Increasing fill volume reduces cardiac performance in peritoneal dialysis

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Abstract

Background. It is generally accepted that peritoneal dialysis (PD) affects systemic haemodynamics less than haemodialysis, but little is known about changes in haemodynamics during PD. It is unknown if increasing PD volume causes changes in cardiovascular haemodynamics possibly increasing the demand on the heart even during normal daily activities.

Methods. Fifteen stable PD patients were included in this randomized, controlled, open-label crossover study. After drainage, we measured blood pressure, pulse rate and cardiac output (CO) after 30 min in the supine position. The measurements were repeated 5 min later in an upright position. Subsequently, following fill, the measurements were repeated after 30 min in the supine and 5 min later in the upright position. The two procedures were repeated twice. The fill was either 21 or 31 of dialysate. CO was measured with a non-invasive device based on foreign gas rebreathing. Stroke volume (SV) and total peripheral systemic resistance were calculated.

Results. In the supine position, no difference was found between drained and 21 fill. With 31 fill both SV and CO decreased and total peripheral systemic resistance increased, while pulse rate and mean arterial blood pressure remained unchanged.

In the upright position, SV and CO decreased and total peripheral systemic resistance increased. Pulse rate and mean arterial blood pressure were unchanged independent of fill volume when compared with the drained situation. During postural change, no significant differences were found between drained and 21 and 31 fill.

Conclusion. The present study showed that cardiac performance decreased when increasing fill volume from 2 to 31 in the supine position. The decreased cardiac performance was already present after 21 fill in the upright position and did not change negatively by increasing fill. It was also shown that cardiovascular response from the supine to upright position was preserved.

Keywords: Peritoneal dialysis; cardiac output; haemodynamics; position

Introduction

During the last decades, the dialysis population has changed from relatively young patients with only one failing organ, the kidney, to elderly patients where several organs are affected due to diabetes or arteriosclerosis. The treatment challenge has thus increased as the lack of reserve capacity in other organs, e.g. the heart, may reduce the patient’s ability to cope with the consequences of reduced kidney function.

Changing from the supine to upright position elicits a decrease in the central blood volume because of venous pooling. This induces an increase in total vascular peripheral resistance (TPR), a decrease in stroke volume (SV) and cardiac output (CO) and a slight increase in pulse rate. In general, cardiovascular haemodynamics is more robust in the supine than in upright position.

The influence of peritoneal dialysis (PD) on repeated daily activities is only scarcely described. In the study by Kong et al. [1] using impedance cardiothocography, the 21 fill did not change the cardiovascular haemodynamics in the supine position compared with the drained situation. During postural change, no significant differences were found between drained and 21 and 31 fill.

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with heart failure grade NYHA II–IV [3], as well as before and after cardiac surgery.

The purpose of the present study was (i) to describe the effect of increasing fill volume on cardiovascular haemodynamics in supine and upright positions and (ii) to describe the effect of postural changes on cardiovascular haemodynamics. We hypothesized that the haemodynamics during positional change from supine to upright is comparable to what is seen in healthy persons, and moreover, that increasing fill volume would decrease SV and increase pulse rate and keep CO unchanged.

The study was performed as a randomized, controlled, open-label crossover study measuring systolic blood pressure (SBP), DBP, pulse rate, TPR, SV and CO comparing the drained situation with the situation after installing 2 l and 3 l dialysate, respectively. Measurements were made after 30 min in the supine position and after 5 min in the upright position.

Materials and methods

Study population

Subjects eligible for study were PD patients stable for at least 3 months, age above 18 years, with a stable body weight and no clinical signs of over hydration. Exclusion criteria were congestive heart failure (NYHA III and IV) and severe pulmonary, infectious or psychiatric diseases and peritonitis in the preceding 3 months.

Fifteen patients were included consecutively at their visit to the outpatient clinic from a population of 100 PD patients. Basic demographics and medication with known cardiovascular effects are shown in Table 1. Residual renal function, Kt/V and peritoneal membrane characteristics were determined from the latest urine and dialysate samples. Peritoneal membrane type was calculated using PD-Adequest version 2.0.

Design

A randomized, controlled, open-label crossover study with the patients serving as their own controls.

Procedure

The patients arrived at the outpatient clinic between 8 and 10 a.m. A clinical examination before the study showed no signs of overhydration. Continuous ambulatory peritoneal dialysis (CAPD) patients had not performed their morning exchange (n = 2). Automated peritoneal dialysis (APD) patients followed their normal dialysis program (n = 13). After arrival at the outpatient clinic, drainage was performed if necessary (Figure 1). Blood pressure, pulse rate and CO were measured after 30 min resting in a supine position and after 5 min in an upright position. Installation of dialysate was followed by 30 min resting in the supine position. Intraperitoneal pressure (IPP) was measured in the supine position. Measurements of blood pressure, pulse rate and CO

| Table 1. Baseline demographics of the 15 peritoneal dialysis patients studied with either 21 or 31 of dialysate in supine and upright positions. Data are given as mean ± SE |
|---|---|
| Sex (male/female) | 13/2 |
| Weight (kg) | 79 ± 11 |
| Age (years, median and range) | 71(29-85) |
| Peritoneal function |  |
| Peritoneal membrane type H/H/A/L/L/L | 0/11/3/0 |
| Total creatinine clearance (l/week/1.73 m²) | 79 ± 35 |
| Total Kt/V | 2.30 ± 0.53 |
| Residual renal function |  |
| (Creatinine clearance l/week/1.73 m²) | 35 ± 35 |
| Residual urine output (ml/day) | 892 ± 693 |
| Blood pressure |  |
| Systolic blood pressure (mmHg) | 137 ± 19 |
| Diastolic blood pressure (mmHg) | 83 ± 15 |
| Medication |  |
| Beta-blokkers | 8 |
| ACEI/ATB | 5/4 |
| Ca-antagonists | 9 |
| Loop-diuretics | 9 |
| Insulin | 2 |
| Kidney disease |  |
| Glomerulonefritis | 1 |
| Nephropathy (Obstructive/Infectious) | 2 |
| Polyzystic | 1 |
| Diabetic | 3 |
| Hypertensive | 1 |
| Unknown/Others | 7 |

* n = 14.
Ethics

Informed consent was obtained from all participants. The study was approved by the Regional Ethics Committee and conducted in accordance with the second Helsinki Declaration.

Methods

Blood pressure, pulse rate and CO were measured with a portable non-invasive device consisting of a three-way respiratory valve with a mouthpiece and a rebreathing bag connected to an infrared photoacoustic gas analyser, a pulse oxymeter and a device for automatic blood pressure measurement (Innocor, Innovaion, Odense, Denmark). The system was connected to a computer integrating control of respiratory valve and the gas analyser system settings and registration of retrieved gas concentration data.

CO was measured by rebreathing in a closed system containing a gas mixture of sulphahexafluoride (SF6, 0.1%) and nitrous oxide (N2O 0.5%) in an O2/N2 mixture. Rebreathing was performed in 15 s with a gas volume of 1.8 l and breathing rate of 14–18 min–1. SF6 indicated incomplete gas mixing. The first two or three concentration plotted against time). The first two or three venous shunt (SaO2 in pulse pressure (PP) was derived parameters.

Nitrous oxide (N2O0.5%) in an O2/N2 mixture. A constant ventilation rate and volume was ensured by synchrony between the graphical tachymeter on the computer screen and the study subject, who was instructed to empty the bag with each breath. The rebreathing software calculated pulmonary blood flow from the rate of uptake of N2O into the blood (slope of regression line through logarithmical transformation of expiratory N2O concentration plotted against time). The first two or three breaths were excluded from analysis if total lung volume changes measured by SF6 indicated incomplete gas mixing. In the majority of patients without pulmonary arterial–venous shunt (Sao2 ≥98%), the pulmonary blood flow value was equal to CO [5,6]. In contrast, in patients with pulmonary shunt, the shunt was calculated and added to CO. The shunt fraction was calculated using the oxygen concentration [7]. The calculations were performed assuming the gases were mixed completely, that equilibration of gases between alveoli and blood was rapid and that lung blood flow was constant.

SBP, DBP, and pulse rate were measured by an automated device connected with the Innocor. Pulse pressure (PP) was calculated as SBP–DBP.

SV and TPR and related indices were mathematically derived parameters.

IPP measurement was performed in the supine position as described by Durand et al. [8]. The mean value of inspiration and expiration was used.

Statistics

Data are presented as mean ± SE unless otherwise stated. The haemodynamic parameters did not differ significantly when comparing the two drained periods in the supine position. Analyses were performed as ANOVA or ANOVA for repeated measurement with correction for multiple comparisons comparing drained and 21 and 31 fills, respectively. When necessary, correction for multi-comparison was performed with Scheffe’s test. When significant differences were found, a paired Student’s t-test was performed to identify which situations were significantly different (drained 21 or 31). Ln transformation was performed if data were not normally distributed. P-values <0.05 were considered statistically significant (STATA version 9.2, Texas, USA).

The two drained periods were statistically processed as one. In the supine position, (SBP: 133±3 mmHg vs 136±4; DBP: 81±3 mmHg vs 81±3; pulse rate: 71±2 min–1 vs 72±3; CO: 4.4±0.3 l/min vs 4.5±0.3; SV: 62±4 ml vs 63±3; TRP: 23.2±2 mmHg × ml/min vs 22±2) and in the upright position (SBP: 124±6 mmHg vs 127±4; DBP: 76±4 mmHg vs 78±4; pulse rate: 75±4 min–1 vs 74±4; CO: 3.6±0.3 l/min vs 3.9±0.4; SV: 49±5 ml vs 54±4; TRP: 26±3 mmHg × ml/min vs 25±5).

Results

Supine position—effects of fill volume

CO decreased significantly with 31 fill compared with both the drained situation (88%, P <0.01) and 21 fill (91%, P <0.01). No statistical difference was found between 21 fill and the drained situation (Figure 2). SV decreased significantly with 31 fill compared with both the drained situation (87%, P <0.02) and 21 fill (88%, P <0.01). No statistical difference was found between 21 fill and the drained situation (Figure 2).

The cardiac workload calculated as CO × SBP was unchanged with 21 fill (599±61 mmHg × l/min, ns) and with 31 fill (555±68 mmHg × l/min, P = 0.07) compared with the drained situation (604±54 mmHg × l/min).

DBP increased significantly with both 21 (103%, P <0.05) and 31 (104%, P <0.05) fills compared with the drained situation (Table 2). No change was found in pulse rate or SBP.

TPR was significantly increased using a 31 fill compared with the drained (114%, P <0.01) and 21 fill (110%, P <0.01) situations (Figure 2). IPP increased significantly with fill volume (21:14±1 cm H2O vs 31:17±1, P <0.003). No significant relations were found between absolute and relative changes of IPP and the haemodynamic parameters (CO: rho =0.57, P = 0.055 and SV: rho = 0.51, P = 0.09).

Upright position—effects of fill volume

CO decreased with 21 (3.3±0.4 l/min, P <0.005) and 31 (3.4±0.4 l/min, P <0.02) fills compared with the drained situation (3.8±0.3 l/min). There was no statistically significant difference between 21 and 31 fills (Figure 1). SV decreased with 21 (44±4 ml, P <0.02) and 31 (44±4 ml, P <0.03) fills compared with the drained situation (51±4 ml). There was no statistically significant difference between 21 and 31 fills (Figure 2).

The CO was reduced both with 21 (419±64 mmHg × l/min, P <0.001) and 31 (460±68 mmHg × l/min, P <0.04) fills compared with the drained situation (492±64 mmHg × l/min).
No changes were found in SBP, DBP and pulse rate (Table 2). TPR was significantly increased both for 2 l (30 ± 2 mmHg/l/min, \( P < 0.01 \)) and 3 l (30 ± 2 mmHg/l/min, \( P < 0.003 \)) fills compared with the drained situation (26 ± 2 mmHg/l/min).

### Change of posture

After shifting to an upright position, CO was reduced by (D: 88 ± 3%, 2 l fill: 69 ± 6%, 3 l fill: 82 ± 6%, D vs 2 l \( P < 0.05 \), D vs 3 l ns, 2 vs 3 \( P < 0.05 \)) compared with the supine position. The SV was reduced by (D: 82 ± 3%, 2 l: 66 ± 7%, 3 l: 83 ± 6%, D vs 2 l \( P < 0.05 \), D vs 3 l ns, 2 vs 3 \( P < 0.05 \)). SBP and DBP decreased and pulse rate and TPR increased with change of posture from the supine to upright position, regardless of fill volume status. The result was not statistically significant.

### Discussion

The present study showed that increasing dialysate fill volume decreased SV and CO and increased TPR and that changes were more pronounced in the upright position. It was also shown that the cardiovascular response from supine to upright position was preserved.

#### Supine position

The unchanged SV in the supine position with 2 l fill compared with the drained situation, which is in concordance with Kong et al. [1]. To our knowledge, the reduced SV after 3 l fill has not yet been described. The reduction in SV resulted in a decrease in CO as the pulse rate was unchanged and blood pressure was maintained by a parallel increase in TPR. The venous return via vena cava accounts for approximately two-thirds of the systemic venous return and the resultant preload is the most important determinant of CO under normal conditions. In the supine position, the mean IPP increased 3 cm H2O when the dialysate volume was increased from 2 to 3 l in accordance with other studies [9]. It is generally accepted that CO decreases with an intra-abdominal pressure of more than 20 mmHg, while the effects of lower intra-abdominal pressure are conflicting [10]. An important
factor in keeping flow to the heart is the difference between intrathoracic and IPPs and the intravascular volume. If 31 fills reach the breaking point where venous return is decreased, then CO would decrease. The present study cannot solve this and further studies with simultaneous measurements of flow and intravascular volume are needed.

A decrease in intravascular volume might decrease SV and increase TPR. According to other studies, we expect the net ultrafiltration to be almost the same after a 30 min dwell with 2 or 31 of dialysate. We, thus, expect the intravascular volume to be the same during the two dwells as no changes in pulse rate could be demonstrated. During the trial day overall hydration status was stable, as haemodynamic measurements were identical during the two drained periods. It, thus, seems reasonable to conclude that the changes in haemodynamics in the supine position are not explained by changes in hydration status.

The rebreathing method might have some weaknesses when used to estimate CO from the pulmonary blood flow. Changes in pulmonary circulation does not make the CO measurements with rebreathing invalid compared with invasive techniques [5,11]. When lung function is halved, there is a tendency to underestimate rebreathing CO [5,6]. In patients with lung oedema, forced expiratory volume in 1 s (FEV1) had to be decreased by 40% before any changes in rebreathing CO could be detected [12]. From a theoretical point of view, the use of N2O as the soluble gas should be advantageous as it is less soluble than acetylene, and thus, less sensitive to uneven distribution of gasses in the lungs. In PD studies of lung function in the sitting position, no or small changes in FEV1 and functional vital capacity were found with fill [13,14]. In comparison, no changes in vital capacity and functional reserve capacity in the supine position could be shown [13]. The small changes seen in lung function in PD patients would not affect the rebreathing technique.

In supine position, an increase in DBP was demonstrated both with 21 and 31 fills compared with the drained situation. This is in accordance with Ventura et al., who demonstrated that increasing fill volume increases DBP [15]. Moreover, it has recently been shown that a fill with 3.86% glucose induces a comparable increase in blood pressure shortly after installation [2,16]. The mean arterial pressure (MAP) was not changed in the present study. It is still unknown whether the mechanism is the same after increasing the fill volume and after installation of a hypertonic solution containing 3.86% glucose.

Other research teams using the same rebreathing technology have, in healthy young persons, found CO between 5.3 and 6.5 l/min and SV from 90 to 110 ml in the supine position. Moreover, in patients with heart failure the same values were 4.0–4.5 l/min and 65–80 ml, respectively [17]. The mean age in the heart failure study was comparable to our study. PD patients have lower SV than patients with heart failure. CO in PD patients is in the same range because they have a higher pulse rate compared with heart failure patients. None of the patients had known clinical cardiac disease, but as congestive heart failure is a difficult diagnosis in dialysis patients, an echocardiographic evaluation of the patients would be advantageous.

Many dialysis patients have neuropathy including affection of the autonomic system which might change the cardiovascular response. In the present study, no a priori evaluation of the autonomic nervous system had been performed. Using the criteria described by Jassal et al. [18], only one of the patients fulfilled the criteria for autonomic dysfunction. The use of antihypertensive drugs might also affect the cardiovascular response. A post hoc analysis could not find any difference between patients with or without β-blocker concerning pulse rate, CO and SV response to a change in position.

Recently, it has been suggested by Selby et al. [16] that hyperinsulinaemia might induce haemodynamic changes in PD patients. In healthy subjects, hyperinsulinaemia has been described to cause a rise in SV and CO coupled with a fall in TPR probably via a direct effect on the endothelium [19]. In chronic heart failure patients, a positive relation between insulin sensitivity and CO has been demonstrated [20] while the results of insulin infusion are inconsistent. In the present study, none of the expected changes induced by hyperinsulinaemia were seen, as TPR was either unchanged or increased and CO was unchanged or decreased. The two patients treated with insulin did not show any different results.

**Upright position**

In order to avoid the changes seen immediately after postural change, we measured the haemodynamics after 5 min in an upright position. SV and CO were significantly decreased after fill, independently of fill volume, and a parallel increase in TRP was seen. When standing up the peripheral muscles and the respiratory pumps return blood to the central blood volume. The return of blood from the legs to the central blood volume might be decreased with dialysate in the abdomen. The decrease is probably pressure-dependent. Unfortunately, we did not measure IPP in the upright position. The respiratory pump is based on exaggerated respiratory movements lowering intrathoracic pressure and increasing abdominal pressure and increasing return of extrathoracic blood volume. In conclusion, the decreased CO and SV found after fill could be based on mechanical changes causing resistance to the return of blood flow.

**Change in posture**

Only a small increase in pulse rate (3 beats per min) was found when changing posture from the supine to upright position. This increase was much smaller than expected [1]. In healthy persons, an increase of 8–10 beats per min has been found [17], and in heart failure
patients an increase of approximately 3 beats per min has been described, independent of their hydration status [17]. In the study by Kong et al. [1], a significant increase in pulse rate was seen in the upright position. This is not in accordance with our study where no change in pulse rate was found. This is probably due to differences in the study population. Our study population was approximately 20 years older and thus had an increased risk of comorbidity. In healthy individuals, SV is reduced \( \sim 25\% \) during postural change. We found a decrease in SV between 18\% and 34\% which is in the same range as described earlier for PD patients [1] and patients with heart failure [17]. The increase in TRP in healthy individuals during postural changes ranges from 20\% to 30\% [17], equivalent to the range seen in our study population. When comparing our data with the literature, the haemodynamic response to postural changes in PD patients is similar to healthy individuals.

In conclusion, the present study showed that increasing dialysate fill volume decreased CO and SV and increased TPR and that the changes were more pronounced in the upright position. Moreover, it was found that PD patients have a CO and an SV similar to what has been found in heart failure patients. It was also shown that the cardiovascular response from the supine to upright position was preserved.

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