Automated peritoneal dialysis with ‘on-line’-prepared bicarbonate-buffered dialysate: technique and first clinical experiences

Reinhard Brunkhorst1, Stefan Fromm1, Eike Wrenger2, Axel Berke3, Ruth Petersen1, Gerhard Riede3, Juergen Westphale1, Enrico Zamore1 and Ingrid Ledebo3

1Division of Nephrology, Medizinische Hochschule Hannover, 2Division of Nephrology, Otto-von-Guericke-University Magdeburg, Germany and 3Gambro, Lund, Sweden and Munich, Germany

Abstract

Background. Automated peritoneal dialysis (APD) has the possibility of increasing the dialysis efficacy by using higher fill volumes, frequent dialysate exchanges, and tidal techniques. It is then possible to treat patients adequately without residual renal function. The drawbacks of the required high amounts of dialysis solution of up to 30 litres per session are the high costs of lactate-based dialysate bags and difficulties for the patients in handling these bags. So far, bicarbonate-based peritoneal dialysate, which may be more biocompatible, is only available for CAPD in double-chamber bags. In APD this could be overcome by ‘on-line’ preparation of bicarbonate-buffered dialysate using advanced technologies originally designed for on-line preparation of substitution fluid for haemofiltration.

Methods. Four patients without residual renal function were treated with APD five times weekly in a crossover study design. Patients received standard lactate-based (35 mmol/l) treatment (25 litres per session each) in weeks 1 and 3. In week 2 on-line-produced bicarbonate-buffered (37 mmol/l) dialysate was used. This dialysate was prepared by an AK 100 Ultra haemodialysis machine. The machine was modified for adding glucose from a 50% concentrate to the desired concentration of 1.7%. Electrolytes, pH, pCO2, and dialysis efficacy parameters were measured. Microbiological testing was carefully performed.

Results. Creatinine clearances, Kt/V, and pCO2 did not vary between the different treatment phases, whereas the pH showed a distinct increase during the bicarbonate phase. Repeated determinations of endotoxins and culturing showed no contamination of the dialysate. The composition of the produced dialysate was reproducible with respect to pH, pCO2, sodium, calcium and bicarbonate, whereas the glucose concentration varied by ± 20%.

Conclusions. On-line preparation of PD fluid with the AK 100 Ultra is easy and safe to handle. APD with dialysate containing 37 mmol/l bicarbonate provides improved acid-base balance and possibly improved biocompatibility, and may lead to a significant cost reduction. Further development in order to provide smaller machines and more precise ways of achieving a desired dialysate glucose concentration is necessary.

Key words: automated peritoneal dialysis; bicarbonate dialysate; on-line-prepared dialysate

Introduction

The number of patients performing automated peritoneal dialysis (APD) is increasing worldwide [1]. Patients often prefer APD during the night because then the day remains free of any manual bag exchange. The other important reason for the success of APD is the frequent necessity to increase efficacy of the standard continuous ambulatory peritoneal dialysis (CAPD) with four dialysate exchanges in order to obtain adequate dialysis [2–4]. High fill volumes (up to 3.5 litres), short dwell times (in patients with high peritoneal transport characteristics) and tidal techniques are also being applied to APD patients to increase the dialysis clearance in patients who have lost their residual renal function [5]. The total amount of dialysate necessary per dialysis session then can reach up to 30 litres. The negative consequences as e.g. the difficulty to handle the multiple 5-litre-dialysate bags and the fact that the cost of treatment becomes even higher than the costs of centre haemodialysis limits the distribution of APD.

These drawbacks could only be overcome by the on-line preparation of the peritoneal dialysis (PD) fluids as it has been introduced by Tenckhoff et al. [6] and used long-term in smaller numbers of IPD patients, and Quellhorst [personal communication]. However, the opportunity to use advanced technologies, introduced for the on-line preparation of bicarbonate-buffered substitution fluid in haemofiltration and
haemodiafiltration [7], in peritoneal dialysis have not yet been realized.

The following paper summarizes our first experiences with the on-line preparation of PD fluid with a commercially available Gambro AK 100 Ultra haemodialysis machine (Gambro, Lund, Sweden) in four APD patients with respect to safety and handling. Furthermore some of the potential advantages of an 'individualized' preparation of PD-fluid are demonstrated.

Subjects and methods

Patients and treatment protocol

Four stable patients (2 males, 2 females, age 22–49 years), on CCPD for more than 6 months without residual renal function and without prior peritonitis were treated with APD in our centre for 3 weeks in a cross-over study design. The first week (Monday to Friday) APD was performed with standard lactate-buffered dialysate in bags. The second week (Monday to Friday), on-line, bicarbonate-buffered dialysate was used. The third week again standard APD (as in week 1) was performed. Each APD was performed with 25 litres of dialysate for 9 h, there was no filling of the abdominal space between the dialysis sessions.

Venous blood samples were taken at the start of the dialysis session three times weekly (Monday, Wednesday, and Friday) for determination of serum electrolytes, creatinine, urea, pH, and pCO₂. At the end of each phase (on the Friday of each week) the total effluent of the APD session was collected for measurement of dialysis creatinine clearance and Kt/V. Twice per day during the first and during the last hour of treatment, dialysate samples from the reservoir bags were taken for analysis for endotoxins, bacterial contamination, electrolytes, glucose, pH, and bicarbonate content.

Fluid preparation

The peritoneal dialysate was prepared by an AK 100 Ultra (Gambro, Lund, Sweden) in the same way as it prepares i.v.-quality substitution solution for haemofiltration and haemodiafiltration (Figure 1). Water treated by reverse osmosis and having a defined chemical and microbiological quality was used. This water was filtered through a U 7000 ultrafilter before entering the machine. Then it was mixed in the proportions set on the machine with electrolytes from a standard acid concentrate and from BiCart® (Gambro, Lund, Sweden). This solution was filtered again in a U 7000 ultrafilter which is part of the AK 100 Ultra. Finally, glucose from a 50% i.v. infusion fluid was added to the desired concentration. The glucose-containing solution was now filtered through a small ultrafilter, U 2000, incorporated in the fluid line. This fluid was transported to the APD machine, a Gambro PD 100, where it was distributed among a set of empty bags, one being the heater bag and the others hanging on the APD machine. This setting 300 ml of fluid were prepared per minute, that means approximately 18 l/h. The on-line-prepared fluid can in parallel be distributed to several APD machines.

The following material was used for the fluid preparation: a bicarbonate column (BiCart®, Gambro, Lund, Sweden); acid dialysate concentrate D246® (Gambro, Lund, Sweden) containing Na⁺ 138 mmol/l, K⁺ 0 mmol/l, Ca²⁺ 1.5 mmol/l, Mg²⁺ 0.75 mmol/l, Cl⁻ 108.5 mmol/l, acetate 3.0 mmol/l, sterile glucose solution (500 g/l, Kabi Pharmacia, Lund, Sweden), special lines for fluid production, a standard AK 100 ULTRA, and a standard PD 100 cycler.

Dialysate composition

In this first clinical test the composition of the on-line prepared dialysate was chosen as follows: 37 mmol/l of bicarbonate, glucose 1.8%, sodium 138 mmol/l, chloride 105 mmol/l, calcium 1.5 mmol/l, and magnesium 0.75 mmol/l. The control lactate solution was a standard dialysate containing 35 mmol/l of lactate, glucose 1.25–2.25%, sodium 132 mmol/l, chloride 102 mmol/l, calcium 1.5 mmol/l, and magnesium 0.75 mmol/l. The higher sodium concentration of the bicarbonate solution was chosen because this solution was at that time the only one applicable in this experimental setting. The testing for the composition of the on-line prepared fluid was performed with electron-sensitive electrodes (Beckman Instruments, Mijdrecht, The Netherlands).

Dialysis efficacy

Dialysis efficacy was measured by standard methods. A 20-ml sample of the effluent on the Fridays of each week was analysed for creatinine and urea and the total drain volume was determined. By these means and the analysis of the serum, the dialysis clearances for creatinine and urea were determined. Kt/V for urea was calculated according to the formula: (urea clearance/week)/total body-water volume. Total body-water volume was estimated by standardized nomograms [8].

Microbiological investigations

A Swinnex filter holder containing a 0.2 µm membrane was inserted into the line between the reservoir bags and the PD 100 cycler. Fluid was collected on the membrane filters. Samples for endotoxin testing were taken directly from the reservoir bags. The membrane filters were cultivated for bacteria on TGEA (tryptone glucose extract agar) for 7 days.
at 20 ± 2°C. The test for endotoxins was performed using a gel clot method (Endo LAL from Chromogenix, Malmö, Sweden) with a sensitivity of 0.03 EU/ml.

**Results**

**Dialysis efficacy**

The creatinine clearances and the Kt/V of the four patients in the three treatment periods together with the means of the pH and the pCO₂ (three measurements each) are summarized in Table 1. There were no marked differences between any of the parameters measured during the standard PD periods and the period of 'on-line' PD except the distinct increase of the serum pH during the 'on-line' PD period (using bicarbonate-buffered dialysate). Plasma sodium concentrations did not differ significantly between the test periods.

**Microbiological investigations**

Repeated determinations (two measurements during each dialysis session) of endotoxins revealed no contamination (<0.03 EU/ml) of the on-line-prepared dialysate. Furthermore, during all test periods no bacterial contamination of the dialysate was detected.

**Dialysate composition**

The composition of the dialysate was reproducible and stable with respect to its pH, sodium and bicarbonate content from one dialysate preparation to another and from the beginning of each session to the end. Mean values in the on-line-prepared dialysate fluid were 135 ± 3 mmol/l of sodium, 36.6 ± 0.6 mmol/l of HCO₃⁻ and 7.3 ± 0.1 pH at the start and 135 ± 4 mmol/l of sodium, 36.1 ± 0.5 mmol/l of HCO₃⁻, and 7.3 ± 0.2 pH respectively at the end of the dialysis sessions. The glucose concentration, however, varied considerably from session to session (1.7 ± 0.4 mg/dl × 10) but remained stable to the end of the dialysis sessions (1.7 ± 0.3 mg/dl × 10).

**Discussion**

This first report on the 'on-line' preparation of PD fluid demonstrates, that this alternative technique is feasible and offers considerable advantages. The basis for our favourable experience is the proof, that the Gambro AK 100 Ultra machine produces a dialysis fluid that is free from bacteria and endotoxins. Our repeated examinations confirmed the results of prior microbiological testings performed when the device was used for the on-line production of intravenous substitution fluids for haemofiltration [9,10].

The composition of the prepared fluid was reproducible with respect to its electrolyte, bicarbonate, and pH content. However, there was a more than 20% variation of the glucose concentration in the dialysate. This finding is attributable to the technique used for adding the necessary 30% glucose solution with a rather insensitive pump, originally designed to transport the substitution fluid during haemofiltration. The dialysate was prepared directly before starting the APD session and remained in polyethylene bags until the end of dialysis (7–9 h). The fluid remained stable during this time with respect to its glucose and electrolyte content. Moreover, the concentrations of CO₂ and HCO₃⁻ did not change considerably over time.

Our four patients showed metabolic acidosis during both periods of standard lactate peritoneal dialysis, which has been described as a problem in some patients on chronic peritoneal dialysis [11,12]; other PD patients have a normal or even alcalotic metabolic state [13,14]. Acidosis disappeared in all four patients after 2 days of peritoneal dialysis with 37 mmol/l bicarbonate-containing dialysis solution.

There are several considerable advantages of the on-line production of PD-fluid: (i) The difficulty of handling 5-litre bags, a disadvantage of home APD at least for handicapped patients, is avoided. Additionally, the amount of waste is reduced. (ii) In the long term the costs are reduced. This becomes relevant with regard to the growing trend towards APD in CAPD patients with inadequate dialysis parameters [15]. (iii) PD fluid can be produced according to the individual needs of the PD patient. The

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Parameters</th>
<th>Standard PD I</th>
<th>On-line PD</th>
<th>Standard PD II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 NH</td>
<td>Kt/V; CreaCl</td>
<td>1.83; 54</td>
<td>1.87; 55</td>
<td>1.79; 53</td>
</tr>
<tr>
<td>2 VS</td>
<td>1.72; 53</td>
<td>1.70; 53</td>
<td>1.79; 53</td>
<td></td>
</tr>
<tr>
<td>3 SS</td>
<td>1.96; 62</td>
<td>1.90; 63</td>
<td>1.92; 60</td>
<td></td>
</tr>
<tr>
<td>4 DR</td>
<td>1.56; 49</td>
<td>1.59; 51</td>
<td>1.60; 62</td>
<td></td>
</tr>
<tr>
<td>1 NH</td>
<td>pCO₂; pH</td>
<td>42; 7.31</td>
<td>48; 7.42</td>
<td>43; 7.34</td>
</tr>
<tr>
<td>2 VS</td>
<td>48; 7.26</td>
<td>43; 7.38</td>
<td>46; 7.29</td>
<td></td>
</tr>
<tr>
<td>3 SS</td>
<td>43; 7.31</td>
<td>46; 7.41</td>
<td>45; 7.32</td>
<td></td>
</tr>
<tr>
<td>4 DR</td>
<td>46; 7.29</td>
<td>48; 7.43</td>
<td>47; 7.35</td>
<td></td>
</tr>
</tbody>
</table>
bicarbonate as well as the calcium or sodium content can be modified as required by the metabolic situation of the patient. (iv) No heat-induced glucose degradation products are generated during the production of the fluid, another factor that might increase the biocompatibility of PD fluid.

In summary the on-line preparation of PD fluid with the AK 100 Ultra is easy and safe to handle. APD with dialysate containing 37 mmol/l bicarbonate provides improved acid–base balance and possibly improved biocompatibility. On-line prepared PD fluid may lead to a significant cost reduction and can be varied (with respect to glucose, electrolyte, and buffer concentrations) according to the needs of the individual patient. It seems urgently necessary that this promising technique will be further developed in order to provide smaller machines and more precise ways of adding the glucose component of the dialysate.

References


Received for publication: 7.1.98
Accepted in revised form: 3.8.98