Noninvasive haemodynamic studies in haemodynamically challenged patients

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Acute effects of peritoneal dialysis on haemodynamics
CHAPTER 6

Introduction

Cardiovascular mortality in patients with end-stage renal disease is extremely high compared to the normal population, in both patients receiving haemodialysis (HD) as renal replacement therapy, and in patients on continuous ambulatory peritoneal dialysis (CAPD). [1] The latter has a theoretical advantage over the former because of the steady-state situation. Better short term control of hypertension [2] and less abrupt changes in intravascular volume are possible advantages of CAPD. Yet, it has been shown that fluid shifts during the first 30 minutes of CAPD can be as large as those observed in HD. [3] Studies on the haemodynamic effects of peritoneal dialysis (PD) have shown conflicting results, [4-6] possibly due to opposing effects of ultrafiltration and intraperitoneal fluid on cardiac output. To investigate the short-term haemodynamic response in relation to ultrafiltration characteristics, we studied the effects of the instillation and dwell of PD solutions on cardiovascular responses. This was done during standard peritoneal permeability analysis (SPA).

Methods

Patients

The study group consisted of 26 consecutive patients on CAPD who underwent a SPA as routine patient care. The mean age of the study group was 54 years (range 29-79). All patients had been stable for at least 3 months on CAPD, with an average of 15 months (range 3 months to 7 years). None of the patients had clinical evidence of overhydration. During the measurements patients sat semirecumbent in a dialysis chair, in a temperature-controlled room with an ambient temperature of 22°C during the whole procedure. Patients had not had anything to eat or drink since 2400 hr the day before, and were asked to refrain from eating, and drinking (with the exception of small amounts of water) during the investigation. Antihypertensive medication had not been taken within 10 hours before the investigation. The registrations of 5 patients were rejected; 4 due to an unreliable plethysmogram of the Portapres [Portapres model-2, TNO Biomedical Instrumentation (TNO-BMI); Amsterdam, The Netherlands] blood pressure recording and 1 patient because of many artefacts in the registration. As a result, 21 recordings were analysed. The characteristics of these patients are presented in Table 1.

SPA procedure

A SPA is a routine investigation, performed in patients on CAPD approximately 3 months after the start of CAPD and every 12 months thereafter to study the function of the peritoneal membrane. [7] The procedure is as follows: Upon arrival in the hospital, the night
Table 1 Patient Characteristics

<table>
<thead>
<tr>
<th>Pt</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Primary renal disease</th>
<th>Time on CAPD (months)</th>
<th>Antihypertensive drugs</th>
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</table>

Abbreviations: Pt, patient; NSAID, nonsteroidal anti-inflammatory drug

dwell dialysate is drained from the peritoneal cavity (phase 1). Thereafter, the peritoneal cavity is rinsed by filling it with a low osmolar dialysate (1.36% glucose, Dianeal; Baxter Utrecht, The Netherlands), phase 2. The rinsing fluid is immediately drained (phase 3). Finally, the peritoneal cavity is filled (phase 4) with a high osmolar dialysate (3.86% glucose, Dianeal), which is primed with dextran 70, 1 g/L. (Hyskon; Medisan Pharmaceuticals AB, Uppsala, Sweden) to study peritoneal fluid kinetics during the SPA. Dialysate samples are taken at regular intervals to determine the time course of the changes in intraperitoneal volume. Peritoneal diffusion capacity is expressed as the mass transfer area coefficient, (MTAC). The methods applied have been described in detail by Pannekeet et al. [7] The amount of instilled dialysis solution, either 1.5 L or 2 L, was similar to the usual amount of dialysate in that patient. As such, the SPA resembles a normal CAPD exchange. The dialysate (rinsing solution and test solution) is warmed in a microwave oven to a temperature of 38°C.
On the day of the SPA residual glomerular filtration rate (GFR), calculated as the mean urea and creatinine clearance, is determined.

**Haemodynamic monitoring**

During the complete phase 1-3 and the first 30 minutes of the phase 4 of the SPA noninvasive finger pressure was measured in all patients with a Portapres model-2, which is the portable version of the Finapres (TNO-BMI). [8] This method has been extensively validated in healthy persons, [8-12] in elderly patients with vascular disease [13] and in patients with septic shock. [14] Portapres usually underestimates mean and diastolic blood pressure in patients with vascular disease. Yet, differences in blood pressure are tracked accurately. [13] This technique has also recently been applied in HD patients. [15]

Measurements were performed on the middle finger of the right hand when no arteriovenous fistula used for dialysis access was or had been present. Otherwise, the left hand was taken. Procedures were started after the signal had been stable for at least 5 minutes. Events were marked with an electronic time marker. The hand that was used for Portapres blood pressure measurement was in the same position throughout the whole registration period. A height correction system, to correct for the difference in height between the hand and the heart, was present. The continuous blood pressure waveform was sampled at 100Hz with 0.25 mmHg resolution and stored on a digital flash-memory card after data compressing.

**Data-analysis**

Off-line artefact rejection of the finger arterial pressure tracing was performed visually. Beat-to-beat values of systolic and diastolic blood pressure (SBP and DBP), mean arterial pressure (MAP) and heart rate (HR) were determined from the continuous finger arterial pressure signal with the Beatfast program (TNO-BMI). Left ventricular stroke volume (SV) was estimated on a beat-to-beat basis using the Modelflow method. [16] This method computes aortic flow pulsations from central or peripheral arterial pressure waveform using a non-linear, time-varying three-element model which consists of the characteristic impedance of the aorta, arterial compliance and peripheral vascular resistance. This method has been validated extensively against thermodilution in healthy subjects, [17] in patients undergoing heart surgery [16,18] and in patients with septic shock. [14] Once calibrated, Modelflow accurately tracks changes in SV, cardiac output (CO) and total peripheral resistance (TPR) with a 2% error (SD 8%). [16] When calibration with thermodilution is not performed, as in our study, changes in BP, SV, CO and TPR, as calculated by Modelflow, are expressed as percentage change from baseline. For more detailed information on the Modelflow method we refer the reader to the study by Harms et al. [17]
**Statistics**

All parameters were tested for the presence of a normal distribution. First, all serial changes in the aforementioned parameters were tested with a two-sided ANOVA. In case of statistically significant changes, further analysis was performed using a 2-way paired Student’s t-test. A correlation coefficient was calculated to investigate the relationship between different parameters. Results were considered statistically significant with a 95% limit of probability. All values are expressed as means ± standard deviation (SD).

**Results**

*Portapres recorded BP and HR*

The baseline SBP after a stable signal had been obtained was 124 ± 22 mmHg, DBP 66 ± 13 mmHg. During phase 1 the BP remained stable, but HR decreased from 85.6 ± 12.1 beats/minute (bpm) to 83.5 ± 11.4 bpm (p<0.005). During the ensuing phases of the SPA no significant changes in HR were seen. Instillation of the rinsing solution (duration: 6.7 ± 1.7 minutes) induced a rise in SBP in 16 of the 21 patients from 127 ± 26 mmHg to 134 ± 27 mmHg (p < 0.005). The DBP rose from 67 ± 13 mmHg to 72 ± 12 mmHg (p< 0.005). During drainage of the rinsing solution, no change was seen in BP, but subsequent instillation and dwell of the test solution was accompanied by a further rise in BP: SBP rose 8 ± 14 mmHg to a maximum of 142 ± 23 mmHg, (p < 0.05), DBP increased 6 ± 8 mmHg to 77 ± 14 mmHg (p<0.005) (Figure 1). These changes were not correlated with the use of the various classes of antihypertensives.

*Haemodynamic parameters*

No significant change in SV could be detected, although there was a tendency to a reduction in SV during phase 4. Cardiac output decreased almost 6% in phase 4 while during other phases, no significant change in CO was seen. The rise in BP during phases 2 and 4 could be attributed to a rise in peripheral resistance, despite the aforementioned decrease in CO, increasing more than 25% almost exclusively during phase 2 and phase 4 (both p<0.05), as shown in Figure 2.

*Peritoneal transport characteristics*

Intraperitoneal volume increased 225 ± 99 ml during the first 30 minutes of phase 4. This was not related to the change in SV during the same period, and also not to SBP, DBP, CO or TPR. The MTAC of creatinine, a measure of peritoneal diffusion capacity, was not correlated with the rise in BP.
Figure 1 Change in systolic, diastolic blood pressure (SBP, DBP) and heart rate (HR) during standard peritoneal permeability analysis (SPA).

* p < 0.05; ** p < 0.01; *** p < 0.005
Figure 2 Change in stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR) during standard peritoneal permeability analysis (SPA).

* p < 0.05; ** p < 0.01; *** p < 0.005
**Residual renal function**

Residual GFR could be determined in all patients except one. The mean value was 2.2 ml/min, range 0 - 8.7 ml/min. Residual renal function was not correlated with the change in BP.

**Discussion**

It is well known that ultrafiltration during haemodialysis affects haemodynamics. [15,19] Although fluid shifts during the first half hour of PD may approach 500 ml/30 min., [3] few studies have investigated the influence of those fluid shifts (as measured by the change in intraperitoneal volume) or the filling of the peritoneal cavity on haemodynamic parameters such as BP, HR, SV, CO and TPR.

In an unselected CAPD population we found a distinct rise in BP during the annual SPA, when measured by means of continuous noninvasive Finapres technique. This rise occurred both during instillation of the rinsing fluid (1.36% glucose, phase 2) and instillation of the test bag (3.86% glucose, phase 4).

A rise in blood pressure upon instillation of PD fluid has been described in a short report of Fleming and co-workers. [6] They found a higher systolic and diastolic blood pressure, when comparing ‘full’ (dialysate instilled) and ‘empty’ (dialysate drained) conditions in 8 subjects. Blood pressure was measured using an oscillometric method, recording BP and HR every 2 minutes. The average rise in SBP in the full condition was 5.6 mmHg, the rise in DBP was 3.5 mmHg. They were not able to describe the underlying haemodynamic changes. The rise in BP in our population was larger, and reproducible with two different dialysate concentrations. Others, however, using invasive monitoring, did not find a rise in blood pressure, but they reported a decrease in CO immediately upon instillation of the dialysate within the intraperitoneal cavity, and a compensatory rise in peripheral resistance. [4,5] Although the same underlying mechanism was probably present in these patients as in those studied by us, BP was not affected. This might be explained by the acute indication for PD in the study of Swartz et al., [4] who investigated patients with acute renal failure, while we investigated patients who were stable on CAPD. Pacifico et al. [5] investigated patients under sedation and analgesia and used a different dialysis solution with a low osmolality.

Stroke volume did not change significantly despite the 225 ml removed from the extracellular volume during the first 30 minutes of the dwell. This might be due to subclinical overhydration, which has been reported before in PD patients, [20] or due to a compensatory increase in stroke volume due to compression of the mesenteric vasculature by the PD fluid. The rise in blood pressure could be fully attributed to an increase in total peripheral
resistance. A possible explanation could be an increment in local splanchnic or systemic resistance due to glucose induced insulin release. This might have been the case because insulin has been shown to induce arteriolar vasoconstriction in case of endothelial dysfunction. [21] However, our observation of a similar, albeit initial, response after 1.36% glucose and 3.68 % argues against a glucose-related effect. Also, the similar reaction in diabetic and non-diabetic patients does not support a direct role for glucose.

Sympathetic activation as a result of stretching of structures within the peritoneal cavity or pain related to fluid instillation might offer alternative explanations for the increased peripheral resistance. Noxious effects of the dialysate might also induce sympathetic activation but, to the best of our knowledge, sympathetic activity has not been studied during instillation of CAPD fluid. Finally, the dialysate might also have a direct mechanical effect on splanchnic vasculature.

In this study we have shown that blood pressure rises upon instillation of PD fluid. This rise is caused by an increase in total peripheral resistance, possibly caused by sympathetic activation or mechanical effects. Despite the continuous nature of the technique, PD patients might be subjected to considerable blood pressure fluctuations.
CHAPTER 6

References


Effect of PD on haemodynamics


