**In vitro** biocompatibility evaluation of a novel bicarbonate-buffered amino-acid solution for peritoneal dialysis

A. Jöres\(^1\), G. M. Gahl\(^1\), K. Ludat\(^1\), U. Frei\(^1\) and J. Passlick-Deetjen\(^2\)

\(^1\)Abteilung für Innere Medizin mit Schwerpunkt Nephrologie und Internistische Intensivmedizin, Virchow-Klinikum der Humboldt-Universität zu Berlin, Berlin; \(^2\)Fresenius Medical Care, Oberursel, Germany

**Abstract**

**Background.** Conventional lactate-buffered peritoneal dialysis fluids containing glucose as the osmotic agent have been shown to compromise important peritoneal host defence functions. The current study employed an *in vitro* model using activated peripheral blood mononuclear leukocytes (PBMC) for the preclinical biocompatibility assessment of a novel bicarbonate-buffered peritoneal dialysis fluid containing 1.0% amino acids as the osmotic agent.

**Methods.** PBMC (5 \times 10^6/ml) were pre-exposed (10–30 mm, 37°C) to bicarbonate-buffered 1% amino-acid solution, bicarbonate- or lactate-buffered 1.5% glucose fluid, or control medium (RPMI). The cells were then washed and stimulated for 2 h at 37°C in RPMI containing 100 ng/ml *E. coli* endotoxin from strain O55:B5. The cytokines IL-6 and TNFα in cell supernatants were assessed using specific enzyme immunoassays, cytokine mRNA expression by reverse transcription polymerase chain reaction.

**Results.** Short, i.e. 10 min, exposure to conventional, lactate-buffered glucose fluid resulted in a significant and time-dependent inhibition of cytokine release and mRNA expression by activated PBMC, whereas the cytokine response was improved even following prolonged (up to 2 h) exposure to bicarbonate-buffered 1% amino-acid solution or bicarbonate-buffered 1.5% glucose fluid.

**Conclusions.** Our results suggest that very short, i.e. potentially clinically relevant, exposure to conventional dialysis fluid impairs the cytokine response by activated leukocytes. In this respect, the use of bicarbonate-buffered solutions containing 1.0% amino acids or 1.5% glucose may result in improved biocompatibility properties.

**Key words:** peritoneal dialysis; peritoneal dialysis fluids; bicarbonate buffer; amino acids; cytokines; interleukin-6; tumour necrosis factor; biocompatibility; *in vitro* study

**Introduction**

The continuous absorption of glucose from the peritoneal cavity of patients treated with continuous ambulatory peritoneal dialysis may lead to the development of obesity and hyperdyslipidaemia [1,2] whereas at the same time, loss of amino acids and proteins into the peritoneal dialysate may contribute to negative nitrogen balance and malnutrition [3,4]. An elegant way to ameliorate both problems could be the substitution of glucose by amino acids as the osmotic agent. Indeed, earlier studies using a lactate-buffered amino-acid solution have shown its clinical feasibility and efficacy [5–10].

In addition to these clinical considerations, the potential bioincompatibility of current dialysis fluids has gained increasing interest of researchers in the field of peritoneal dialysis. The background of these thoughts is the fact that the composition of conventional peritoneal dialysis fluids is clearly unphysiological: (i) in order to achieve water ultrafiltration their osmolality is increased to 360–511 mOsm/kg by addition of high glucose concentrations (15.0–42.5 g/l), and (ii) their pH is buffered to 5.2–5.5 with high lactate concentrations (35–40 mmol/l) in order to prevent glucose caramelization during the industrial heat sterilization process. In the past years several studies have therefore used *in vitro* experimentation for the evaluation of potential adverse effects of these dialysis fluids on various cell populations (for reviews see [11,12]). Among other things it has been shown that current dialysis fluids impair the capacity of leukocytes regarding phagocytosis, oxygen radical production, and killing of micro-organisms [13–17] as well as their ability to produce and secrete different immune mediators which are believed to play a pivotal role in the initiation and control of peritoneal inflammation [18–22]. In addition, adverse effects of conventional dialysis fluids on mesothelial cell viability and function...
have been reported recently [23–26]. Although the potential clinical relevance of these in vitro findings is unclear, since conclusive clinical data are at present lacking, the fact that the average CAPD patient is exposed to approximately 3000 litres of dialysis fluids per year has stimulated a search for alternative solutions with a more physiological composition and, at least theoretically, improved biocompatibility properties.

An earlier study investigating two different amino-acid solutions suggested that these fluids may exert even worse adverse effects with regard to peritoneal macrophage function as compared to glucose fluids with similar hyperosmolality [27]. These solutions, however, contained very high concentrations of lactate (48 mmol/l) so that a distinction between intrinsic effects of the amino acids and of the high lactate content [28] is not possible.

The current study employed an established in vitro model [19,20,29] using activated peripheral blood mononuclear leukocytes (PBMC) for the preclinical biocompatibility evaluation of a novel, bicarbonate-buffered peritoneal dialysis fluid (Aminobic, Fresenius) containing 1.0% amino acids as the osmotic agent. The finding that even short (10–30 min) exposure to conventional dialysis fluids impairs the cytokine response of PBMC to bacterial endotoxin challenge, whereas at the same time cell function is preserved following exposure to Aminobic, suggests improved biocompatibility properties of this bicarbonate-buffered amino-acid solution.

**Materials and methods**

**Peritoneal dialysis solutions**

The composition of the test fluids is shown in Table 1. All solutions were obtained from Fresenius AG, Bad Homburg, Germany. CAPD 2 fluid was supplied in a standard one-chamber bag, the bicarbonate-buffered solutions in two-chamber bags.

**Cell separation and incubation procedures**

PBMC were isolated from the peripheral blood of healthy volunteers by Ficoll density gradient centrifugation (Ficoll–Hypaque, Pharmacia, Uppsala, Sweden) under strictly sterile conditions (laminar air flow) as described previously [19,20,29]. All reagents used for cell separation and incubation experiments were LAL negative. The PBMC fraction consisted of 15–30% monocytes, 60–70% lymphocytes, <10% granulocytes, and few erythrocytes and thrombocytes, as established by light-microscopy and dual-colour flow cytometry. Cell viability by trypan blue exclusion test was >95% before incubation.

Aliquots obtained from one individual donor, each containing 5 × 10⁶/ml PBMC, were used for each series of the incubation experiments. All materials used were cell culture grade (Nunc, Wiesbaden, Germany). For experiments targeting cytokine release, aliquots were pre-exposed (10–30 mm, 37 °C) to Aminobic bicarbonate-buffered (Bic 20), or conventional lactate-buffered (CAPD 2) 1.5% glucose fluid, bicarbonate-buffered 4.25% glucose solution (Bic 30), or control medium (RPMI-1640, Sigma, Deisenhofen, Germany). Subsequently the cells were washed in RPMI and stimulated for 2 h at 37 °C in RPMI medium containing 100 ng/ml endotoxin from E. coli O55:B5 (Sigma). Parallel experiments were performed coincubating PBMC (2 h, 37 °C) in the respective fluids in order to assess maximum toxicity.

The incubation experiments were terminated by rapid centrifugation, and the supernatants were frozen (−80 °C) until cytokine determination. Parallel experiments targeting cytokine mRNA expression were performed coincubating PBMC (1 × 10⁶ cells/ml) in the different test fluids for 45 min followed by RNA extraction (see below).

**Table 1. Composition of test fluids**

<table>
<thead>
<tr>
<th></th>
<th>CAPD 2</th>
<th>Bic 20</th>
<th>Bic 30</th>
<th>Aminobic*</th>
</tr>
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<tbody>
<tr>
<td>Na+ (mmol/l)</td>
<td>134</td>
<td>134</td>
<td>134</td>
<td>137</td>
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<tr>
<td>CL (mmol/l)</td>
<td>103.5</td>
<td>104.5</td>
<td>104.5</td>
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<tr>
<td>Ca²⁺ (mmol/l)</td>
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<td>1.75</td>
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<tr>
<td>Mg²⁺ (mmol/l)</td>
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<tr>
<td>Lactate (mmol/l)</td>
<td>35</td>
<td>–</td>
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<td>–</td>
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<tr>
<td>HCO₃⁻ (mmol/l)</td>
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<td>34</td>
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<tr>
<td>Glucose (g/l)</td>
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<tr>
<td>Ammonium* (g/l)</td>
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<td>–</td>
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<td>Osmolality (mOsm/kg)</td>
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<td>7.2–7.6</td>
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* Amino acid composition of Aminobic:

<table>
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<th>Essential amino acids (mmol/l):</th>
<th>Non-essential amino acids (mmol/l):</th>
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</thead>
<tbody>
<tr>
<td>L-histidine 3.222</td>
<td>L-alanine 6.73</td>
</tr>
<tr>
<td>L-isoleucine 5.72</td>
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<td>L-lysine 7.18</td>
<td>Proline 3.91</td>
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<tr>
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</tr>
<tr>
<td>L-phenylalanine 3.33</td>
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</tr>
<tr>
<td>L-threonine 7.05</td>
<td>L-tyrosine 0.52</td>
</tr>
<tr>
<td>L-tryptophan 2.01</td>
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</tr>
<tr>
<td>L-valine 14.51</td>
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</table>

TNFα and IL-6 in cell supernatants

TNFα and IL-6 in cell supernatants were determined by specific enzyme immunoassay as described previously [20,30]. For TNFα determination, microtitre strips (Nunc, Wiesbaden, FRG) were coated with an affinity-purified polyclonal goat anti-human TNFα antibody (Bissendorf Biochemicals, Hannover, Germany) as the solid phase. The TNFα in samples and standards was then detected by a sequence of incubations with (i) a mouse monoclonal anti-human TNFα IgG antibody (Bissendorf Biochemicals, Hannover, Germany); (ii) a goat anti-mouse IgG antibody coupled to horse-radish peroxidase (Jackson, West Grove, PA, USA), and (iii) 3,3′,5,5′-tetramethyl benzidine substrate buffer for colour development (Fluka, Buchs, Switzerland). The TNFα content of unknowns was calculated from a standard curve using recombinant human TNFα standards (Boehringer, Mannheim, Germany) ranging from 20–2000 pg/ml. The lower detection limit of the assay was 8 pg/ml (zero mean ± 3 standard deviations). No cross-reactivity with recombinant TNFβ, interleukin-1α IL-1α, IL-2, IL-3, IL-4, and IL-6 was observed when these cytokines were added to blank samples.
in amounts up to 50 ng/ml (recombinant cytokines were obtained from British Biotechnology, Cowley, Oxford, UK).

The materials used for IL-6 determination were:
(a) Coating antibody: affinity-purified polyclonal rabbit anti-mouse IgG antibody (Dakopatts, Hamburg, Germany)
(b) Primary antibody: mouse monoclonal anti-human IL-6 antibody (Serva, Heidelberg, Germany)
(c) Secondary antibody: polyclonal anti-human IL-6 antibody coupled to biotin (R&D Systems, Minneapolis, USA)
(d) Standards (20–2000 pg/ml): recombinant human IL-6 (Janssen, Beerse, Belgium).

The lower detection limit of the IL-6 assay was 20 pg/ml. No cross-reactivity with recombinant TNFα or TNFβ, interleukin-1α, IL-1β, IL-2, IL-3, and IL-4 was observed when these cytokines were added to blank samples in amounts up to 50 ng/ml (recombinant cytokines were obtained from British Biotechnology, Cowley, Oxford, UK).

RNA extraction, reverse transcription and polymerase chain reaction (PCR)

RNA extraction, reverse transcription, and PCR were performed essentially as described previously [29]. Briefly, total RNA was extracted from the cell pellets of the incubations by the RNAzol method as described by the manufacturer (Cinna-Biotex Laboratories, Houston, TX, USA). One microgram total RNA was heat denatured at 95°C for 3 min in the presence of 100 pmol random hexamer (Pharmacia, Freiburg, Germany) and cooled on ice for 2 min. The RNA was reverse transcribed in a final volume of 20 μl of lx PCR buffer (10 mM Tris (pH 8.3), 50 mM KCl, 1.5 mM MgCl2, 0.001% gelatin) and 625 nM of each dNTP (Boehringer, Mannheim, Germany), 20 U of RNAsin (Promega, Heidelberg, Germany), 10 mM dithiothreitol, and 200 U of MMuLV reverse transcriptase (Gibco-BRL, Berlin, Germany). The reaction mixture was incubated for 10 min at room temperature, 45 min at 42°C, and 5 min at 95°C.

PCR amplification of TNFα cDNA was carried out in a total volume of 50 μl (2 ml of reverse transcription product and 48 ml master mix (36.25 ml H2O, 1.25 ml 3-primer (20 μmol/l), 1.25 ml 5-primer (20 μmol/l), 4 ml nucleotide triphosphate, 5 ml lx PCR buffer, and 0.25 ml Taq polymerase (2.5 U, Amplitaq, ILS Ltd, London, UK)) using a Perkin-Elmer model 480 thermocycler (Perkin-Elmer, Überlingen, Germany). The PCR protocol was as follows: first cycle, 94°C for 3 min, 55°C for 1 min, 72°C for 1 min; second to 24th, 25th or 32nd cycles, 94°C for 1 min, 55°C for 1 min, 72°C for 1 min. The final cycle was 94°C for 1 min and 60°C for 10 min. PCR was performed for 25 cycles with 3-actin, for 26 cycles with IL-6, and for 33 cycles with TNFα.

One-tenth of the PCR reaction products was separated by electrophoresis on 1.5% agarose gels, stained with ethidium bromide, and photographed. The negatives were scanned for densitometry (Scanpack System, Biometra, Göttingen, Germany), and the relative density of the TNFα and IL-6 transcripts was compared to the actin controls.

Oligonucleotide primers

The sequences of the amplification primers were as follows:

Statistical analysis

All data was analysed on IBM PC 486–66 using SPSS8 for Windows version 5.0.2 (SPSS, Munich, Germany). The Wilcoxon signed-ranks matched-pairs test or non-parametric ANOVA statistics were used where appropriate, and a two-sided P value of <0.05 was considered as being statistically significant.

Results

Effect of dialysis fluids on steady-state cytokine mRNA content of PBMC

Unstimulated control PBMC showed weak constitutive expression of both TNFα and IL-6 mRNA transcripts, which were markedly enhanced following stimulation of control PBMC with E. coli LPS. Intact mRNA expression was observed in cells stimulated in the presence of either Aminobic or low-glucose, bicarbonate-buffered solution (Bic 20). In contrast, both conventional, lactate-buffered low-glucose fluid (CAPD 2) and high-glucose, bicarbonate-buffered solution (Bic 30) reduced TNFα and IL-6 mRNA expression to unstimulated background levels (Figures 1, 2).

Effect of short fluid exposure on TNFα release from activated PBMC

Unstimulated control PBMC after 10 min pre-exposure to RPMI medium followed by 2 h recovery in RPMI released only background levels of TNFα (21 ± 7 pg/ml, mean ± SEM; n = 7). TNFα secretion was markedly enhanced following LPS stimulation of control cells (2170 ± 438 pg/ml, P < 0.02). In contrast, 10 min exposure of PBMC to conventional, lactate-buffered low-glucose fluid (CAPD 2) was sufficient to significantly impair the stimulated TNFα response despite a 2 h recovery period (890 ± 291 pg/ml, P < 0.05). The inhibitory effect of CAPD 2 was time dependent, that is, further enhanced following 20 min and 30 min pre-exposure when stimulated TNFα release was reduced to 175 ± 62 and 80 ± 28 pg/ml respectively (P < 0.02). On the other hand neither low- or high-glucose bicarbonate-buffered solution nor Aminobic showed a significant impairment of the TNFα response after 10 min pre-exposure; however, in the case of the hyperosmolar Bic 30 solution, a significant depression of TNFα release was observed after 20 and 30 min pre-exposure, whereas at the same time, cells exposed to Bic 20 and Aminobic showed normal TNFα secretion (Figure 3).

Effect of short fluid exposure on IL-6 release from activated PBMC

Unstimulated control PBMC after 10 min pre-exposure to RPMI medium followed by 2 h recovery in RPMI released only background levels of IL-6 (52 ± 22 pg/ml, mean ± SEM; n = 5). IL-6 secretion was markedly enhanced following LPS stimulation of control cells (1133 ± 385 pg/ml, P < 0.05). In contrast, 10-min exposure of PBMC to conventional, lactate-buffered low-glucose fluid (CAPD 2) significantly impaired the stimulated IL-6 response during the 2 h recovery period (331 ± 117 pg/ml, P < 0.05). In the case of IL-6....
Table II. Sequences of amplification primers

<table>
<thead>
<tr>
<th>Gene</th>
<th>Primers</th>
<th>Product size</th>
<th>Ref.</th>
</tr>
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<tr>
<td>TNFα</td>
<td>5'-ACACCATGAGCACTGAAAGC-3'</td>
<td>525 bp</td>
<td>[31]</td>
</tr>
<tr>
<td></td>
<td>5'-TGATGGCAGAGGAAGGTTG-3'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-6</td>
<td>5'-TACATCTCCGCGATCCCTC-3'</td>
<td>465 bp</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>5'-GGAGCAATGATCTTGATCTT-3'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-Ac tin</td>
<td>5'-TGCTGAGGTACGGGTCTCC-3'</td>
<td></td>
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</table>

Fig. 1. RT-PCR evaluation of IL-6 (upper) and TNFα (lower) mRNA expression as compared to α-actin as an internal control in PBMC exposed to dialysis fluids. Negatives from one representative experiment out of three performed with cells from different donors are shown.

secretion, both low- and high-glucose bicarbonate-buffered solution showed a significant impairment of the IL-6 response after 20–30 min pre-exposure, and Aminobic exerted a significant IL-6 inhibition after 30 min pre-exposure (382 ± 127 pg/ml, P < 0.05). Both Bic 20 and Aminobic, however, showed a significantly improved IL-6 response as compared to conventional, lactate-buffered CAPD 2 (P < 0.05) (Figure 4).

Effect of prolonged fluid exposure on TNFα release from activated PBMC

Unstimulated control PBMC after 2 h incubation in RPMI released only background levels of TNFα (55 ± 25 pg/ml, mean ± SEM, n = 10). TNFα secretion was markedly enhanced following LPS stimulation of control PBMC (2175 ± 519 pg/ml, P < 0.01). The TNFα response was reduced to background levels following 2 h of coincubation in both CAPD 2 and Bic 30 (87 ± 39 pg/ml and 98 ± 34 pg/ml respectively, P < 0.01), whereas no significant change was observed following prolonged exposure to either Bic 20 (1413 ± 596 pg/ml) or Aminobic (1740 ± 484 pg/ml) (Figure 5).

Fig. 2. Densitometric evaluation of PCR gels shown in Figure 1. Data are given as the optical density (O.D.) ratio of either IL-6 (hatched columns) or TNFα (open columns) to α-actin.

Fig. 3. TNFα release from PBMC exposed to test fluids for 10 min (open columns), 20 min (hatched columns), or 30 min (cross-hatched columns) followed by 2 h LPS stimulation in control medium (RPMI). Data are mean ± SEM of seven series of experiments. Asterisks indicate statistical significance (P < 0.05) as compared to stimulated controls (+Control) at the corresponding time-point. Unstimulated controls: (−Control).
Biocompatibility of a bicarbonate-buffered amino-acid solution for CAPD

Equilibration as well as water ultrafiltration, which cannot be perfectly mimicked *in vitro*. Still, *in vitro* models may constitute a useful tool in the preclinical biocompatibility evaluation of novel dialysis solutions since they allow for the detailed study of solution characteristics such as pH/buffer or osmolality/osmotic agent effects under tightly controlled conditions. In the current experimental setup, very short, i.e. potentially clinically relevant, exposure periods followed by a prolonged recovery phase are compared to an ‘unphysiological’ prolonged fluid exposure in order to also assess potential maximum cytotoxicity.

The major findings of this study are the following:

(a) Even very short, i.e. 10-min, exposure to a conventional low-glucose, lactate-buffered dialysis fluid is sufficient to impair the stimulated TNFα response despite a 2 h recovery phase. Since *in vivo*, pH equilibration of instilled dialysis fluids will at least take 20–30 min to reach nearly neutral values, this finding suggests that repeated exposure of peritoneal leukocytes to conventional, acidic solutions may, at least temporarily, reduce their potential to release proinflammatory cytokines in response to bacterial stimuli. With respect to TNFα this might be particularly problematic since this cytokine is believed to be an important factor in the interactions between peritoneal macrophages and mesothelial cells during the initial phase of peritoneal inflammation, inducing mesothelial cells to produce prostaglandins and cytokines [30,34–38].

(b) In keeping with many earlier studies [15,26,29,39–41], the initial low pH of conventional fluids appears to be of primary importance for potentially negative effects on leukocyte functions, since exposure to a bicarbonate-buffered, low-glucose fluid completely reverses the inhibition observed with an otherwise identical lactate-buffered, low-pH solution. Longer pre-exposure periods to a high-glucose fluid, however, lead to a marked inhibition despite the neutral pH of the solution. In this respect it is important to note that unlike pH, the hyperosmolality of instilled dialysis solutions is equilibrated much more slowly, suggesting that a hyperosmolality/glucose effect is likely to occur *in vivo* even when bicarbonate-buffered solutions with very high glucose concentrations are applied.

(c) The novel, bicarbonate-buffered amino-acid solution Aminobic offers improved *in vitro*-biocompatibility properties as compared to conventional fluid or high-glucose bicarbonate fluid in that neither cytokine mRNA expression nor cytokine release are affected following short incubation, and the cytokine response remains improved even after prolonged coincubation (up to 2 h). This is obviously due to the fact that the initial pH of the amino-acid solution is neutral and the hyperosmolality is moderate (369 mOsm/kg). Moreover, the high concentrations of amino acids present in

Discussion

The current study investigated the *in vitro*-biocompatibility of Aminobic, a novel bicarbonate-buffered amino-acid solution for peritoneal dialysis, thereby employing an established model of LPS-activated PBMC. These cells are the circulating precursors of the peritoneal macrophages, and are therefore believed to constitute a valid target for this type of study [11,12]. Compared to *in vitro*-models using peritoneal macrophages isolated from peritoneal dialysis effluent they offer several advantages: (i) they are available in essentially unlimited numbers; (ii) they have not previously been exposed to dialysis solutions, which are the study objective; (iii) they permit the evaluation of fluid effects independent from potential influences of the uraemic milieu. It has to be kept in mind, however, that the direct extrapolation of data obtained during *in vitro* studies to the clinical situation of the CAPD patient is not allowed, since the CAPD cycle *in vivo* constitutes a dynamic cascade of events involving fluid equilibration as well as water ultrafiltration, which cannot be perfectly mimicked *in vitro*. Still, *in vitro* models may constitute a useful tool in the preclinical biocompatibility evaluation of novel dialysis solutions since they allow for the detailed study of solution characteristics such as pH/buffer or osmolality/osmotic agent effects under tightly controlled conditions. In the current experimental setup, very short, i.e. potentially clinically relevant, exposure periods followed by a prolonged recovery phase are compared to an ‘unphysiological’ prolonged fluid exposure in order to also assess potential maximum cytotoxicity.

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this fluid do not appear to have an intrinsic effect on cytokine production by PBMC, at least not during short-term exposure.

In summary, Aminobic as well as the bicarbonate-buffered glucose solutions exhibit, at least under in vitro experimental conditions, improved biocompatibility profiles compared to conventional dialysis fluids. A major point that needs addressing and discussion, however, is whether dialysis fluid biocompatibility is likely to matter in a biological sense, that is, potentially to influence the clinical outcome of the treatment. Quite clearly there is no direct evidence available to date as to this effect since current clinical trials of alternative solutions primarily target at safety and efficacy of these solutions. There are, however, two well-known facts suggesting that biocompatibility of dialysis fluids might, indeed, matter for the long-term outcome of peritoneal dialysis patients. Firstly, many CAPD patients are lost from the programme due to therapy failure within very few years: up to 50% of the patients starting CAPD leave the programme within the first 3 years, frequent reasons being recurrent infections, loss of solute transport capacity or ultrafiltration failure [42,43]. On the other hand, temporary withdrawal of peritoneal dialysis has been reported to restore peritoneal function at least in some patients [44,45]. This strongly suggests that the treatment adversely affects the long-term function of the peritoneal membrane, an effect which might be (partially) reversible in some cases. Secondly, the primary patient-treatment interface in peritoneal dialysis is the dialysis fluids whose current composition is unphysiological. In particular, there are several lines of evidence, obtained in vitro [15,26,29,39-41] as well as ex vivo in peritoneal dialysis patients [46], hinting at the low pH and/or the high lactate content as being of primary importance. Hence, dialysis fluid composition is an obvious primary angle from which a potential improvement of peritoneal dialysis treatment may be attempted. Since the technical problem related to the caramelization of glucose during autoclaving at neutral pH can now practically be solved by the availability of two-chamber bags for the fluids, we believe that (i) dialysis solutions with neutral pH urgently need further (preclinical and clinical) evaluation and (ii) the development of alternative solutions, e.g. alternative osmotic agents such as amino acids or glucose polymers, should principally include pH neutralization. Whether the choice of the buffer is also important, however, is still open to discussion. In addition to bicarbonate-buffered peritoneal dialysis solutions, lactate–bicarbonate mixtures [47] or pyruvate [48] have been suggested recently. As can be derived from the current in vitro study, amino acids in combination with bicarbonate buffer constitute another promising option.

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References


