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Effect of Antibiotic Therapy on Asymptomatic Bacteriuria in Kidney Transplant Recipients

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ABSTRACT

Purpose: Asymptomatic bacteriuria is a very common complication after kidney transplantation and the need for antibiotic therapy is controversial. The aim of this study was to evaluate the effect of antibiotic therapy on the clinical course of asymptomatic bacteriuria in renal transplant recipients.

Materials and Methods: In the present study, 88 kidney transplant recipients with asymptomatic bacteriuria were divided into two groups of cases and controls. The patients had been selected from among those with at least 1 year follow-up. In the case group, asymptomatic bacteriuric episodes were treated with antibiotics, and in control group, they were followed without antibiotic therapy. The follow-up period was 9 to 12 months. Bacteriuric episodes, symptomatic urinary tract infection (UTI) episodes, and changes in plasma creatinine level were recorded and compared between the two groups.

Results: The rate of bacteriuric episodes and symptomatic UTIs were not significantly different between the two groups (P >0.05). In addition, level of plasma creatinine did not increase significantly in neither of the groups during the study (P >0.05).

Conclusion: It seems that treatment of asymptomatic bacteriuria in kidney recipients does not decrease the rate of UTI episodes afterwards. Asymptomatic bacteriuria does not affect renal function in short term. Thus, we can abandon antibiotic therapy, subject to careful follow-up.

KEY WORDS: antibiotic therapy, asymptomatic bacteriuria, kidney transplant

Introduction

Urinary tract infection (UTI) is the most common infection after renal transplantation.[1] If left untreated, it has proved harmful effect on allograft function and survival, in addition to infectious complications.[2] Asymptomatic bacteriuria is also very common in these patients; however, its negative effect on patient and transplanted kidney has not been proved, yet.[3] In general, treatment of asymptomatic bacteriuria is not useful in non-pregnant patients with normal immune system,[4] and has no positive effect on later incidence of UTI. In kidney recipient patients, however, it can be of benefit if antibiotic therapy of asymptomatic bacteriuria can decrease later symptomatic infections. Otherwise, if we cannot change the incidence of infections by medication, it will

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impose a burden of potential side effects as well as the excessive costs on these patients. This study was performed to evaluate the short-term effects of antibiotic therapy in asymptomatic bacteriuria on subsequent incidence of UTI and also on graft function in kidney recipients.

Materials and Methods

In a clinical trial, 50 male and 50 female renal transplant recipients with asymptomatic bacteriuria entered the study, from March 2002 to February 2003. Asymptomatic bacteriuria was defined as pyuria and bacteriuria in urine analysis, positive culture with colony count greater than 100000 of one organism, and the absence of irritative voiding symptoms, fever, and chills.

All of the selected patients were older than 18 years old and had at least one year post-transplantation follow-up. None of the patients had indwelling urethral catheter or ureteral stent. Etiologies of renal failure in these patients were hypertension, diabetes mellitus, urinary stones, and glomerulonephritis (table 1).

All of the patients underwent urinalysis, urine culture, colony count, and plasma creatinine level tests. Patients with Proteus infection were excluded from the study because of high risk of stone formation and emphasis on their treatment.

According to the order of patients' transplant code, they were divided into two groups of case and control, in every other one manner. Afterwards, they were informed about the study, in detail, and informed written consent was taken.

In case group, a 10-day oral antibiotic therapy (according to antibiogram) was administered and the patients were asked to return two weeks later (3 to 4 days after antibiotic therapy period). After resolving bacteriuria, confirmed by urine culture, the patients were asked to return for follow-up one month later. The patients in control group were left untreated and followed one month later with urinalysis and urine culture.

In each group, monthly visits continued, assessing urinalysis, urine culture, creatinine serum level, and BUN in addition to history and physical examination. In case of bacteriuria and positive culture in case group, treatment would be repeated. Standard treatment for symptomatic urinary tract infection would be done in both groups, if any, and when eradication of infectious organism was confirmed by repeat culture, the patients would return to their respective group. All of the patients were followed for 9 to 12 months. The patients with lost follow-up visits, acute rejection, and pyelonephritis leading to hospitalization during the study were excluded.

Collected data were analysed using SPSS 9.0 software. Chi-square test was used to compare categorical variables and *t* test to compare normally distributed continuous variables, considering P value less than 0.05 as significant.

TABLE 1. *Etiologies of renal failure in case and control groups*

Etiology	Case group (%)	Control group (%)	Total (%)
Hypertension	20 (46.5)	18 (40)	38 (43.1)
Diabetes mellitus	6 (13.9)	7 (15.6)	13 (14.8)
Glomerulonephritis	3 (6.9)	8 (17.8)	11 (12.5)
Urolithiasis	4 (9.3)	5 (11.1)	9 (10.2)
Polycystic kidney	1 (2.3)	4 (8.9)	5 (5.7)
Chronic pyelonephritis	2 (4.6)	3 (6.7)	5 (5.7)
Gout	2 (4.6)	2 (4.5)	4 (4.6)
Tuberculosis	-	2 (4.5)	2 (2.3)
Kidney hypoplasia	1 (2.3)	1 (2.2)	2 (2.3)
Lupus Erythematosus	1 (2.3)	-	1 (1.1)

Results

Twelve patients were excluded of the study, 11 because of lost follow-up visits and 1 because of acute pyelonephritis, and eventually, data from 88 patients were analyzed.

There were 43 patients in the case group (20 males and 23 females) and 45 ones in control group (20 males and 25 females). Mean ages of case and control groups were 44.2 ± 12.7 (range 19 to 62) years and 40.9 ± 13.2 (range 20 to 70) years (P >0.05).

TABLE 2. *Pathogen organisms isolated at the first bacteriuria episode*

Pathogen	Case group (%)	Control group (%)
E. coli	30 (69.7)	27 (60)
Klebsiella	3 (6.9)	6 (13.4)
Pseudomonas	4 (9.3)	3 (6.7)
Streptococcus-beta	2 (4.6)	1 (2.2)
Coagulase negative Staphylococcus	2 (4.6)	3 (6.7)
Enterobacter	1 (2.3)	2 (4.5)
Gram positive cocci	1 (2.3)	3 (6.7)
Total	**43**	**45**

TABLE 3. *Comparison of the number of bacteriuric episodes between the two groups*

Number of episodes	Case group (%)	Control group (%)	Total
1	11 (25.6)	17 (37.8)	28
2	7 (16.3)	10 (22.3)	17
3	2 (4.6)	1 (2.2)	3
4	3 (6.9)	1 (2.2)	4
5	1 (2.3)	1 (2.2)	2
6	1 (2.3)	2 (2.5)	3
9	-	1 (2.2)	1
Total	**25 (58.1)**	**33 (73.3)**	**58**

The most common organisms in the patients at the first episode of bacteriuria were Escherichia coli in 57 patients, Klebsiella in 9, and Pseudomonas in 6 (table 2).

Recurrence of bacteriuria developed in 25 cases (58.1%) and 33 controls (73.3%) (P >0.05). Among these patients, mean number of bacteriuria episodes were 2.15 (range 1 to 6) and 1.58, respectively (range 1 to 9) (P >0.05, table 3).

Nine patients in case group and 14 patients in control group were affected with symptomatic urinary infection (21% vs. 31%, P >0.05).

In case group symptomatic infection occurred once, twice, and three times in 5, 3, and 1 patients, respectively; while in the control group, it was seen once, twice, three times, and four times in 7, 4, 2, and 1 patients, respectively (P >0.05).

Mean plasma creatinine level was 1.16 ± 0.27 mg/dL and 1.42 ± 0.67 mg/dL in case and control groups, respectively (P >0.05), which changed to 1.2 ± 0.55 mg/dL and 1.43 ± 0.56 mg/dL at the end of the study (t and paired *t* tests, P >0.05).

Discussion

To preserve renal function and prevent or treat acute allograft rejection, kidney transplant recipients require immunosuppressive therapy. However, any kind of immunosuppressive therapy can lead to the development of infections. Among renal transplant recipients, UTI is the most common type of infection and the most common cause of septicemia.[1,5,6] UTI can present as asymptomatic bacteriuria, acute cystitis, pyelonephritis, and septicemia. Goya et al detected UTI in 20.8% of hospitalized patients and 4.2% of outpatients, of whom 40% were symptomatic and the remainder were asymptomatic.[3]

Two aspects of the effect of bacteriuria on transplant recipients should be considered: first, morbidity and mortality caused by the infection; and second, potential effects of infection on developing rejection and its clinical course. Risk of bacteremia accompanying UTI in these patients is nearly 12% and gram negative bacteria are the most common pathogens; however, gram positive bacteria such as Enterococcus and Staphylococcus are also the potential causes.[5]

In a study by Muller et al, they evaluated the relationship between UTI and biopsy proven chronic rejection. The patients were followed for 5 years and it was found that patients with chronic rejection had had more episodes of UTI comparing to those without rejection. Microbial antibodies can result in TNF-α, IF-δ, and IL-6 production, which have important roles in chronic rejection process.[1]

Morbidity accompanying UTI depends on the time of its occurrence after transplantation.[6] UTI is very common in the first weeks after transplantation and is usually diagnosed faster in this period. Mean interval between the beginning of infection and clinical manifestations is about 4 to 7 days.[7] If left untreated with a standard antibiotic therapy course in the first month, it often results in pyelonephritis, bacteremia, and recurrence.[8] Thus, treatment for all nosocomial urinary infections or infections accompanying bacteremia or pyelonephritis should be started with parenteral antibiotic therapy and be continued until the culture is negative. Thereafter, depending on the sensitivity of organism, the oral antibiotic therapy should be administered for 2 to 6 weeks. Urinary infection in outpatients during the first three months after operation should be also treated with oral antibiotic therapy for 6 weeks. A shorter treatment period of 10 to 14 days is usually accompanied by higher risk of recurrence.[6]

Urinary infections are usually more benign after the first 3 to 6 post-transplant months and, not differing from urinary infection in general population, they could easily be treated with a standard 10- to 14-day antibiotic therapy. However, increasing urinary infection episodes is associated with a higher risk of chronic rejection.[9] But, Takai did not find any significant difference between kidney recipients with and those without urinary infection in a 3-year follow-up.[10]

Due to high prevalence of urinary infection within the first post-transplant weeks and

months, high risk of urinary infections leading to bacteremia and sepsis, and high susceptibility of kidney allograft to parenchymal infection, in most centers, they use prophylactic oral antibiotic therapy continuously during the first months. Duration of prophylaxis may alter; it continues at least 3 to 4 months, but in some centers, it may last up to 1 year.[11]

Asymptomatic bacteriuria is commonly seen in kidney transplant recipients. There is a direct relation between bacterial accumulation, diuresis, and renal function. Colony count decreases by increasing urine outflow and subsequent bacterial dilution.[3] Most of the authors recommend antibiotic therapy for asymptomatic bacteriuria in the first months after transplantation. There is no consensus about the period of therapy and also it is not clear yet whether to treat every episode of asymptomatic bacteriuria after the first months or not. Stein and Funfstruck recommend treating every episode of bacteriuria with or without symptoms.[12] Sayegh has also recommended antibiotic therapy for a period of 10 to 14 days in these cases.[6] On the other hand, some authorities recommend that asymptomatic bacteriuria, occurring after the first post-transplant months, must be carefully followed and we should warn patients of symptoms and begin antibiotic therapy when clinical manifestations are present.[1]

In our study, we studied only the patients who had undergone transplantation at least one year before. The two case and control groups were matched for sex in order to eliminate the intruding effect of this factor. The recurrence rate of bacteriuria and symptomatic urinary infection were slightly higher in the case group, but the differences between the two groups were not statistically significant. In other words, antibiotic therapy in asymptomatic bacteriuria did not decrease recurrence of bacteriuria and incidence of symptomatic infection. In addition, there was not a significant difference in the number of bacteriuria or symptomatic infection episodes. Analyzing serum creatinine level at the beginning and at the end of the study showed increase in neither of the groups. Thus, it seems that asymptomatic bacteriuria does not affect kidney allograft function in a short-time period.

Conclusion

Asymptomatic bacteriuria after transplantation is a benign condition which commonly recurs; although most of the patients will have symptomatic urinary infection in the future, antibiotic therapy cannot decrease the rate of bacteriuria recurrence or impending urinary infections. Furthermore, asymptomatic bacteriuria and its recurrence do not adversely affect allograft function in short-time. Thus, it seems that if asymptomatic bacteriuria is carefully followed after the first year of transplantation, we can abandon antibiotic therapy.

References

1. Abbott KC, Oliver JD 3rd, Hypolite I, et al. Hospitalizations for bacterial septicemia after renal transplantation in the United States. Am J Nephrol. 2001;21:120-7.
2. Muller V, Becker G, Delfs M, Albrecht KH, Philipp T, Heemann U. Do urinary tract infections trigger chronic kidney transplant rejection in man? J Urol. 1998;159:1826-9.
3. Goya N, Tanabe K, Iguchi Y, et al. Prevalence of urinary tract infection during outpatient follow-up after renal transplantation. Infection. 1997;25:101-5.
4. Gleckman R. The controversy of treatment of asymptomatic bacteriuria in non-pregnant women–resolved. J Urol. 1976;116:776-7.
5. Burgos Revilla FJ, Pascual Santos J, Marcen Letosa R, et al. [Renal transplantation and urinary infection. Review]. Actas Urol Esp. 1999;23:95-104. Spanish.
6. Mohammad HS. Urinary tract infection in renal transplant recipients. In: Rose BD, editor. Uptodate. Wellesley: 2001;9(3). [CD-ROM].
7. Kentouni-Noly JC, Cloix P, Martin X, Rabodonirina M, Lefrancois N, Sepetjan M. Analysis of nosocomial infections in renal transplant and pancreas transplant recipients. Transplant Proc. 1994;26:284.
8. Tolkoff-Rubin NE, Rubin RH. Urinary tract infection in the immunocompromised host. Lessons from kidney transplantation and the AIDS epidemic. Infect Dis Clin North Am. 1997;11:707-17.
9. Tolkoff-Rubin NE, Cosimi AB, Russell PS, Rubin RH. A controlled study of trimethoprim-sulfamethoxazole prophylaxis of urinary tract infection in renal transplant recipients. Rev Infect Dis. 1982;4:614-8.
10. Takai K, Tollemar J, Wilczek HE, Groth CG. Urinary tract infections following renal transplantation. Clin Transplant. 1998;12:19-23.
11. Barry JM. Renal transplantation. In: Walsh PC, Retik AB, Vaughan ED Jr, et al, editors. Campbell's urology. 8th ed. Philadelphia: WB Saunders; 2002. p.345-76.
12. Stein G, Funfstuck R. [Asymptomatic bacteriuria]. Med Klin (Munich). 2000;95:195-200. German.