One-dose cefuroxime i.v. and i.p. reduces microbial growth in PD patients after catheter insertion

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Abstract

Background. When a peritoneal dialysis catheter is inserted intra-abdominally in a patient starting peritoneal dialysis (PD) there is always a risk for postoperative wound infection and peritonitis. At our centre, PD is started immediately after the dialysis catheter is inserted. This may increase the postoperative risk for peritonitis and wound infection.

The aim of this prospective, randomized, study was to evaluate whether the incidence of microbial growth postoperatively (within 10 days) after catheter insertion could be reduced by prophylactic antibiotic therapy.

Subjects and methods. During a period of 27 months, 38 patients, who consecutively entered the PD programme, (11 women and 27 men, mean age 57 years) were included in the study. Eighteen patients were given cefuroxime 1.5 g i.v. preoperatively and 250 mg i.p. in the first dialysis bag (containing 1 litre fluid) as prophylaxis. Twenty patients were not given prophylactic antibiotics (control group). All catheter insertions were performed in an operating theatre by the same surgeons using the same technique.

Results. In the test group, none of the patients showed microbial growth in the dialysis fluid during the postoperative period, while in the control group six of 20 patients (30%) suffered from such growth (P = 0.021).

Conclusion. Prophylactic treatment by cefuroxime i.v. pre- and i.p. perioperatively may reduce the risk for microbial growth and peritonitis after insertion of a Tenckhoff catheter.

Key words: CAPD; microbes; bacteria; catheter insertion; antibiotic prophylaxis; exit site; wound infection; peritonitis
present at the operative site [4], and the choice of an antibiotic should therefore be based on this type of pathogen. The aim should be to reduce the bacterial concentration in the tissue at the operative incision site to below the level which can cause infection (usually $10^5–10^6$ organisms per gram of tissue) [4].

Administration of antibiotics i.v. 2 h before surgery results in the lowest rate of surgical wound infections; administration postoperatively in the recovery room is less effective [4,5].

Single agent cephalosporins are considered to be the most effective agents to reduce postoperative infections in adults after, for instance, cardiac surgery [6]. Generally these antibiotics are useful prophylactic agents as they have sufficient activity against Staphylococcus [6].

Patients with uraemia, diabetes mellitus, malnutrition, concomitant heart failure, or malignant diseases have an impaired host defence which increases their risk for infections [7,8]. Additionally, patients hospitalized for some time before an operation have an increased risk of more aggressive/resistant nosocomial bacterial infections [1,9].

Peritonitis after catheter insertion, apart from the pain and suffering for the patient, is also a threat to well-functioning CAPD, since it can reduce ultrafiltration, complicate the training programme, and prolong the stay in the hospital [10].

There are only a few retrospective studies concerning antibiotic prophylactics in PD catheter insertion [11–13]. Some of them recommend administration of 1 g vancomycin i.v. prior to surgery to prevent exit-site infections [11,12]. However, to our knowledge, there is no evidence that prophylactic antibiotics i.v. before catheter placement will prevent subsequent infection [13,14].

The aim of the present study was to investigate if cefuroxime, a second-generation cephalosporin, administered i.v. preoperatively and i.p. perioperatively, during the PD catheter insertion, could reduce the risk of microbial growth within the peritoneal cavity or the exit site (including tunnel infection) postoperatively.

Subjects and methods

During a period of 27 months, 38 patients who consecutively entered the PD programme were included in the study (11 women and 27 men, mean age 57 years, range 33–84). Thirteen of them suffered from diabetes mellitus. The patients were randomized to receive antibiotics or not by a co-ordinating nurse by using closed envelopes. The group I patients received cefuroxime prophylactics; the group II patients did not. All patients were Caucasian. All were informed and consented to take part in the study.

Group I consisted of 18 patients (6 women, 12 men) with a mean age of 56 years (range 33–84); six of the patients suffered from diabetes mellitus.

Group II consisted of 20 patients (5 women, 15 men) with a mean age of 61 years, (range 34–84); seven patients had diabetes mellitus. One patient in group II was being treated with cephradroxil p.o. for a urinary tract infection. None of the other patients had any infection at the time of the catheter insertion.

One patient in group I and two patients in group II had been hospitalized for more than 3 weeks before the catheter was inserted. The other patients were admitted to the hospital a few days before the operation. Seven patients, four in group I and three in group II, were on steroid treatment at the time of the catheter insertion. All patients were prepared for surgery in the same way except for the antibiotic prophylactics.

No routine check was performed to detect nasal carriers of Staphylococcus aureus.

Cefuroxime (Zinacef® Glaxo AB, Mölndal, Sweden), a second-generation cephalosporin, was used for prophylaxis. The patients in group I received 1.5 g cefuroxime i.v. 0.5–2 h prior to surgery, and 250 mg intraperitoneally in the first dialysis bag containing 1 litre fluid (Dianeal Twin Bag; Baxter Healthcare, SA Castlebar, Ireland) starting perioperatively.

All operations were performed by either of two experienced surgeons, in an operating theatre under sterile conditions. Double-cuffed straight Tenckhoff catheters were used in all patients. In our unit the Tenckhoff catheter is inserted with a lateral insertion technique and two purse-string sutures anchor the inner cuff. Dialysis is started perioperatively onwards with initial instillation of 1 litre fluid, gradually increasing the volumes to 2 or 3 litres [15].

Experienced PD educated staff performed the dialysis exchanges during the first days after the operation; thereafter the patient training was taken care of by either of two PD nurses. The same type of connective system was used in both groups (Dianeal Twin Bag; Baxter Healthcare, SA Castlebar, Ireland). Wound care and dressing routines were identical in the two groups. Insulin was administered intraperitoneally to all patients with diabetes mellitus. Leukocyte count of the drained dialysate was performed daily using Multistix® (defined below).

Postoperative infection occurring within 10 days after surgery was defined in the present study as: Wound infection. Localized pain, tenderness, redness, pus and/or positive culture from the wound.

Exit site/tunnel infection. Pus or positive culture from exit site and/or localized pain, tenderness or redness over the tunnel area or exit area.

Peritonitis. Positive culture from the dialysis fluid and/or cloudy effluent with an increase in the leukocyte concentration in peritoneal fluid, measured either by manual counting ($>100 \times 10^6/l$) or by a dipstick test with grade 2 or grade 3 in at least two consecutive bags (by Multistix® 8SG test, Bayer Diagnostika, Gothenburg, Sweden) representing $70–125 \times 10^6$ white blood cells/litre.

Microbial growth. This was defined as a microbial growth on culture of dialysis fluid in a patient without clinical signs of an invasive infection, including normal C reactive protein. The patient had to be asymptomatic with lack of fever. Culture was taken due to a positive Multistix® with grade 1, which represents about $15 \times 10^6$ leukocytes/litre, or findings of fibrin veils and threads in the drained fluid.

Thus the patients did not have to show symptoms or cloudy peritoneal fluid to initiate culture for microbes in the dialysis fluid.

Normally peritonitis is considered when the leukocyte count is $>100 \times 10^6$ leukocytes/litre [14,18].

All cultures of the peritoneal dialysate were performed both on anaerobic and aerobic blood culture media. Laboratory analyses and cultures were performed accord-
Antibiotic prophylaxis was performed according to local routines at the Department for Microbiology at the hospital.

Statistics

Analyses were performed by Fisher exact test with a computer software program [16] and the unpaired Student $t$ test.

Results

In group I, after cefuroxime prophylactics, none of the 18 patients developed growth of microbes in the dialysis fluid within the first 10 days after the Tenckhoff catheter implantation and dialysis start. In patients without prophylactic antibiotic treatment, six of 20 patients suffered from microbial growth ($P=0.021$). The bacteria cultured from the dialysis fluid of the patients were *Staphylococcus epidermidis* ($n=1$), *Staphylococcus aureus* ($n=1$), *alpha-Streptococcus* ($n=1$) and in one patient two types of bacteria were cultured (*Enterobacter* and *Staphylococcus epidermidis*). Five of these patients had bacteria which were sensitive to cefuroxime. One of them also had *Enterobacteriaceae*, which have a minimal inhibiting concentration of 16 mg/l [21]. We were not able to analyse the *Clostridium fragilis* strain for sensitivity to cefuroxime because the strain died. This patient had only growth of bacteria with no evidence of a progressive peritonitis, which was also found in another patient, who had fibrin veins in the effluent as the only finding, and the subsequent bacterial culture showed the presence of *Staphylococcus epidermidis*.

All patients were given antibiotics according to the sensitivity test and responded well to therapy within a couple of days.

Peritonitis developed in four of the six patients. Two of the patients in whom bacteria were cultured had shown no symptoms. Three of the patients with microbial growth had glomerulonephritis, two had diabetes mellitus (one of them also heart failure), and one had chronic pyelonephritis as the reason for chronic renal failure.

The diagnosis diabetes mellitus was not significantly more common in patients with microbial growth than in the others.

The mean age of the patients with peritonitis (51 years, range 33–69) was lower ($P=0.054$) than those who did not get peritonitis (67 years, range 34–84).

Two of the three patients being treated with steroids in group II developed a post-catheter-insertion microbial growth.

One patient with severe heart failure and diabetes mellitus had been hospitalized for three weeks before the Tenckhoff catheter insertion. He suffered from post-catheter-insertion microbial growth with *Staphylococcus aureus*. The bacteria cultured were not resistant to cefuroxime.

During the observation time no exit-site or tunnel infections were seen in any of the patients.

Discussion

The test group that received the antibiotic prophylactics was comparable to the control group in terms of gender, distribution of age, and the number of patients with diabetes mellitus. The number of patients reported in this study is small. However, due to intermediate analysis of data the differences in outcome resulted in termination of the study.

This study included two routes of antibiotic administration in an attempt to reduce the risk for post-catheter-insertion microbial growth. The preoperative i.v. antibiotic routine used was mainly aimed at inhibiting growth of bacteria in the operation wound and the soft tissue in the exit site/tunnel area according to suggestions by Twardowski [11].

Our choice to give cefuroxime 1–2 h prior to surgery was based on studies in surgical practice [4,5]. Thus, for optimal prophylactics, antibiotics have to be present in sufficient concentration in the blood and tissue fluids before the clot is formed, since antibiotic penetration into a clot is poor. Administration prior to operation, and not at the start of anaesthesia in the preoperative room, is therefore of great importance [5,17]. This regime enables prophylactic antibiotics to be present during the operation as well as during the lag phase time of the growth cycle of bacteria contaminating the wound towards the end of the operation [9]. A 2-h operation requires that the antibiotic concentration should still be above the minimal bactericidal concentration for contaminating organisms 6 h after incision. These criteria would be satisfied in this study, since cefuroxime has a half life of 1.3 h for a 1.5-g dose in non-uraemic patients, and in a patient on CAPD the half-life is 15 h [14,18].

The choice of cefuroxime was based on studies showing that cephalosporins are among the most effective single agents in reducing infections in adults after cardiac surgery [6]. Findings by del Rio et al. [19] supported the use of single dose administration. They investigated urological patients and found that a monoagent cephalosporin with half-life > 4 h given as a single dose was just as effective as multiple-dose therapy. In addition, the monodose was less likely to select resistant strains [19] with negligible risk for oto- and nephrotoxicity and superinfections [1].

In the present study none of the patients who received prophylactic cefuroxime suffered from microbial growth after the catheter insertion, in contrast to 30% of the patients in the control group without prophylactics. This differs from other (not prospective) studies using only i.v. administration and other antibiotic prophylactic regimes, which failed to show significant advantages regarding exit-site infection and subsequent peritonitis [11–13,20].

We believe that using only i.v. prophylactics would not be sufficient to eliminate bacteria contaminating the peritoneal cavity during the operation. The i.v.-administered antibiotics which penetrate from the blood into the peritoneal cavity are rapidly diluted by
the dialysis fluid. The minimal inhibiting concentration would therefore be too low to kill most bacterial strains. By intraperitoneal administration, cefuroxime acts directly on bacteria ‘trapped’ in the peritoneal cavity perioperatively, and the dose used corresponds to a minimal inhibiting concentration of 250 mg/l, which is sufficient to kill most bacteria. The i.v. dose may be more effective in preventing bacteria in the exit-site/tunnel area.

As expected, skin bacteria were the most frequent organisms cultured from the drained dialysate in the present study, indicating perioperative transmission from the skin area. The other organisms were intestinal bacteria, which may have been released through microtrauma of the intestine during the surgery. The minimal inhibitory concentration would have been attained i.p. for both types of bacteria because the doses used corresponded to 250 mg/ml intraperitoneally [21,22].

In conclusion, pre- and perioperative prophylaxis with cefuroxime seems to reduce greatly the risk of postoperative infections, with little risk of side-effects.

References


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Received for publication: 20.10.95
Accepted in revised form: 10.9.96