

**A single-dose vancomycin application after standard protocol in peritoneal dialysis patients with recurrent peritonitis**

Sir,

Peritonitis remains the major cause of catheter removal in peritoneal dialysis (PD) patients suffering from recurrent attacks, despite appropriate antibiotic therapy. Bacteria such as coagulase-negative staphylococci (CNS) from the exit site of the catheter and contaminated dialysis fluids can grow into microcolonies in biofilms on the surface of the catheter [1,2]. In the preliminary study, we evaluated the outcome of administration of a single-dose intracatheterial vancomycin just after primary response to the treatment of the last peritonitis attack with cefazolin in continuous ambulatory PD patients with recurrent peritonitis.

Among 166 patients who underwent routine PD, six cases with recurrent peritonitis attacks were treated with initial empiric antibiotic therapy consisting of intraperitoneal cefazolin given in each exchange for gram-positive organisms. The characteristics and data regarding peritonitis attacks are given in Table 1. Six patients had three to five peritonitis attacks with intervals of ~1–7 weeks following the completion of a standard 2- or 3-week course of antimicrobial therapy. Four cases out of six had no history of peritonitis, tunnel or exit-site infection before. One

patient (fourth case in the table) had exit-site infection. For *S. aureus* positive culture, the patient received mupirocin pomade and Sodium Fusidate (1 g/day per oral for 7 days). After therapy, exit-site infection completely resolved, and the two cultures taken afterwards were negative. Then, she also had a peritonitis attack with *S. aureus* on 21 February 2006. The other patient (third case in the table) had a culture-negative peritonitis attack on 1 May 2006. They were treated with cefazolin. The wives of the two male patients (one having diabetic retinopathy) helped during the dialysis exchanges, and the remaining patients were on their own. Six patients and the two assistants (wives) were negative for nasal carriage state. However, prophylactic mupirocin was given to all patients, but the peritonitis attacks recurred. None of the patients had tunnel infection. After complete resolution of peritonitis by cefazolin alone in the last attack, 50 cc peritoneal dialysate was mixed with 2 g vancomycin after drainage of the entire peritoneal fluid and left in the catheter lumen for 8 h. Then, without drainage, a normal dialysis session was carried out. During the mean follow-up of 25 ± 0.8 months, none of the six patients had recurrence peritonitis.

Many episodes of peritonitis appear to be unrelated to obvious causes. Bacterial biofilm formation on the dialysis catheter represents a concern for PD patients in terms of our ability to eradicate the infection [2]. However, there is sometimes no clear relationship between biofilms and clinical peritonitis. Indeed, one exception may occur in patients with multiple episodes of peritonitis who were likely to have

**Table 1.** Characteristics of peritoneal dialysis patients with recurrent gram-positive peritonitis

Patient no	Age (year)	Gender (F/M)	Aetiology	PD starting date	Episode number	Peritonitis starting date	Organisms	Infection types	Intraperitoneal treatment
1	57	F	Diabetes mellitus	01 February 2005	3	29 December 2006	Culture-negative	–	C
						07 February 2007	Culture-negative	Relapse	C
2	47	M	Idiopathic	09 March 2005	5	16 March 2007	<i>S. aureus</i>	Repeat	C + V <sup>a</sup>
						22 December 2006	<i>S. epidermidis</i>	–	C
						30 January 2007	<i>S. epidermidis</i>	Relapse	C
						08 March 2007	<i>S. epidermidis</i>	Relapse	C
3	76	M	Idiopathic	31 December 2004	5	12 April 2007	Culture-negative	Relapse	C
						02 May 2007	Culture-negative	Relapse	C + V <sup>a</sup>
						04 December 2006	Culture-negative	–	C
						03 January 2007	<i>S. aureus</i>	Relapse	C
						28 January 2007	Culture-negative	Relapse	C
						11 March 2007	<i>S. epidermidis</i>	Re-infection	C
4	54	F	Diabetes mellitus	01 January 2004	4	12 April 2007	Culture-negative	Relapse	C + V <sup>a</sup>
						11 December 2006	<i>S. aureus</i>	–	C
						20 January 2007	<i>S. aureus</i>	Relapse	C
5	45	F	Idiopathic	01 April 2006	5	28 February 2007	<i>S. aureus</i>	Relapse	C
						01 May 2007	<i>S. aureus</i>	Repeat	C + V <sup>a</sup>
						12 October 2006	Culture-negative	–	C
						11 November 2006	Corynebacterium	Relapse	C
						29 November 2006	Culture-negative	Relapse	C
						29 January 2007	Culture-negative	Repeat	C
						09 March 2007	<i>S. epidermidis</i>	Re-infection	C + V <sup>a</sup>
6	52	F	Idiopathic	07 October 2004	3	01 January 2007	<i>S. hominis</i>	–	C
						21 February 2007	MRSE	Re-infection	V <sup>b</sup>
						28 March 2007	Culture-negative	Relapse	C + V <sup>a</sup>

F, female; M, male; PD, peritoneal dialysis; MRSE, methicillin-resistant staphylococcus epidermidis; C, cefazolin (a loading dose 500 mg/L and maintenance dose 125 mg/L in all exchanges for 14 to 21 days), V, vancomycin (<sup>a</sup>a single dose of 2 g intracatheterial. <sup>b</sup>Loading dose of 2 g and repeat dosing 1 g in long dwell every 7 days).

stable biofilms, positive biofilm cultures and a high incidence of catheter loss. Recently, examination by electron microscopy of catheters of patients who experienced PD peritonitis revealed biofilm formation; however, no biofilm formation was found in PD catheters removed from patients without infection [3]. The risk associated with administering cefazolin continuously (in every PD bag) is that the organisms survive and continue dividing in biofilms. Our current antimicrobial protocols may not permit adequate dosing to penetrate the biofilm and be a reason for recurrent episodes of peritonitis. To evaluate the differences in the antibiotic sensitivity patterns of CNS, minimum inhibitory concentrations (MIC) and minimum biofilm eradication concentration (MBEC) assays were compared in CNS isolates from patients with PD-associated peritonitis in a study [4]. In the PD effluent sample from patients with repeat infection, the rate of first-generation cephalosporin (FGC) or gentamicin or both resistances was higher. MBEC results were higher than those with standard MIC assays. Although no vancomycin resistance was observed with MIC assays, a small number of cases were identified with MBEC assays. There was no resistance when a vancomycin/rifampin 1:1 combination was used. All patients with repeat infections had high degrees of FGC resistance, and infection cycles were terminated when their treatment protocol included vancomycin. In conclusion, we assume that adequate antibiotic levels will be achieved within the catheter-contained biofilm with a single dose of vancomycin of 2 g at the end of the treatment course that will prevent recurrent peritonitis and catheter loss. These results are difficult to compare because patient numbers are small. In our opinion, this observation should be confirmed by other investigators.

*Conflict of interest statement.* None declared.

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## **Biocompatibility of peritoneal dialysis solutions determined by genomics of human leucocytes: a cross-over study**

Sir,

Peritoneal dialysis (PD) is based on passive movement of water and soluble molecules across the peritoneum. In continuous ambulatory peritoneal dialysis (CAPD), the patient's abdomen is filled with a dialysate fluid introducing an osmotic gradient driven by electrolytes and glucose, or macromolecules such as icodextrin. Biocompatibility of PD fluids is the most important criterion to enable long-term dialysis without introducing clinically significant changes in the functional characteristics of the peritoneum and systemic inflammatory effects [1]. The effects of biocompatibility on clinical outcome include changes in the physiology of cell populations constituting the peritoneal cavity (leucocyte, mesothelial and endothelial cells, and fibroblasts) and the gene expression of peripheral blood mononuclear cells (PBMCs) triggering alterations in cytokine, chemokine and growth factor networks, upregulation of proinflammatory and profibrotic pathways, and induction of carbonyl and oxidative stress [2–4].

Our study objective was to compare the genome-wide gene expression signature of PBMCs of PD patients using glucose-based (GBF) and icodextrin-based peritoneal fluids (IBF) to allow a direct comparison of biocompatibility relevant intracellular processes with respect to the PD fluid used. This pilot study should give us first insights into the alterations in gene expression of leucocytes triggered by different PD fluids and should provide an informative basis for future research.

Therefore, we conducted a random cross-over study in five stable ESRD patients being treated with CAPD between 4 and 18 months (demographic data are provided on our laboratory homepage in Table 1 (<http://www.meduniwien.ac.at/nephrogene/data/pd/>)). Blood samples (10 ml) were collected immediately after a 4- to 6-h dwell of GBF (Physioneal<sup>®</sup> 40, Glucose 2.27% w/v, 395 mOsmol/l) and an overnight dwell of IBF (Extraneal<sup>®</sup>, icodextrin 7.5%, 284 mOsmol/l) [study approved by the local Institutional review board (Ethical Committee # EK-318/06, see <http://ohrp.cit.nih.gov/search/asearch.asp>)]. Oligoarrays were obtained from the Stanford University Functional Genomics core facility. All microarray experiment protocols can be found on the Stanford University webpage at <http://cmgm.stanford.edu/pbrown/protocols/index.html>. Stratagene Universal human reference RNA was used as a reference. Raw data files as well as the MIAME checklist are available at our laboratory webpage.

A paired *t*-test ( $P < 0.05$ ) of log-transformed expression values was used to evaluate differences between IBF and GBF treatment. Differentially expressed genes (DEGs) were hierarchically clustered and graphically represented using the MultiExperiment Viewer (MeV) (Pearson correlation, complete linkage) [5]. DEGs were furthermore analysed with respect to their molecular functions, biological processes and interaction partner using gene ontology terms