Long term follow up of active management versus minimization of immunosuppressives of bk virus

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Introduction

There is no active treatment for post-renal transplant BK virus associated nephropathy (BKVAN) that has proven to be effective so far.

We aimed to assess effectiveness of active management of BKVAN with combined leflunomide, IVIG and ciprofloxacin on the long term graft outcome compared to minimization of immunosuppressives.

Materials and methods

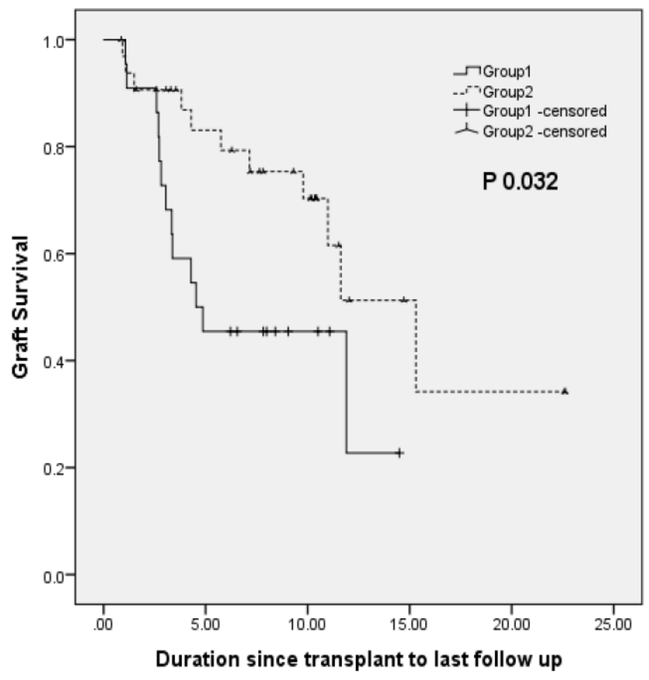
Our kidney transplant recipients were screened for BKVAN. Group1 (n=22): was composed of kidney transplant recipients with twice positive BK virus-PCR in urine and blood who underwent graft biopsy to confirm BKVAN. Once BKVAN is diagnosed, anti-metabolite (mycophenolate mofetil or azathioprine) was changed to leflunomide and a course of IVIG and oral ciprofloxacin were given. Group 2(n=33): was composed of BKVAN patients treated conventionally with reduced immunosuppressives.

Results

Fifty five patients were treated, 69%were males (), 50.9% were diabetics, mean HLA mismatches was 3.65 and 50.9% of patients were CW7 negative. All patients received induction therapy (thymoglobulin in 55.6%) and 52.7% received antirejection therapy before BKVAN diagnosis. Maintenance immunosuppression was prednisolone (96.3%), mycophenolate mofetil (94.5%) and tacrolimus (50.9%). Subsequent rejection episodes have occurred in 38% of the patients after BKVAN diagnosis. Basal mean eGFR was 52.5 25.5 which has reduced significantly to 38.1 27.8 ml/min/1.73m2 (p <0.0001) at the end of the study without significant differences between the groups (p 0.08 and 0.17respectively). Follow up period was 7.3 4.99 years. There was no significant difference in the patient outcome. Graft survival was significantly better in group2 (p 0.032).

	Total (n=55)	Group1 (n=22)	Group2 (n=33)	P value
Mean time from transplant to first viremia(months)	25.9 29.4	19.5 29.1	30 39.4	0.29
Mean time from transplant to maximum viremia(months)	28.8 36.1	25.6 29.7	30.9 40.2	0.6
Mean time from first viremia to established BKVAN diagnosis (months)	3.95 6.8	4.78 6.45	3.24 7.2	0.49
Mean time from BKVAN diagnosis to maximum viremia(months)	1.2 2.9	1.1 3	1.3 2.9	0.82
Number of BK virus copies (mean SD)	283098 581227	564500 1109000	189297 294711	0.28
Mean time from BKVAN diagnosis to clearance of viremia(months)	14.6 9.1	13.1 3.6	15.5 11.4	0.5
Patients with BK viremia at the end of the study, n (%)	1(1.8)	nil	1(3)	0.71
Patients with BK viruria at the end of the study, n (%)	4(7.2)	1(4.5)	3(9)	0.67
Basal serum creatinine[a]	184 81	189 50	179 98	0.73
Serum creatinine at the end of the study[b]	360 261	431 293	306 225	0.09
	***P*[a,b] <0.0001**	***P*[a,b] 0.047**	***P*[a,b] 0.001**	
Baseline eGFR[c]	52.5 25.5	45.1 17.9	57.1 29	0.08
eGFR at the end of the study[d]	38.1 27.8	31.9 27.2	42.7 27.9	0.17
	***P*[c,d] <0.0001**	***P*[c,d] <0.0001**	***P*[c,d] <0.0001**	
Patients with positive CMV-PCR required treatment, n (%)	7(12.7)	3(13.6)	4(12.1)	0.59
Associated infections required hospitalization (Urinary, chest, gastrointestinal, skin, multiple)	19/15/5/5/9	6/6/2/2/2	13/9/3/3/7	0.39
Follow up period after BKVAN (years)	7.3 4.99	5.9 3.75	8.2 5.5	0.09
Mean time from BKVAN diagnosis to graft failure (years)	4.5 3.3	4.0 2.8	4.8 3.6	0.39
Graft survival at last follow up, n (%)	31(56.3)	9(40.9)	22(66.6)	**0.032**
Patient survival at last follow up, n (%)	50 (92.5)	21(95.4)	29(87.9)	0.49

Table1: Results



Long term graft survival of kidney transplant patients since transplant to last follow up (Kaplan-Meier estimator).

Conclusion

Minimization of immunosuppressive drugs was more effective than actively treating BKVAN with a combination of leflunomide, IVIG and ciprofloxacin regarding long term graft outcome.

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