The combination immunosuppressive therapy of Everolimus with low dose Tacrolimus in de novo kidney transplantation in children

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Purpose

Little information is available whether de novo immunosuppression with the mammalian target of rapamycin (mTOR) inhibitor evelolimus (EVR) and low dose tacrolimus (TAC) is advantageous for kidney transplantation (KT) in children.

The purpose of this study is to evaluate the efficacy and safety of the new immunosuppressive regimen with EVR/TAC in pediatric kidney transplant recipients.

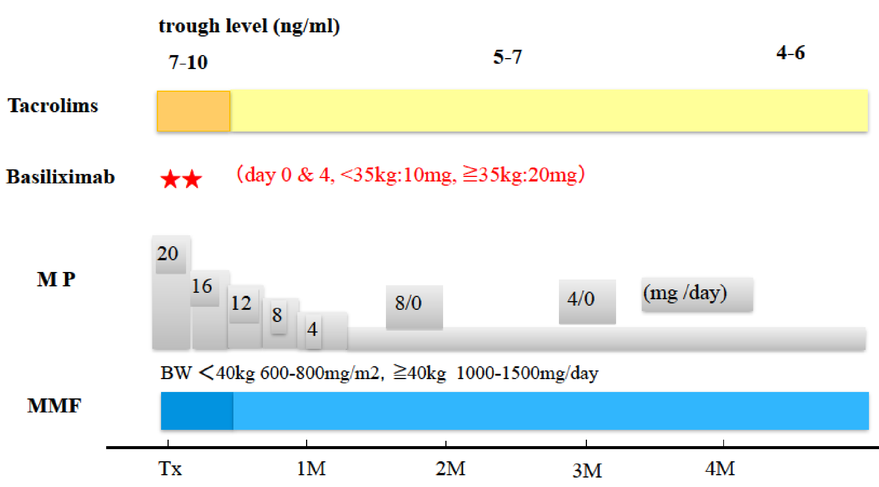
Methods

Twenty-five pediatric patients who received KT were enrolled in this study. All children received an induction therapy with Basiliximab on day 0 and 4.

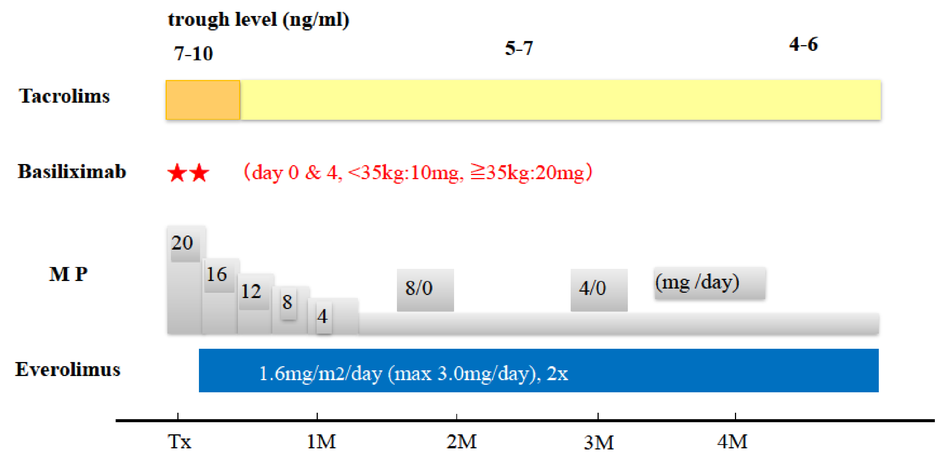
Posttransplant immunosuppression was EVR/TAC and methylpredonisolone (MP) in 10 patients, while 15 recipients received a standard therapy with TAC/mycophenolate mofetil (MMF) and MP (Figure1). EVR was started 7 days after transplantation with target trough level of 3-8 ng/ml until 6 month followed by 3-5 ng/ml. (Figure2)

Acute rejection (AR) rates, adverse events and renal function at the last follow-up were analyzed between the both groups.

【Figure 1】Protocol of treatment, tacrolimus/ MMF



【Figure 2】Protocol of treatment, tacrolimus/ everolimus



Results

Table 1. Patient characteristics

	Tacrolimus/EVR (N=10)	Tacrolimus/MMF (N=15)
Sex (male/female)	6 / 4	6 / 9
Age (year)	13.4± 4.7	7.3±5.4
Primary disease, N	Hypoplastic/dysplastic kidney 5 Posterior urethral valves 1 TMA after BMT 1 Wilms tumor 1 Neonatal shock 1 Unknown 1	Hypoplastic/dysplastic kidney 6 Posterior urethral valves 2 ARPKD 2 Nephronopthisis 2 Henoch-Schonlein nephritis 1 Congenital nephrotic syndrome 1 Denys-Drash syndrome 1
Cytomegalovirus (R-/D+)	4/10 (40%)	9/15 (60%)
Epstein-Barr virus (R-/D+)	1/10 (10%)	9/15 (60%)

TMA, thrombotic microangiopathy; BMT, bone marrow transplantation

Table 2. Efficacy and survival

	Tacrolimus/EVR (N=10)	Tacrolimus/MMF (N=15)	*P-value*
Clinical acute rejection <3 months	1/10 (10.0 %)	1/15(6.7%)	0.33
Protocol biopsy at 3 months	3/10(30.0%) Borderline 2 Grade I A 1	2/15(13.3%) Borderline 1 Grade I A 1	0.38
Protocol biopsy at 1 year	1/6(16.7 %) Borderline 1	3/11(27.3%) Borderline 3	0.76
eGFR at last visit (ml/min/1.73m2)	68±21	66±20	0.80
Patient survival	100 %	100 %	-
Graft survival	100 %	100 %	-

eGFR, estimated glomerular filtration rate

Table 3. Infections after transplantation

	Tacrolimus/EVR (N=10)	Tacrolimus/MMF (N=15)	*P-value*
Cytomegalovirus (viremia)	2	9	0.05
BK virus	1	1	0.76
EBV/PTLD	0	1	0.40
Adenovirus	0	0	-
UTI	1	0	0.40

EBV, Epstein-Barr virus; PTLD, posttransplantation lymphoproliferative disorder; UTI, urinary tract infection

Table 4. Adverse events associated with Everolimus

	Tacrolimus/EVR (N=10)	Tacrolimus/MMF (N=15)	*P-value*
Hypertension	5	1	0.01
Hyperlipidemia	2	1	0.31
Hyperuricemia	1	3	0.50
Proteinuria	0	1	0.40
Glucose tolerance abnormality	1	1	0.76
Delayed wound-healing	0	0	-
Stomatitis	2	0	0.07
Hyperkalemia Metabolic acidosis	0	2	0.23
Diarrhea	0	2	0.23

Conclusion

The current study using an EVR with low-dose TAC has shown a low number of rejections and good renal function after pediatric KT. The number of side effects was acceptable.

Furthermore, this regimen may provide some beneficial effect on preventing the posttransplant viral infection.

Reference

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