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Alemtuzumab in paediatric kidney transplantation, five years' experience at the Pablo Tobón Uribe Hospital in Medellín, Colombia☆

Alemtuzumab en trasplante renal pediátrico: experiencia de 5 años en el Hospital Pablo Tobón Uribe de Medellín, Colombia

Dear Editor,

Kidney transplantation is the treatment of choice in the paediatric population with end-stage renal disease (ESRD).[1] There are few studies evaluating the long-term effectiveness and safety of alemtuzumab for kidney transplantation in the paediatric population.

This is a descriptive study conducted at the Hospital Pablo Tobón Uribe (HPTU). All kidney transplant patients under 18 years of age from 2005 to 2012 who received alemtuzumab as induction therapy were included.

The immunosuppression protocol used included administering alemtuzumab and a triple maintenance therapy, with a calcineurin inhibitor (tacrolimus or cyclosporine), antimetabolite (azathioprine or mycophenolate), and steroids. This study was approved by the Hospital Pablo Tobón Uribe ethics committee.

During 2005–2012, 21 paediatric kidney transplants were performed with alemtuzumab received as the induction therapy; 57.1% were boys, and the median age was 13 years (p25–75: 9–15); malformations of the urinary tract were the most common cause of chronic kidney disease (42.9%). The serological status for cytomegalovirus was recipient negative/donor positive in 23.8%, recipient positive/donor positive in 71.4%, and recipient positive/donor negative in 4.8%. The median cold ischaemia time was 18 h (p25–75: 12–20).

The 6-, 12-, 24-, 36-, and 60-month patient survival rate after the kidney transplant was 100%, 100%, 95.2%, 95.2%, and 95.2%, respectively. One patient died during the study. Post-transplant 6-, 12-, 24-, 36-, and 60-month kidney graft survival were 95.2%, 95.2%, 90.5%, 85.7%, and 85.7%, respectively.

The median GFR 1 week, and 1, 2, and 5 years after the transplant were: 72.5 ml/min (p25–75: 45–94; $n = 21$), 70.5 ml/min (p25–75: 61–88.5; $n = 20$), 89 ml/min (p25–75: 66–108; $n = 19$), and 76 ml/min (p25–75: 61–101.5; $n = 14$), respectively. At 1, 2, and 5 years of follow-up, 28.6%, 19.1%, and 29.4% of patients, respectively, presented a GFR under 60 ml/min/1.73 m^2. By grouping the patients according to CKD stage, we found that, during the 5-year follow-up, a high percentage of patients were in stage 1 and 2 (Fig. 1). Table 1 describes the main complications found.

This study describes the clinical outcomes of paediatric kidney transplant patients who received alemtuzumab as induction therapy. Among the most important findings, a good kidney graft survival stands out, with a low incidence of rejection and few complications. One patient who lost the graft 18 months after transplantation died. The patient was admitted, placed on haemodialysis and died due to decompensated heart failure. The other three patients who lost the kidney graft were secondary to acute rejection, due to poor adherence to the immunosuppressant therapy.

Other benefits that we found with the use of this therapy was GFR stability over time. Furthermore, in our study, only 28.6%, 19.1%, and 29.4% of the patients had a GFR under 60 ml/min/1.73 m^2 at 1, 2, and 5 years. According to this, most

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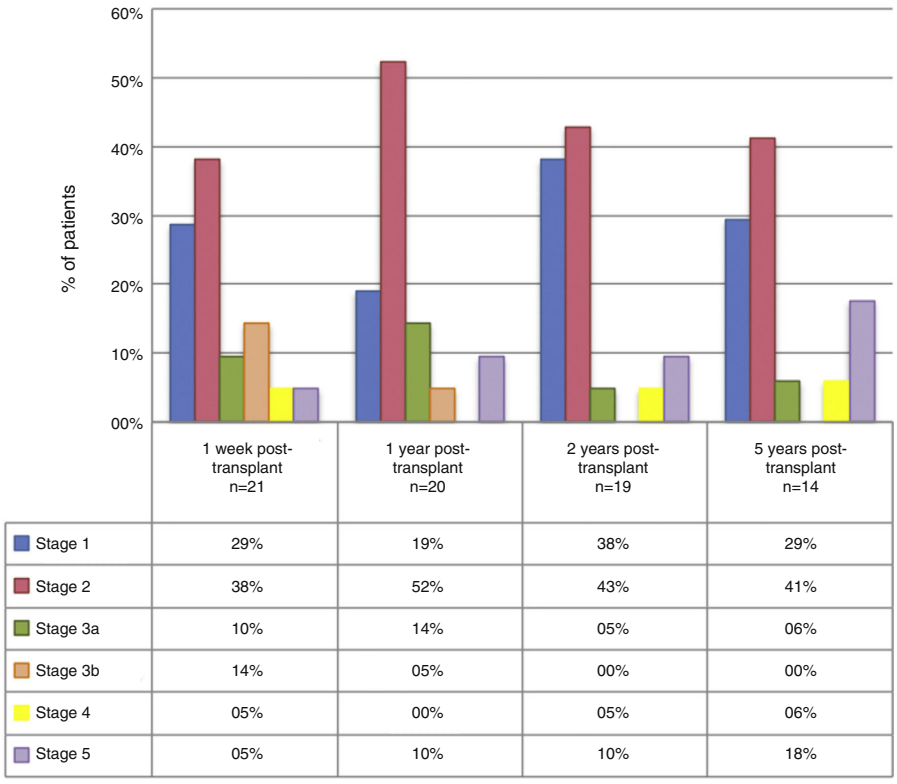

Fig. 1 – Stage of chronic kidney disease, grouped by time of progression in the paediatric kidney transplant population at HPTU 2005–2012.

of the study population remained in stage 1 and 2 chronic kidney disease during the follow-up period, which involves a low future risk of kidney disease-related complications.

The cumulative 1-, 2-, and 5-year incidence of acute rejection in our patients was 14.3%, 21.1%, and 35.7%, respectively. Poor adherence to the immunosuppressant treatment was documented in all these patients, and 3 of them subsequently lost the kidney graft. Only one of the rejections was classified as antibody-mediated.

One of the main fears with the use of alemtuzumab has been its safety profile. In this study, the incidence of CMV infection was found to be 23.8% in the year after transplant, which is very high in comparison with other studies, and which can be explained because we did not use universal prophylaxis against this virus.[2–9] As for other infectious complications such as BK virus and tuberculosis, both infections only presented in one patient throughout the entire follow-up period (incidence of 1.1% person-years).

During the follow-up period, which had a median of 6 years, no cases of PTLD was documented in the study population, which is consistent with the literature[10]; in addition, 23.8% of the patients in this cohort were seronegative for the Epstein–Barr virus. None of the studies with which we compared our outcomes found cases of PTLD.[5,7–9,11] One of the possible explanations why alemtuzumab has a low rate of PTLD is its T and B lymphocyte depletion effect, which arguably prevents abnormal lymphocyte clone proliferation, as the clones cause this type of lymphoproliferative disorder.

In conclusion, induction immunosuppression therapy with alemtuzumab, in paediatric kidney transplant recipients, is effective in preventing acute rejection, provides a suitable short- and long-term safety profile, encourages an adequate glomerular filtration rate, and good patient and kidney graft survival.

Table 1 – Complications one year after kidney transplantation.

Complications	One-year incidence percentage *n* (%)	One-year incidence rate (events person-years)	5-Year incidence rate (events person-years)
Delayed graft function	2 (9.5)	10.1% person-years	–
One-year acute graft rejection	3 (14.3)	16% person-years	5.6% person-years
CMV infections	5 (23.8)	26% person-years	6.7% person-years
BK virus infection	1 (4.8)	5.2% person-years	1.1% person-years
Tuberculosis	1 (4.8)	5.2% person-years	1.1% person-years
Total	21 patients		

CMV: cytomegalovirus.

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Subacute interstitial pneumonitis due to *Mycobacterium bovis* after intravesical bacillus Calmette-Guérin instillation in a renal transplant patient☆

Neumonitis intersticial subaguda por *Mycobacterium bovis* tras instilaciones vesicales de bacilo de Calmette-Guérin en un trasplante renal

Dear Editor,

The estimated incidence rate of urothelial bladder carcinoma is 1.4–2.2% in kidney transplant (KT) patients.[1] However, the clinical course may be more aggressive than in the general population, with higher rates of progression and relapse.[2]

Intravesical administration of bacillus Calmette-Guérin (BCG), an attenuated live strain of *Mycobacterium bovis*, is one of the main adjuvant therapies for managing non-invasive bladder cancer. BCG instillation produces a massive local immune reaction with antitumour activity.[3] However, both local and systemic infectious complications have been reported in relation to this treatment, especially in immunocompromised patients. Disseminated infection as a result of the systemic absorption of BCG may occur in 0.4% of cases and it is usually manifested as fever, weight loss, night sweats or dyspnoea, and even multiple organ failure in severe cases.[4,5] Interstitial pulmonary involvement is a rare complication.

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