determined for the lowest and the highest concentration levels were: 1.2% and 1.0% (urea), 1.7% and 0.8% (creatinine), 1.9 and 0.5 (urate). β2-Microglobulin was determined using a microparticle enzyme immunoassay (IMx® System, Abbott diagnostics, North Chicago, USA). Albumin, transferrin, and IgG were determined by nephelometry (BN100, Behring, Marburg, Germany), and α2-macro­globulin by another nephelometric method (Cobas Bio, Roche Diagnostics, Basel, Switzerland). The lower detection limits and the coefficients of variation for the lowest and the highest concentration of the protein assays were: 0.1 mg/l, 5 and 5% for β2-microglobulin; 1.8 mg/l, 1.8 and 3.0% for albumin; 2.4 mg/l, 1.1 and 2.4% for transferrin; 4.8 mg/l, 1.0 and 3.2% for IgG; and 0.5 mg/l, 6.8 and 4.6% for α2-macroglobulin. Total dextran 70 was determined in all dialysate samples by high-performance liquid chromatography [22]. The coefficient of variation of this method was 1.5%.

**Calculations**

The peritoneal fluid parameters, that is, the transcapillary ultrafiltration and the lymphatic absorption, were calculated as described previously [9,13–15,23]. Briefly, fluid loss from the peritoneal cavity, both subdiaphragmatic and interstitial are included in the definition of the absorption rate, which was calculated as the dextran disappearance rate. The dilution of dextran 70 was used to calculate the changes in the in situ intraperitoneal volume after correction for incomplete recovery. The transcapillary ultrafiltration was calculated as the sum of the change in in situ intraperitoneal volume and the effective lymphatic absorption. The mass transfer area coefficients (MTAC) of urea, creatinine and urate were calculated according to the model of Waniewski et al. [25], in which the solute concentration in plasma was expressed per volume of plasma water [26]. The protein clearances were calculated as described previously [9]. The intrinsic permeability of the peritoneal membrane can be characterized functionally by the peritoneal restriction coefficient to macromolecules (RC). This is the slope of the power relationship between the clearance (Cl) of various serum proteins and their free diffusion coefficients in water (Dw): Cl=constant DwRC [9–11]. The values of the free diffusion coefficients in water (Dw) for all proteins were: β2-microglobulin 13.3 [27]; albumin 6.1, transferrin 5.0, IgG 4.0 and α2-macro­globulin 2.41 [28]. The restriction coefficient was calculated using the five above-mentioned proteins. The higher its value the lower is the intrinsic permeability of the membrane.

**Statistical analysis**

Results are given as mean values ± SEM. All peritoneal fluid and solute parameters are expressed per 1.73 m² body surface area. The paired Student's t test was used for comparison of means in two positions. Correlations were calculated by the linear regression method. The variance ratio test was used for comparison of variances. The delta method [29] was used for distinguishing biological variance from analytical variance (see Appendix).

**Results**

The residual volume at the end of the first examination was not different from the mean residual volume obtained during the following five tests: 358 ± 85 ml (1st day) and 360 ± 64 ml (2nd to 6th day) (P = 0.97), implying that the accuracy of the examinations done at home was not different from those performed in the hospital.

The parameters of peritoneal fluid transport are given in Table 2. No significant differences were found for effective lymphatic absorption rate and transcapillary ultrafiltration rate. As the effective lymphatic absorption rate was 8% higher in the upright position than in the recumbent position (P = 0.40) and the mean transcapillary ultrafiltration rate 5% lower in the upright position (P = 0.23), the net ultrafiltration after the 4-h exchange was 16% lower in the upright position.

**Table 2.** Peritoneal fluid parameters in eight CAPD patients: studies in the recumbent and upright positions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recumbent</th>
<th>Upright</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective lymphatic absorption rate (ml/min/1.73 m²)</td>
<td>0.91 ± 0.09</td>
<td>0.98 ± 0.07</td>
</tr>
<tr>
<td>Mean transcapillary ultrafiltration rate during 4 h (ml/min/1.73 m²)</td>
<td>2.05 ± 0.12</td>
<td>1.94 ± 0.08</td>
</tr>
<tr>
<td>Net ultrafiltration rate (ml/min/1.73 m²)</td>
<td>1.14 ± 0.12</td>
<td>0.96 ± 0.09*</td>
</tr>
</tbody>
</table>

Mean ± SEM. *P < 0.05 compared to the recumbent position.
Day-to-day variability of fluid and solute transport during CAPD

The intraperitoneal pressure is influenced by body posture [30]. Iberti et al. [31] studied 16 patients postoperatively and compared intra-abdominal pressures in the supine and semi-erect position. The intraperitoneal pressure increased from 6.0 mmHg (supine) to 8.9 mmHg in the semi-erect position. A higher intra-abdominal pressure could also be achieved when contracting the muscles around the abdominal cavity during exercise [32,33]. It is likely therefore that the intraperitoneal pressure during CAPD will rise when changing from the recumbent to the upright position. However, during CAPD the differences in the measured intraperitoneal pressure between the horizontal and the vertical position [16] are also influenced by differences in the hydrostatic fluid column in both positions. In the present study the intraperitoneal pressure difference between the recumbent and the upright position averaged 6 mmHg. Part of this can be explained by the fact that the hydrostatic column, estimated from the distance of the umbilicus level to the table during recumbency and from the distance of the xiphoid process to the pubic symphysis in the upright position,

Discussion

Changing from the supine to the upright position was accompanied with modest changes in the lymphatic absorption (+8%) and the transcapillary ultrafiltration (-5%). As a consequence the net ultrafiltration decreased significantly by 16%. These differences are small when compared with our previous study, in which the intraperitoneal pressure was increased by means of external compression [15]. In that study all experiments were performed in the recumbent position. A rise of 10 mmHg led to an increase in the effective lymphatic absorption of 74%, while the transcapillary ultrafiltration decreased by 14% [15].

Table 3. Intraperitoneal pressures (IPP) in the recumbent and the upright positions, the distance of the umbilicus level to the table d(UT) during recumbency, and the distance of the xiphoid process os pubis d(XP) during upright position are given for all patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>IPP Recumbent (mmHg)</th>
<th>IPP Upright (mmHg)</th>
<th>d(UT) (cm)</th>
<th>d(XP) (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.7</td>
<td>9.4</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>3.9</td>
<td>9.2</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>5.8</td>
<td>12.3</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>4</td>
<td>6.1</td>
<td>13.0</td>
<td>32</td>
<td>34</td>
</tr>
<tr>
<td>5</td>
<td>10.8</td>
<td>14.7</td>
<td>36</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>7.0</td>
<td>15.2</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>8.0</td>
<td>11.8</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>5.5</td>
<td>15.0</td>
<td>32</td>
<td>38</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>6.7 ± 0.8</td>
<td>12.6 ± 0.8</td>
<td>31.2 ± 1.0</td>
<td>34.2 ± 1.2</td>
</tr>
</tbody>
</table>

*P < 0.001; **P < 0.05 vs the recumbent position.

than in the recumbent position (P = 0.05). The intraperitoneal pressure is given in Table 3 for all patients. Also the distances of the length of the xiphoid process to the symphysis pubis in the upright position, and the height from the table to the umbilicus level in the supine position are given in Table 3. The intraperitoneal pressure was higher in the upright position than during recumbency: 12.6 ± 0.8 mmHg (upright) and 6.7 ± 0.8 mmHg (recumbent) (P < 0.0005). No differences in the intraperitoneal pressure were found between the sitting position and the standing position.

The MTACs of the low-molecular-weight solutes, and the clearances of the serum proteins are given in Figure 1. Greater values were found in the supine position. The peritoneal restriction coefficient was: 2.23 ± 0.08 (upright) and 2.07 ± 0.09 (recumbent) (P = 0.05).

Relationships between fluid kinetics and intraperitoneal pressure in the supine position are given in Figure 2. A good correlation was present between net ultrafiltration and intraperitoneal pressure (r = -0.71, P = 0.05). The relationship between the intraperitoneal pressure and the effective lymphatic absorption rate did not reach statistical significance (r = 0.52, P = 0.19). No correlation was present between the transcapillary ultrafiltration rate and the intraperitoneal pressure (r = -0.35, P = 0.39). In the upright position no correlations between the intraperitoneal pressure and the parameters of fluid transport were found. The effective lymphatic absorption rate was related to the MTACs of low-molecular-weight solutes in the upright position (Figure 3), but not during recumbency.

The coefficients of variation for the parameters of fluid and solute transport and the contribution of the biological variance to the total individual variance are shown in Table 4. Only 5–30% of the total variance could be ascribed to errors in measurements. The remainder was due to biological variation.

Fig. 1. The mass transfer area coefficients of low-molecular-weight solutes (left panel) and the clearances of five serum proteins are given for the recumbent (open bar) and the upright (hatched bar) positions. Values are presented as mean ± SEM. *P < 0.05. **P < 0.01.
was larger in the upright position than during recumbency. It implies that comparisons of the intraperitoneal pressure during CAPD in different positions are difficult to make. The small effect of changing to the upright position on the effective lymphatic absorption may therefore be due to the fact that the real increase in the intraperitoneal pressure at the level of the tissues was much lower than 6 mmHg. Also an effect of haemodynamic changes (changes in cardiac output and splanchnic blood-flow) while changing from recumbency to the upright position, cannot be excluded. However, in animal experiments the effect of hypotension on peritoneal solute clearances was only small [34].

The marginal effect of increased peritoneal pressure on peritoneal transport caused by standing up may also be due to a counteracting effect of gravity on the fluid-filled peritoneal cavity for the following reasons. First, the lymphatic absorption of intraperitoneally instilled dye-labelled protein in anaesthetized rabbits decreased about 50% in the inclined 45° pelvis-down position compared to the horizontal position [35]. Second, obstruction of the peritoneal lymphatics in cats by abrasion of the inferior surface of the diaphragm led to a more than 10-fold reduction in the removal rate of serum by the lymphatics [36]. Third, sealing of the diaphragm reduced the appearance rate of RISA in the plasma by 55%. Only 30% could be ascribed to visceral lymphatics, and some 10–15% to the parietal lymphatics [37]. These results suggest that the subdiaphragmatic lymphatics are the main pathway for convective fluid loss from the abdominal cavity during CAPD [38], provided that there is contact of the dialysate with the diaphragm. In the upright position the contact of the dialysate with the subdiaphragmatic lymphatics is probably less extensive. Therefore, fluid absorption by other pathways e.g. across the mesothelium to the interstitium and from there to the lymphatics that drain the interstitium is likely to be more important in the vertical position. Such mechanism is in accordance with the submesothelial oedema often found in specimens of peritoneum from CAPD patients [39], and also with the experiments in rats showing that more macromolecules move into the peritoneal tissues when the pressure gradient between the peritoneal cavity and the peritoneal tissue is increased [40,41]. It is also in accordance with the relationship between the effective lymphatic absorption rate in the upright position and the MTACs of low-molecular-weight solutes, found in the present study.
This can be explained as follows: interstitial uptake and removal of fluid and dextran will be dependent on the lymphatic drainage of the interstitial tissues. It is known from anatomy that the lymphatics of e.g. the anterior abdominal wall accompany the blood vessels. The number of perfused peritoneal capillaries is an important determinant of the effective peritoneal surface area. Fluctuations in this area in individual patients are reflected in fluctuations in the MTACs of creatinine [9]. Our results suggest that the number of functioning interstitial lymphatics is related to the number of perfused capillaries.

In the supine position, a high intraperitoneal pressure was related with a low net ultrafiltration. These results are in accordance with those of others [42,43]. But, our results suggest that the effect of pressure on lymphatic absorption is of more importance to this relationship, than that on transcapillary ultrafiltration. This may explain why no relationship was found between the intraperitoneal pressure and net ultrafiltration in the upright position.

Changing from the recumbent to the upright position caused a decrease in the MTACs of low-molecular-weight solutes that averaged 7%. This points to an effect on the number of perfused peritoneal capillaries, similar to that of external compression in the supine position [15]. The mechanisms involved are most probably (1) compression of those peritoneal capillaries that are hardly perfused, and (2) arteriolar constriction that occurs when the intraperitoneal pressure, and hence the intravenous pressure, is raised [15,44]. Both phenomena will reduce the number of pores available for solute transport. The 8% increase in the restriction coefficient for macromolecules suggests that the upright position also leads to some decrease in the average large pore radius.

The coefficients of variation of the parameters of fluid and solute transport were alike in the upright and recumbent position. Those for the clearances of serum proteins were similar to previously reported data obtained during night dwells [10]. The coefficients of variation for the mass transfer area coefficients of low-molecular-weight solutes were smaller than the 15–20% reported previously [18–20]. This difference may be explained by the following two reasons: first, in the studies mentioned the body position during the examinations was not standardized; second, the accuracy in the determination of the peritoneal fluid parameters has improved in the last years. The lower coefficients of variation for the MTACs of low-molecular-weight solutes compared to those for protein clearances may be caused by the fact that the former are determined by the effective peritoneal surface area only, whereas the latter are influenced by both surface area and intrinsic permeability.

This can be concluded that net ultrafiltration is decreased in the upright position, because of a modest increase in the effective lymphatic absorption rate and a marginal decrease in the transcapillary ultrafiltration rate. These results are most probably caused by counteracting effects of a higher intraperitoneal pressure and the effect of gravity leading to a decreased contact between the dialysate and the subdiaphragmatic lymphatics. Also the smaller effective peritoneal surface area and the lower intrinsic permeability in the upright position are probably due to the higher intraperitoneal pressure. The variability of the parameters of peritoneal transport also leads to some decrease in the average large pore radius.

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### Table 4. The estimates of the mean intraindividual coefficients of variation* in eight CAPD patients** for the parameters of peritoneal fluid and solute transport: the contribution of the biological variation to the total variance***(%); and the 95% confidence interval (CI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean intraindividual coefficients of variation (%) and (95% CI)</th>
<th>Contribution of biological variation (%) to the total variance and (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recumbent Upright</td>
<td>Recumbent Upright</td>
</tr>
<tr>
<td>Effective lymphatic absorption rate</td>
<td>23 (15–30) 17 (7–26)</td>
<td>79 (54–93) 67 (24–95)</td>
</tr>
<tr>
<td>Mean transcapillary ultrafiltration rate</td>
<td>14 (8–20) 12 (5–18)</td>
<td>88 (71–96) 79 (52–90)</td>
</tr>
<tr>
<td>Net ultrafiltration rate</td>
<td>17 (10–25) 23 (7–39)</td>
<td>80 (51–95) 85 (63–98)</td>
</tr>
<tr>
<td>MTAC creatinine</td>
<td>7 (4–10) 7 (2–12)</td>
<td>69 (51–95) 73 (33–97)</td>
</tr>
<tr>
<td>MTAC urea</td>
<td>7 (2–11) 8 (3–13)</td>
<td>34 (7–7) 58 (22–92)</td>
</tr>
<tr>
<td>MTAC urate</td>
<td>8 (5–11) 13 (8–18)</td>
<td>38 (7–85) 72 (41–97)</td>
</tr>
<tr>
<td>Cl-β2-microglobulin</td>
<td>16 (8–23) 18 (14–22)</td>
<td>75 (40–97) 73 (46–89)</td>
</tr>
<tr>
<td>Cl-albumin</td>
<td>17 (9–24) 18 (8–27)</td>
<td>95 (86–100) 92 (80–99)</td>
</tr>
<tr>
<td>Cl-transferrin</td>
<td>19 (9–29) 20 (12–28)</td>
<td>97 (91–100) 93 (85–98)</td>
</tr>
<tr>
<td>Cl-IgG</td>
<td>21 (12–29) 24 (14–34)</td>
<td>93 (86–100) 95 (88–100)</td>
</tr>
<tr>
<td>Cl-x2-macroglobulin</td>
<td>19 (9–28) 28 (11–45)</td>
<td>93 (78–100) 96 (84–100)</td>
</tr>
</tbody>
</table>

Values are presented for the recumbent and the upright positions. The differences of the mean coefficients of variation between the two positions are far from statistical significance. * The observed intraindividual coefficients of variation, each obtained from only three observations, were corrected for bias to get nearly unbiased estimates, by dividing them by $\sqrt{3/n(1+(\bar{x}/\bar{y})^2)^2}$. These corrected estimates were used for a Student confidence interval for the population of intraindividual coefficients of variation for the position under consideration. ** For MTAC urea one patient was not included because of outlying values caused by dividing by a difference much smaller than the theoretical measurement errors of the two numbers. *** The total variance is an unbiased estimate of the true variance, but heavily skewed with three observations. Therefore first a Student confidence interval was constructed for the population mean of their logarithms, whereafter the obtained limits (left and right) were transformed to $\exp(\text{left} + \frac{1}{2} \text{W}^2)$ and $\exp(\text{right} + \frac{1}{2} \text{W}^2)$ where $\text{W}^2$ is the sample variance of the $\ln s_i^2 (i = 1, \ldots 8)$ and removes most of the bias introduced by the log transform.

**Note:**

The mean intraindividual coefficients of variation are calculated as $\sqrt{\frac{\sum_{i=1}^{n} (x_i - \bar{x})^2}{n}}$, where $x_i$ is the $i$th observation, $\bar{x}$ is the mean of the observations, and $n$ is the number of observations. The contribution of biological variation to the total variance is calculated as $1 - \frac{\text{Total Variance}}{\text{Intraindividual Coefficients of Variation}}$.
fluid and solute transport was not affected by body posture.

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Appendix

The variance of a variable due to random measurement errors in the basic variables from which it was calculated can be computed by a statistical method, sometimes called the 'delta method' [29]. A simple example will show how it works.

Let  be a variable calculated from basic variables, , ,  by the equation

\[ u = f(x, y, z) \]  \tag{1}

and let  be a value of  calculated from observed values , , of , ,  respectively. Let , ,  be repeated basic measurements and  the mean value of the corresponding  be calculated from equation (1).

Let , ,  be the partial derivates of  with respect to , , . Then, assuming small random errors in , , and continuous partial derivates of , we have approximately

\[ u_i - \bar{u} = a(x_i - \bar{x}) + b(y_i - \bar{y}) + c(z_i - \bar{z}) \]  \tag{2}

Squaring both sides gives

\[ (u_i - \bar{u})^2 = a^2(x_i - \bar{x})^2 + b^2(y_i - \bar{y})^2 + c^2(z_i - \bar{z})^2 + 2ab(x_i - \bar{x})(y_i - \bar{y}) + 2ac(x_i - \bar{x})(z_i - \bar{z}) + 2bc(y_i - \bar{y})(z_i - \bar{z}) \]  \tag{3}

Summing both sides for  yields a more useful equation describing error propagation:

\[ \text{var}(u) = a^2 \text{var}(x) + b^2 \text{var}(y) + c^2 \text{var}(z) + 2bc \text{cov}(x, y) + 2ac \text{cov}(x, z) + 2bc \text{cov}(y, z) \]  \tag{4}

From eq.4 we can calculate the variance of  without knowing all the sample points , ..., . It is sufficient to know the variance–covariance matrix of , , and the partial derivates , , of  at , , . If errors are small, as should be in good laboratory practice, , and can be approximated by the partial derivates of  at the observed point .

Finding the exact equations for the partial derivates can be difficult or tedious. However, we can calculate them with sufficient accuracy for our purpose, e.g. for

\[ b = \frac{f(x_1, y_1, z_1 + \delta) - f(x_1, y_1, z_1)}{2\delta} \]  \tag{5}

where \( \delta \), 'delta', is a small positive number not greater than the standard deviation of the error of  at level . If the coefficients of variation in repeated measurements of , , and  are known for the usual ranges of these variables, than the variances of , , and can be calculated as the squares of these coefficients multiplied by the squares of , , respectively.

Mostly covariances are zero by the independence of measurements of , , and . This simplifies eq. (4), especially when  has to be calculated from more than three basic variable, since, with  basic variables we have  covariances in eq. (4). However, basic measurements may be interdependent. This was the case for the MTAC calculations, which use, besides other basic variables, three different concentrations of the same type of molecule. These three concentrations were measured in one run of the measuring device. The within-run coefficient of variation (CV) for this device was known to be smaller than the day-to-day (total) coefficient of variation (CV), probably due to components of the error which affected the three measurements in the same direction. In order to calculate the covariance between the results, , , or two of such concentration measurements, we assumed the following model:

\[ x = \bar{x} + pd + v \]
\[ y = \bar{y} + qd + w \]

where  and  are the unknown true values, , and  constants which may depend on  and  respectively,  and  the correlated errors due to day-to-day variation, and  and  the uncorrelated within-run errors. The variables , , and  are assumed to have zero means and to be uncorrelated. This model implies the equations:

\[ \text{var}(x) = p^2 \text{var}(d) + \text{var}(v) \]
\[ \text{var}(y) = q^2 \text{var}(d) + \text{var}(w) \]
\[ \text{cov}(x, y) = pq \text{var}(d) \]  \tag{7}

From these equations we easily get

\[ \text{cov}(x, y) = \sqrt{(\text{var}(x) - \text{var}(v))(\text{var}(y) - \text{var}(w))} \]  \tag{8}

For a pair of observations , we can now calculate the corresponding covariance by substituting in eq.8:

\[ x_1^2 CV^2_Y(x_1, y_1^2 CV^2_Y(y), x_1^2 CV^2_x(x_1, y_1^2 CV^2_Y(y)) \]  \tag{9}

for the total variances , , and the within-run variances , and respectively.

For each of the three types of molecules and for both total and within-run errors, CV values were available for two levels of concentration. For a concentration result under the lower level or above the higher one we used the corresponding CV. For a result between these levels we used linear interpolation with the logarithms of both level and CV. This has the advantage of giving equal results for CV and CV squared.
References


15. Imholz ALT, Koomen GCM, Struijk DG, Arisz L, Krediet RT. Effect of an increased intraperitoneal pressure on fluid and solute transport during CAPD. *Kidney Int* 1993; 43: 1339–1346


