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Induction Therapies in Kidney Transplantation: The Experience of Hospital Pablo Tobon Uribe, Medellín, Colombia 2005–2010

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ABSTRACT

Background. Induction therapies in kidney transplantation have led to prescriptions of lower doses of maintenance immunosuppression and fewer acute rejection episodes. We sought to assess the use of an affordable monoclonal antibody in terms of the incidences of rejection episodes as well as graft and patient survivals and cytomegalovirus (CMV) and opportunistic infections among our kidney transplant recipients between August 2005 and December 2010. Data were obtained for patients who had more than 20 months' follow-up.

Materials and methods. We retrospectively analyzed data from kidney recipients between August 2005 and December 2010, using descriptive statistics and Kaplan-Meier survival analysis. We performed a multivariate analysis with logistic regression for the dependent variables of rejection episodes and death.

Results. Among 425 transplant patients graft survival was 89.2% and patient survival was 94.1% after 76.2% of patients received alemtuzumab, 10.7% daclizumab, 3.6% basilixi-mab, 2.4% thymoglobulin, and 7%, no induction therapy. Rejection incidence in general in the first year was 10.8% and CMV incidence 10%. There was an increased risk of rejection among subjects without any us with alemtuzumab induction therapy.

Conclusion. Induction therapies show an important reduction in kidney transplant rejection incidence during the first year, allowing low doses of maintenance immunosuppressants, thereby diminishing long-term adverse effects. Alemtuzumab seemed to be a safe alternative with similar results to those obtained with standard immunosuppression.

INDUCTION THERAPIES in kidney transplantation have significantly improved results over the past 10 years. Nowadays they are used in more than 70% of the patients who received a kidney transplant in the United States.[1] Stronger, more specific induction regimens have led to reduced doses of maintenance immunosuppressants and fewer rejection episodes. The main problems with induction therapies are infections and neoplasms.[2–4]

Alemtuzumab, a potent monoclonal antibody directed against the CD52 receptor on T and to a lesser extent B cells, induces complement-mediated cell lysis not only in peripheral blood but also in secondary lymphoid organs as well as bone marrow. The effects last several months.[5] Given the socioeconomic circumstances of our country, we sought to assess the use of a more affordable monoclonal antibody compared with other available therapies in terms of acute rejection episodes, graft and patient survivals, as well as cytomegalovirus (CMV) and oportunistic infections.

MATERIALS AND METHODS

We retrospectively studied kidney transplant recipients between August 2005 and December 2010. Initially, we characterized the transplant population according to the variables of interest and performed normalized tests. To compare the data among the studied groups, we performed χ^2 and Pearson tests for categorical variables and Mann-Whitney U tests for continuous variables.

We evaluated cross-tab calculations between induction therapies and all other variables using χ^2 test and Fisher exact tests. Survival was calculated using the Kaplan-Meier method for grafts compar-

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0041-1345/–see front matter
doi:10.1016/j.transproceed.2011.09.006

ing estimates using the log-rank test for alemtuzumab versus other induction agents or no induction.

We constructed a multivariate model using logistic regression for the dichotomous dependent variables of rejection and death. The independent variables inputted into the model due to clinical interest were sex, age, pretransplant CMV status, CMV disease after transplantation, and transplant number, although some of them did not meet the criteria of Hosmer and Lemeshow ($P < .25$).

Induction therapy was included as a dummy variable with alemtuzumab as the reference category, for comparison with other inductors (basiliximab, daclizumab, and thymoglobulin) and with no induction.

RESULTS

Among the 425 transplanted patients, 60.5% were males and 39.5% females of overall mean age of 46.2 years. The causes of end-stage renal disease were diabetes (14.6%), glomerulopathies (12.2%), hypertension (11.5%), polycystic kidney disease (7.1%), or unknown (30%). It was the first transplant for 91.1%, second for 8.7%, and third for 0.2%. Mean cold ischemia time was 15.6 hours. Mean follow-up was 21.1 months (standard deviation 16.7). The induction therapy was alemtuzumab (76.2%), daclizumab (10.7%), basiliximab (3.6%), thymoglobulin (2.4%), or none (7%). CMV immunoglobulin G (IgG) was positive among 91.5% and Epstein Barr IgG in 90% of patients prior to transplantation. The maintenance immunosuppression was: steroids (100%), cyclosporine (86.7%), tacrolimus (10.3%), azathioprine (21.8%), mycophenolate (17%), and/or mammalian target of rapamycin (13%). In the first year the overall rejection incidence was 10.8%; CMV, 10%; BK virus, 1.4%; histoplasmosis, 0.5%; aspergilosis, 0.9%; and stongyloidiasis, 0.2%. Among the lost grafts, 4.5% of the patients had received alemtuzumab; 2.5%, daclizumab, and; 4.5%, basiliximab. We did not lose any grafts among patients who received thymoglobulin.

During the follow-up there were two posttransplant lymphoproliferative disease (PTLD) cases: one with multiple myeloma and one with lymphoma (PTLD incidence: 0.47%). One of them received alemtuzumab (incidence of 0.3%) and the other one thymoglobulin (10%). There were no PTLD cases among patients without induction or with basiliximab or daclizumab treatment.

Graft survival was 89.2% and patient survival 94.1% (Fig 1). We did not observe a significant difference comparing Kaplan-Meier graft survival curves with alemtuzumab versus other or no induction treatment (Figs 2 and 3).

When we compared rejection as a variable with the recipient characteristics according to the induction therapy, we noted a significant difference between alemtuzumab and the composite of other two alternatives other agents or no induction (Table 1). Compared to alemtuzumab, patients with other treat-

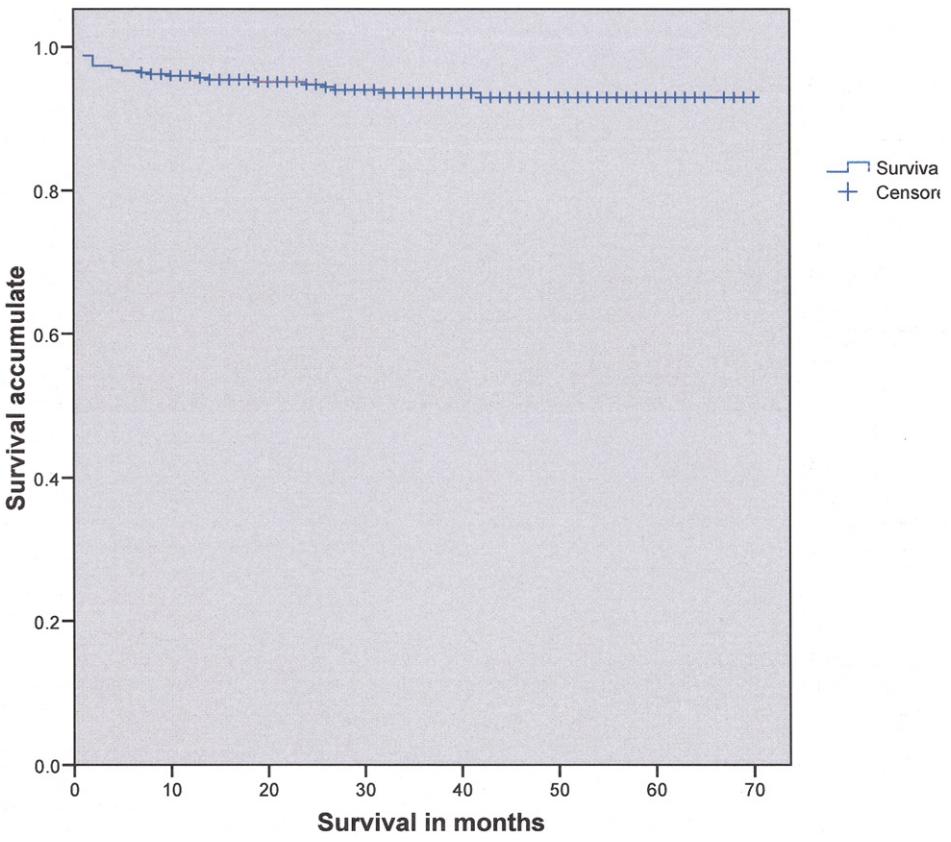

Fig 1. Kaplan-Meier plot of graft survival.