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# The effect of intravesically applied antibiotic solution in the prophylaxis of infectious complications of renal transplantation

**K. Salmela, B. Eklund, L. Kyllönen, H. Isoniemi, C. Korsbäck, K. Höckerstedt, and J. Ahonen**

The Fourth Department of Surgery, Helsinki University Central Hospital, Kasarmikatu 11–13, SF-00130 Helsinki, Finland

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**Abstract.** The effect of intravesically applied antibiotic solution in the prevention of infectious complications of renal transplantation was evaluated in a prospective, randomized study. The bladder was filled preoperatively with saline solution containing cephalotin in the test group, and with saline solution only in the controls. Both groups of patients received IV doses of cephamandole during, and once after, surgery. Two hundred consecutive patients were randomly allocated to the study groups. The overall incidence of urinary tract infection was 10.4% during the first 4 postoperative weeks; that of wound infections was 1.6% and of septicemia 3.3%. The addition of cephalotin to the bladder irrigation fluid did not have any effect on the overall incidence of infectious complications.

**Key words:** Urinary tract infection, prophylaxis – Bladder irrigation, antibiotics – Antibiotics, bladder, prophylaxis

Urinary tract infection (UTI) can lead to major morbidity in renal transplant patients. UTI has been reported to be associated with deep wound infections, septicemia, and impaired graft survival in kidney transplant recipients [1, 2, 3, 6, 7]. It has been shown that patients with chronic renal failure harbor organisms in their bladder [6]. Although it has been postulated that irrigation of the bladder with antibiotic solution may reduce the incidence of postoperative infectious complications of renal transplantation [9], no randomized study has been published. We, therefore, conducted a prospective, randomized study to analyze the incidence of early infectious complications in renal transplant recipients when the bladder was irrigated with saline solution with or without cephalotin.

## Patients and methods

This prospective, randomized study on 200 consecutive kidney transplant recipients was conducted at our center during the period from September 1987 to February 1989. Retransplantations comprised 17% of the cases (12% second, 3% third, and 2% fourth). The patients were randomly allocated to two groups by the closed envelope method. Prior to surgery the bladder was filled either with 200 ml or to capacity in those few cases with bladder volume less than 200 ml. In one group (cephalotin group; $n = 100$), the bladder was filled with saline solution (NaCl 0.9% in water) containing 1 g cephalotin sodium (Keflin, Eli Lilly, Indianapolis, Ind). In the other group (saline group; $n = 100$), it was filled with saline solution only. During the transplant operation and 12 h postoperatively, 1 g cephamandol (Mandokef, Eli Lilly, Indianapolis, Ind) was given to the patients. Eighteen patients were excluded because of additional antibiotic use for different reasons within 3 weeks after transplantation (Table 1). The remaining 182 patients with no additional antibiotic therapy were included in the study. The cephalotin and saline groups were comparable with regard to age, sex, source of kidney graft, primary disease, pretransplant oliguria/anuria, onset of graft function, and number of rejection episodes (Tables 2, 3). There were no significant differences between the groups. The infectious complications occurring within 4 weeks post-transplantation were analyzed in this study.

The surgical technique used for the transplant operation was the same for all of the patients. The kidney graft was placed extraperitoneally in the iliac fossa, the allograft artery was anastomosed to the internal or external iliac artery and the allograft vein to the external iliac vein. The ureter was anastomosed to the recipient bladder as an open intravesical ureteroneocystostomy. In one patient with a pyeloureteral stenosis in the graft, the ureteral continuity was primarily restored using a pyeloureterostomy. No drains were left in the operation area. The indwelling bladder catheter was left in place for 5 days. A bacterial culture of the urine was taken preoperatively, during the transplant operation, and postoperatively every 5th day. Immunosuppressive treatment included azathioprine (2 mg/kg per day tapered to 1 mg/kg per day at 2 weeks), methylprednisolone (1 mg/kg per day tapered to 0.25 mg/kg per day by 2 weeks), and cyclosporin (initially 10 mg/kg per day, dose-adjusted according to the trough level). For recipients of kidneys from living related

**Table 1.** Causes for antibiotic use in excluded patients

| | |
|---|---|
| Upper respiratory tract infections | 4 |
| Prophylactic antibiotics | |
| Skin infections | 5 |
| Tuberculosis in history | 1 |
| Osteitis in history | 1 |
| Postsplenectomy | 1 |
| Extended operation time | 1 |
| Colon dilatation | 1 |
| Positive legionella antibody | 1 |
| Positive culture | |
| Urine preoperatively | 1 |
| Peritoneal catheter exit site | 1 |
| Transplant preservation fluid | 1 |
| Total | 18 |

*Offprint requests to:* K. Salmela

**Table 2.** Diagnosis of the primary disease

| | Cephalotin group | Saline group |
|---|---|---|
| Diabetes | 23 | 27 |
| Amyloidosis | 5 | 3 |
| Glomerulonephritis | 32 | 34 |
| Polycystic disease | 11 | 8 |
| Pyelonephritis | 7 | 7 |
| Nephritis NUD | 6 | 12 |
| Other | 6 | 1 |
| Total | 90 | 92 |

**Table 3.** Patient characteristics

| | Cephalotin group | Saline group |
|---|---|---|
| Age (mean ± S.D.) | 42.0 ± 11.4 | 43.9 ± 10.7 |
| Sex (male/femle) | 55/35 | 58/34 |
| Living related grafts | 3 | 3 |
| Cadaveric grafts | 87 | 89 |
| Pretransplant oliguria (< 500 ml) | 39 | 38 |
| Delayed onset of graft function (> 7 days) | 23 | 34 |
| One rejection episode | 22 | 30 |
| Two rejection episodes | 1 | 4 |

**Table 4.** Infectious complications

| | | Urinary tract infection | Wound infection | Septicemia |
|---|---|---|---|---|
| Cephalotin group | ($n$ = 90) | 11 (12.2%) | – | 4 (4.4%) |
| Saline group | ($n$ = 92) | 8 (8.7%) | 3(3.3%) | 2 (2.2%) |
| Total | ($n$ = 182) | 19 (10.4%) | 3 (1.6%) | 6 (3.3%) |

donors, immunosuppression consisted of azathioprine and methylprednisolone. Acute rejection episodes were treated with methylprednisolone, 3 mg/kg per day for 5 days.

Urinary tract infection was defined as one positive ($10^5$ or more bacteria per ml urine) culture associated with pyuria. The diagnosis of wound infection was made when pus was drained from the wound. The onset of graft function was defined as the day when serum creatinine decreased without dialysis. Results were analyzed using the chi-square test.

## Results

Urinary tract infection during the first 4 weeks post-transplant developed in 19 out of 182 (10.4%) patients (11/90 in the cephalotin group and 8/92 in the saline group; Table 4). Of these 19 patients, 10 were female and 9 were male. The mean time for detection of UTI was 13 days post-transplant. The most common organism cultured from urine was *Escherichia coli*. In no case was UTI associated with bacteremia, and in all patients UTI responded to treatment with appropriate antibiotics. There were no major urological complications. Minor urological problems occurred in 24 patients: bladder catheter left prophylactically in place for more than 5 days because of a scarred or thin bladder wall in 9 patients, change of catheter due to clot obstruction two or more times in 15 patients, bladder lavation through the catheter due to tamponade in 4 patients, and a temporary percutaneous nephrostomy due to ureteral obstruction or leakage in 4 patients. Five of these 24 patients developed UTI, all in the saline group. Thus, the rate of UTI in patients with post-transplant problems with catheter or manipulation of the urinary tract was 21%, whereas it was 9% in patients with uncomplicated recovery (chi-square = 3.19, NS). In 5 out of 15 (33%) patients in the saline group, urological manipulation was followed by UTI, whereas none of the 9 patients with urological complications in the cephalotin group developed UTI.

UTI was more common in diabetics (14%) and in patients with chronic pyelonephritis (21%), but the number of patients in these groups was too small for a relevant statistical analysis. Ten percent of the patients with pretransplant oliguria had UTI, as did 12% of those with diuresis from their own kidneys. UTI developed in 11% of the cases with late onset of graft function, whereas it was seen in 10% of the cases with immediate graft function. Antirejection treatment did not increase the incidence of UTI (12% versus 10%). Three patients were reoperated because of postoperative bleeding. None of them developed UTI.

Bacteremia occurred in six patients, detected 13 days (mean) post-transplant, four of them in the cephalotin group. The organisms isolated in the blood were *E. coli*, salmonella, streptococcus, and staphylococcus, respectively; all patients survived. Two patients in the saline group had bacteremia: one with listerial sepsis was treated successfully, and another with clostridial sepsis died.

Wound infection developed in three patients, all in the saline group. The micro-organism cultured from the wound excretion was staphylococcus in all cases. None of these patients had UTI and none of them had been reoperated.

Peritonitis developed in two patients who had been on peritoneal dialysis before transplantation. One with a nonfunctioning kidney graft developed peritonitis caused by enterococcus and pseudomonas 8 days post-transplant and died 18 days later from clostridium sepsis, as described above. Another patient with a functioning kidney graft had peritonitis caused by staphylococcus 13 days post-transplant, and he recovered without further complications.

The mean follow-up time for the patients was 14.4 months (range 6–23 months). Graft survival and patient survival at 6 months were 92.7% and 96.1%, respectively.

## Discussion

The 10.4% incidence of early UTI for this group of patients is markedly lower than that reported in earlier studies [2, 8, 12, 13]. In kidney transplant recipients, bacteria in the urinary tract have been considered a potential source of severe septic and wound complications [10, 11]. During the period of acute tubular necrosis in particular, infectious complication rates as high as 70% have been reported [7]. Repeated catheterization in the post-transplant period and prolonged retaining of the indwelling ca-

theter are among the urological complications reported to be risk factors.

As early as in the 1960s, the antibacterial irrigation of the urinary bladder in conjunction with kidney transplant operation was suggested by Hinman and Belzer [6]. Our data demonstrate that the addition of cephalotin to the saline solution used in bladder irrigation does not affect the number of infectious complications as a whole. Whether the instillation of saline solution as such into the bladder is beneficial is not known. Yet, data from the registry of infectious complications at our hospital shows that the incidence of UTI in renal transplant patients in 1985, when no irrigation was used, was 15.7%.

The use of antibiotic irrigation in the present study seemed to be beneficial in patients who had problems postoperatively with the indwelling catheter or who encountered other urological complications; however, the small number of patients with these complications precludes statistical comparisons.

Contrary to earlier reports [4, 5], sex, antirejection treatment, and late onset of graft function were not predisposing factors in our study. The incidence of UTI in diabetics and in patients with chronic pyelonephritis tended to be higher than in the other patients; again, however, because the number of patients with infectious complications was small, the numbers are without statistical support.

The organisms cultured from infected wounds were, in all cases, staphylococci. Thus, our experience does not support the earlier findings that organisms of the urinary tract may be responsible for wound infections in kidney transplant patients. The low number of wound infections – 1.6% – can probably be attributed to the meticulous preparation of the patients prior to the transplant operation, to the short operation time, and to the restricted number of surgeons performing the transplant operations. The overall wound infection rate in clean contaminated operations at our hospital during the same period of time was 3.1%, according to the hospital registry.

All of our patients with septicemia were free from UTI. The organism responsible for sepsis was *E. coli* in one case only, while in the other cases organisms atypical to the urinary tract were cultured from the blood.

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