

## 만성혈액 투석환자에 대한 요로감염\*

— A Prospective Study —

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= Abstract =

### Urinary Tract Infection in Chronic Dialysis Patients

— A Prospective Study —

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We studied prospectively 48 patients with end stage renal disease on chronic dialysis (hemodialysis or chronic ambulatory peritoneal dialysis). Of these 48 patients, 9(19%) had urinary tract infection (UTI), 4(8%) had symptomatic UTI, and 14(29%) had sterile pyuria. Among 16 patient who had documented previous UTI, 8(50%) had repeated UTI at presentation compared to 1 of 32 patients who had not documented previous UTI. Daily urine out put in all patients with sterile pyuria was lesser than 500ml. No significant correlation was seen between frequencies of UTI and duration of dialysis therapy. Successful cure with oral antibiotic treatment for 1-2 weeks achieved in 6 of 9 patients with UTI. However, recurrence of infection occurred in 3, one patient was diabetic with neurogenic bladder, another was patient with chronic pyelonephritis who had experienced perinephric abscess. Third was patient with chronic pyelonephritis complicated with chronic UTI, paraplegia, and vesico-renal reflux. This patient was admitted to hospital for intravenous gentamycin therapy.

### INTRODUCTION

During the last decade, considerable dialysis technics have improved the prognosis of patients undergoing maintenane hemodialysis or chronic ambulatory peritoneal dialysis. However, infection continues to be a major medical problem in chronic dialysis patients. A high incidence of UTI among patients with chronic

renal failure has been reported<sup>1-5)</sup>. Patients with chronic renal failure on chronic dialysis are known to have suppressed cellular and humoral immunity and increased susceptibility in infection<sup>6)</sup>. Several authors have presented high occurrence of vesicorenal reflux<sup>7)</sup>, acquired cystic renal disease<sup>8)</sup>, and perinephric abscess in patients with polycystic disease undergoing hemodialysis<sup>9)</sup>. The concentraing defect commonly found

\*본 연구의 요지는 1987년도 아리조나대학 병원에서 연구한 것임.

in patients with chronic renal failure might well interfere with the development of optimal concentrations of antibacterial substances in the urine<sup>10</sup>.

We frequently encountered with unexpected serious complications in patients on chronic dialysis such as bacteremia or complicated UTI. However, it is difficult to find the exact cause of predisposing factors of such an infection especially in oliguric patients who received chronic dialysis treatment. In this study, the incidence and other factors related to UTI in chronic dialysis patients have evaluated.

## PATIENTS and METHODS

48 patients undergoing chronic dialysis (hemodialysis or chronic ambulatory peritoneal dialysis) at Desert Dialysis Center for 3 months or more who granted informed consent have studied. There were 16 males and 32 females. Mean age was 58 yrs (range 21–81 yrs) have been dialyzed for an average of 31 mo (range 3–111 mo). Mean serum creatinine level was 10.2 mg/dl.

Primary renal disease included diabetic in 15 cases, hypertension in 11, chronic glomerulonephritis in 10, chronic pyelonephritis in 6, polycystic kidney disease in 4, and unknown in 2.

Urine volume has been collected for 3 consecutive days (Friday 8 : 00 AM–Monday 8 : 00 AM, or Saturday 8 : 00 AM–Tuesday 8 : 00 AM) and then 3 days urine volume divided by 3 was recorded daily urine volume.

A separate urine specimen was collected for microscopic examination and culture with antibiotic sensitivity tests. In male patients, a clean voided midstream specimens was obtained. In female patients, we obtained a catheterized specimen after appropriate cleaning of the urethral meatus and vulva. In severely oliguric male patients, urine samples was obtained by catheterization. In anuric patients, bladder washings were obtained by instillation of 50ml sterile saline into the bladder and subsequent drainage.

Pyuria was defined as more than 5 white blood cells

per high power field in the centrifuged sediment. Significant bacteriuria was defined as the presence of  $>10^4$  colony forming units (cfu)/ml of urine on catheterized specimens,  $>10^5$  cfu on clean catch midstream specimens. UTI was defined as significant bacteriuria and pyuria.

In all patients with significant bacteriuria were selected for the detection of antibody-coated bacteria in urine specimens. Aliquots of urine specimen (1ml) were centrifuged at 3000 rpm for 15 mins. The sediments were washed twice in phosphate-buffered saline (PBS) at PH 7.3. The washed sediments were mixed with 0.2ml of a 1 : 5 dilution of fluorescein-conjugated antihuman globulin of horse origin, incubated at 37°C for 30 mins. and rewashed in PBS. Smears were examined microscopically for fluorescence with a 8x eyepieces, a 100x oil objective. The intensity of fluorescence was recorded as negative or positive.

## RESULTS

Of 48 patients 9(19%) had UTI, 4(8%) had symptomatic UTI, and 14(29%) had sterile pyuria (Table 1). Presenting clinical symptoms in patients with symptomatic UTI were fever in 4 cases, flank pain in 2, dysuria in 1, and hematuria in 1. Over a period of 9 yrs, 16 of 48 patients had experienced at least one episode of UTI. 8 of 16 patients who had documented previous UTI developed repeated UTIs at presentation while only 1 patient developed among remaining 32 patients who had not documented (Table 2). There was significant difference in frequencies of UTI at presentation between the patients who had and had not documented previous UTI ( $P < 0.01$ ). UTI occurred in 5 women and 4 men, and there was no sex differences in frequencies of UTI. Among 9 patients with UTI, antibody-coated bacteria in urine was positive in 3 including 2 patients with symptomatic UTI (Table 1). UTI occurred most frequently in patients with chronic pyelonephritis (3 of 10) and chronic glomerulonephritis (4 of 10) while only one patient had UTI in diabetic patients.

Table 1. Patients studied

	No. Pts	Sex		UTI No. (%)	Symptomatic UTI No. (%)	Positive for antibody coated bacteria No. (%)	Sterile pyuria No. (%)
		M	F				
Diabetic nephropathy	15	4	11	1(7)	0	1	4
Hypertensive nephropathy	11	4	7	0	0	0	5
Chronic glomerulonephritis	10	3	7	4(40)	2	1	1
Chronic pyelonephritis	6	3	3	3(50)	1	1	2
Polycystic kidney diseases	4	1	3	0	0	0	2
Unknown	2	1	1	1(50)	1	0	0
Totals	48	16	32	9(19)	4(8)	3(6)	19(29)

UTI : Urinary Tract Infection

Table 2. Frequencies of UTI occurred in patients who had and had not documented previous UTI

	No. Pts	Previous Documented UTI	Non-documented Previous UTI
		No.(No of UTI at Presentation)	No.(No of UTI at Presentation)
Diabetic nephropathy	15	4(1)	11(0)
Hypertensive nephropathy	11	2(0)	8(0)
Chronic glomerulonephritis	10	4(4)	5(0)
Chronic pyelonephritis	6	4(3)	2(0)
Polycystic kidney disease	4	2(0)	4(0)
Unknown	2	0	2(1)
Total	48	16(8)*	32(1)*

\*Significance difference( $p < 0.01$ ) in frequencies of UTI at presentation between patients who had and had not documented previous UTI.

The frequencies of UTI among the various groups for daily urine volume did not increase in proportion to minimizing urine output. However, all the sterile pyuria was presented in groups whose daily urine volume was less than 500ml (Table 3). There was no correlation in frequencies of UTI and sterile pyuria among the various groups for duration of dialysis (Table 4). In all 9 patients with UTI, urine cultures grew  $>10^5$  organisms combined with pyuria by urinalysis. The most frequencies encountered urinary organisms

isolated from patients with UTI were *E. coli* in 5 episodes and *Klebsiella pneum.* in 4 episodes (Table 5). All patients with UTI were treated with ampicillin and trimethoprim-sulfamethoxazole for 1-2 wks. However, significant bacteriuria persisted in 3 patients (symptomatic UTI in 1, asymptomatic UTI in 2). One patient was diabetic with neurogenic bladder, another was patient with chronic pyelonephritis who had experienced perinephric abscess. Third was patient with chronic pyelonephritis complicated with chronic UTI,

**Table 3.** No. of UTI among groups classified according to daily urine output

Daily Urine Output(ml)	No. Pts	Urinary tract infection	Sterile pyuria
< 100	18	4	6
100 - 300	10	0	3
300 - 500	11	2	5
500 - 1000	8	3	0
> 1000	1	0	0
Totals	48	9	14

**Table 4.** No. of UTI among groups classified according to duration of dialysis

Duration of Dialysis(months)	No. Pts	Urinary tract infection	Sterile pyuria
3 - 6	4	2	1
6 - 12	13	4	3
12 - 24	11	0	3
24 - 36	6	0	3
36 - 60	5	2	0
> 60	9	1	4
Totals	48	9	14

**Table 5.** Organisms isolated from patients with UTI

Organisms	No. of episodes
Escherichia coli	4
Klebsiella pneumoniae	3
Protus mirabilis	1
G(D) streptococci	1
Candida albicans	1
Providence stuart II	1
Totals of episodes	11

amyloidosis, paraplegia, and vesico-renal reflux. This patient was frequently admitted to hospital for intravenous gentamycin treatment.

## DISCUSSION

The incidence of UTI was high among the patient with chronic renal failure as pointed out by Montgomerie, and associates(1) ; 44%, Erben and associates (2) ; 45.5%.

Keane and associates have respectively analysed UTI in 445 patients undergoing chronic hemodialysis and were documented an incidence of 2.3 episodes per 1000 treatment months<sup>(4)</sup>. Rault reported 11(11.6%) of 95 patients on maintenance hemodialysis during 3 year period. Saitoh and associates reported that 19% had UTI and 7% had symptomatic UTI<sup>(5)</sup>.

Our incidence of UTI(19%) and symptomatic UTI(8%) was accordance with those of Saitoh and associates. The incidence of UTI may be differed according to underlying primary renal disease. In this study, it should be clear that UTI in patients with chronic pyelonephritis and chronic glomerulonephritis is much more common than other primary renal diseases. The remarkably low incidence of UTI among diabetes suggest that the risk may not be so great as generally is believed. Interestingly, the incidence of UTI was much higher in the group who had documented previous UTI. Moreover, all of the patients with chronic glomerulonephritis who had experienced previous UTI developed repeated UTI at presentation. It suggest that ei-

ther previous history of UTI or primary renal disease may contribute to increased risks of repeated UTI. Reznicek and associates observed pathological changes in the lower urinary tract in 7 of 35 patients on chronic hemodialysis and emphasized the possibility of a recurrent UTI<sup>11</sup>.

Urine flow and mucosal barrier are the main defense mechanism which prevent bacteria that have entered the bladder from establishing UTI<sup>12</sup>.

Friedman and associates demonstrated that changes in urine flow and bladder transit time had profound effects on urine colony counts<sup>13</sup>. In our study incidence of UTI has not increased as oliguria become more pronounced while sterile pyuria is more frequent in oliguric patients. However, the significance of this sterile pyuria in these patients is unclear. In our study, duration of dialysis did not influence the incidence of UTI. UTI was likely to occur any time during the course of long-term dialysis.

In asymptomatic men where the chance of contamination is lower, a more acceptable criteria for defining significant bacteriuria is  $10^4$  cfu/ml. Urine samples obtained from asymptomatic women by short term catheterization are less apt to be contaminated and may warrant the lower criteria for significant bacteriuria of  $10^4$  cfu/ml<sup>14</sup>. Our all patients with UTI being developed at presentation had both pyuria and significant bacteriuria of  $>10^5$  cfu/ml.

Bennett and associates reported ampicillin and trimethoprim-sulfamethoxazole are both excellent choice in the treatment of urinary tract infection in patients with severe renal failure<sup>15</sup>. In this study all of the patients with UTI were treated with appropriate antibiotics (ampicillin and trimethoprim-sulfamethoxazole) based on culture and sensitivity test. 3 of 9 patients with UTI did not respond to 1–2 weeks course of antibiotics and significant bacteriuria persisted. It is likely that resistant organisms have already persisted for a long time in two asymptomatic patients who had diabetic with neurogenic bladder and chronic pyelonephritis with complicated UTI. One was symptomatic patient with chronic pyelonephritis, who was frequen-

tly admitted to hospital due to chronic UTI, paraplegia and vesicorenal reflux. Vaziri and associates reported 42 of 43 patients with spinal cord injuries and end stage renal disease undergoing dialysis had chronic UTI for prolonged periods<sup>16</sup>.

We were able to detect 5 cases of unsuspected UTI prospectively. It leads to an improved understanding of when it is necessary to treat such infections, and when it is appropriate to accept such infections as a "normal" aspect of end stage renal disease.

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