ORIGINAL ARTICLE

Clinical study of different immune induction and BK virus infection after renal transplantation

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ABSTRACT

Objective: To monitor the incidence of BK virus infection in hematuria of renal transplant recipients induced by different immunizations.

Methods: A total of 109 patients who underwent renal transplantation in Baogang Hospital of Inner Mongolia from January 2019 to December 2022 were analyzed retrospectively. The results of BK virus DNA detection in urine and blood were observed after operation. They were divided into three groups according to different immunosuppressive induction regimens; 35 patients in group A, 42 patients in group B, and 32 patients in group C (basiliximab). To explore the effect of different immune induction regimens on BK virus infection in renal transplant recipients.

Results: The positive rate of urine BK virus in all patients in 1 month after operation was 10.09% (11/109), which was significantly higher than that of blood BK virus 0% (0/109), and the difference had a statistical significance ($p < .05$). The positive rate of urine BK virus in all patients in 6 months after operation was 31.19% (34/109), which was significantly higher than that of blood BK virus 3.67% (4/109), and the difference had a statistical significance ($p < .05$). The positive rate of urine BK virus in all patients in 12 months after operation was 35.79% (39/109), which was significantly higher than that of blood BK virus 5.50% (6/109), and the difference had a statistical significance ($p < .05$). The urinary BK virus infection rate was increased significantly from 1 month to 6 months after operation, but was not increased significantly from 6 months to 12 months after operation. There was a statistically significant difference between the two groups ($p < .05$). The BK virus infection rate in renal transplant recipients induced by basiliximab within the first month was significantly lower than that in patients using polyclonal antibodies, but the urinary BK virus infection rate after one year was not significantly different from that in patients using polyclonal antibodies.

Conclusions: There are slight differences in BK virus infection after early renal transplantation with different immune induction therapies, but there is no significant difference in the long-term. It is recommended to strengthen the early monitoring of BK virus after renal transplantation, timely adjust immunosuppressive regimens to achieve the early detection and early treatment.

Key Words: Kidney transplantation, Immunosuppressants, Immune induction, BK virus

1. INTRODUCTION

Currently, renal transplantation is the most effective method for the clinical treatment of uremia and other diseases. Since January 1, 2015, Chinese government has comprehensively banned the use of organs from dead prisoners, and organ donation and transplantation has become the main way of kidney transplantation after the citizens' death. Because most donor organs have went through complex pathophysiological processes before acquisition, resulting in decreased quality of donor kidneys and high immune risk for recipients.

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Hence, it is particularly important to booster immunization induction therapy. The increase in the immune intensity, results in postoperative BK virus infection. BK virus (BKV) is widespread in the normal population, and its positive rate is reported to be $\geq 80\%$ in the epidemiological survey, and the initial infection occurs in childhood in the majority of population, followed by incubation periods, and reactivation can occur in immunocompromised conditions affecting the long-term survival of the transplanted kidney.[1,2] Therefore, the prevention and diagnosis of BK virus infection is very important for protecting the function of transplant kidney. This study retrospectively analyzed the clinical data of renal transplant recipients in Baogang Hospital, Inner Mongolia, and explored the infection of BK virus in urine and blood with different immunization induction regimens to provide a basis for clinical BK virus infection, progression and diagnosis and treatment.

2. Data and methods

2.1 Subjects and grouping

From January 2019 to December 2022, 109 cases of renal transplantation in our hospital were analyzed retrospectively. There were 70 male cases and 39 female cases in this study, with the age of (43.4 ± 11.3). Preoperative BK virus showed negative results, and preoperative lymphotoxic and anti-donor-specific antibodies showed negative results. They were divided into three groups according to different immunosuppressive induction regimens; 35 patients in group A (R-ATG), 42 patients in group B (ATG-F), and 32 patients in group C (basiliximab). Postoperative maintenance immunosuppressive regimen was cyclosporine/tacrolimus + mycophenolic acid (MPA) + glucocorticoid triple immunosuppressive regimen; BK virus copy number in urine and blood was monitored in 3 months, 6 months and 12 months after surgery.

2.2 Experiment methods

BK virus DNA was amplified by PCR instrument from ABI Company (USA), and the copy number was analyzed; the viral nucleic acid quantitative detection kit was purchased from Beijing SinoMed Gene Detection Technology Co., Ltd.10-20 ml of urine and 2 ml of venous blood were collected from patients after renal transplantation in the morning for detection. In this study, if PCR results showed more than 107 copies/ml in urine and more than 104 copies/ml in blood, the results were considered to be positive.[3,4]

2.3 Statistical methods

The statistical analysis was conducted by using SPSS 22.0 software. Measurement data were represented by mean $\pm$ standard deviation ($\bar{x}\pm$s), and all rates were compared by use of χ^2 test. The difference was statistically significant (p < .05).

3. Results

3.1 BK virus infection in hematuria after operation

BK virus infection in hematuria in 1 month, 6 months and 12 months after operation (see Table 1): (1) The positive rate of BK virus in urine in 1 month after operation was 10.09% (11/109), which was significantly higher than that in blood (0/109), and the difference was of statistical significance (p < .05). (2) The positive rate of urine BK virus in all patients in 6 months after operation was 31.19% (34/109), which was significantly higher than that of blood BK virus 3.67% (4/109), and the difference had a statistical significance (p < .05). (3) The positive rate of urine BK virus in all patients in 12 months after operation was 35.79% (39/109), which was significantly higher than that of blood BK virus 5.50% (6/109), and the difference had a statistical significance (p < .05). The urinary BK virus infection rate was increased significantly from 1 month to 6 months after operation, but was not increased significantly from 6 months to 12 months after operation. There was a statistically significant difference between the two groups (p < .05). Blood BK virus infection in 1 month after surgery was not statistically significant (p > .05).

3.2 Comparison of BK virus infection in different immune-induction regimens in 1 month after surgery

3.2.1 *One month after operation*

The BK virus infection rates of patients in the three groups were compared and listed in Table 2. The positive rate of urinary BK virus in group A (R-ATG) was 17.14% (6/35) and 11.90% (5/42) in group B (ATG-F) (χ^2 = 1.013, p = .605), and the difference was not statistically significant (p > .05). In group C (basiliximab), no positive results of urinary BK virus infection were found in one month after surgery. There was a statistically significant difference in urinary BK infection between group C and group A & B (χ^2 = 3.036, p = .043) (p < .05). Blood BK infection occurred in all three groups in one month.

3.2.2 *Six months after operation*

BK virus infection rates in the three groups of patients were compared (see Table 3). In Group A (R-ATG), the positive rate of urinary BK virus infection was 40.00% (14/35) and the positive rate of blood BK virus was 2.86% (1/35); in Group B, the positive rate of urinary BK virus infection was 30.95% (13/42) and the positive rate of blood BK virus was 7.14% (3/42); in Group C, the positive rate of urinary BK virus infection was 21.88% (7/32), and there were no signifi-

cant difference in urinary and blood BK virus infection rates in 6 months among the three groups ($\chi^2 = 1.032$, $p = .713$) ($p > .05$).

3.2.3 *12 months after operation*

BK virus infection rates in the three groups of patients were compared (see Table 4). In Group A (R-ATG), the positive rate of urinary BK virus infection was 40.00% (14/35) and the positive rate of blood BK virus was 8.57% (3/35); in Group B, the positive rate of urinary BK virus infection was 33.33% (14/42) and the positive rate of blood BK virus was 7.14% (3/42); in Group C, the positive rate of urinary BK virus infection was 34.88% (11/32), and there were no significant difference in urinary and blood BK virus infection rates in 12 months among the three groups ($\chi^2 = 1.047$, $p = .683$) ($p > .05$). No blood BK virus infection occurred in group C.

Table 1. BK virus infection

	January	June	December
Urinary BK Virus Positivity	11 (10.09)	34 (31.19)	39 (35.78)
Blood BK Virus Positivity	0 (0%)	4 (3.67%)	6 (5.50%)

Table 2. Comparison of BK virus infection rates in different immune-induction regimens in 1 month after surgery

Item	Group A(35)	Group B(42)	Group C(32)	AB		ABC	
				χ^2	*p*	χ^2	*p*
Urinary BK Virus Positivity	6	5	0	1.013	.605	3.036	.043
Blood BK Virus Positivity	0	0	0				

Table 3. Comparison of BK virus infection rates in different immune-induction regimens in 6 months after surgery

Item	Group A(35)	Group B(42)	Group C(32)	χ^2	*p*
Urinary BK Virus Positivity	14	13	7	1.032	.713
Blood BK Virus Positivity	1	3	0		

Table 4. Comparison of BK virus infection rates in different immune-induction regimens in 12 months after surgery

Item	Group A(35)	Group B(42)	Group C(32)	χ^2	*p*
Urinary BK Virus Positivity	14	14	11	1.047	.683
Blood BK Virus Positivity	3	3	0		

4. Discussion

The primary infection of BK virus mostly occurred in childhood and shows a latent infection state in healthy people, and there are generally no obvious clinical symptoms during the initial infection with the application of potent immune-inducing agents.[5,6] BK virus infection is increased significantly, which reaches up to 48.3% after one year in our center. BKV nephropathy due to BK virus infection has become an important cause of dysfunction of transplant kidney due to the lack of effective antiviral drugs. At present, the biopsy for transplant kidney is the gold standard for the diagnosis of BKV nephropathy, but it is mostly used after the patient's creatinine level is elevated, and it is an invasive examination that cannot identify BKV infection in the early stage. Prevention and early diagnosis and treatment are therefore key to the treatment of BKV infection.[7,8]

In our center, the dynamic monitoring of BK viral load in hematuria is performed to reduce the incidence of post-operative BK virus infection by applying different immunization induction regimens. The BK virus infection rate in renal transplant recipients induced by basiliximab within the first month was significantly lower than that in patients using polyclonal antibodies, but the urinary BK virus infection rate after one year was not significantly different from that in patients using polyclonal antibodies. Basiliximab-induced blood BK virus infection did not occur in patients within 12 months, considering that most of the donors were relatives and the quality of donated kidneys was better. Elfadawy et al. showed that transient and sustained high serum loads of BKV can adversely affect the outcome of transplant kidney after renal transplantation.[9] In this study, it was found that the period of 3-6 months after renal transplantation was the peak period of BK virus infection, the monitoring of BK

virus should be strengthened and prolonged in these patients in clinical practice to protect against the possibility of BK virus-associated nephropathy.

There are no specific antiviral therapies against BK virus infection, and the basic treatment is to reduce immunosuppressive drugs.[10–12] Patients undergoing renal transplantation often need to use immunosuppressive agents for a long time after surgery, and how to achieve immunosuppression and prevent infection is of great importance.[13–15] Compared with mycophenolate mofetil, mizoribine has a more significant immunosuppressive effect with antiviral characteristics. It has a good anti-infective and immunosuppressive effect, and plays an important role in the prevention of BK virus infection after renal transplantation.

5. Conclusion

In summary, with the widespread use of new immunosuppressive agents, the incidence of BKV infection after renal transplantation is still high, and the early screening for BK after renal transplantation is particularly important for preventing BK virus replication and further progression. The selection of different immune regimens and the application of postoperative immunosuppressive agents are effective treatments for our prevention and treatment of BK virus infection. Because the sample size is small and the study period is limited, which affects the accuracy of the results, it is still necessary to expand the sample size clinically, prolong the study period, and further rationalize the application of immunization induction and immunization regimens.

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Conflicts of Interest Disclosure

The authors declare they have no conflicts of interest.

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