Corticosteroids have proved to be very effective for the immunosuppressive treatment of organ transplant patients, but unfortunately they are responsible for many undesirable side effects, such as cataracts, delayed growth in children, skin fragility, bone diseases, and other manifestations considered to be cardiovascular risk factors, such as glucose intolerance, arterial hypertension, and dyslipemias.1 The reduction in the incidence of acute rejection in patients treated with mycophenolate mofetil in combination with anticalcineurin agents (cyclosporine or tacrolimus) has led to the design of studies to reduce or suppress corticosteroid treatment.2–7 We analyzed the 2-year course of cadaveric kidney transplant patients treated with a triple therapy of tacrolimus, mycophenolate mofetil, and corticosteroids in whom steroid therapy was withdrawn after the 3rd posttransplant month.

**MATERIALS AND METHODS**

A prospective, randomized open study of steroid suppression in 120 cadaveric kidney transplant patients was conducted. The primary aim was to analyze the incidence of acute rejection and kidney function 2 years after steroid withdrawal.

A secondary objective was to analyze the influence on arterial hypertension, posttransplant diabetes mellitus, and hyperlipidemia of maintaining the steroids. All the patients received immunosuppressive therapy with tacrolimus at an initial dose of 0.2 mg/kg/day, adjusted to plasma levels of 15 to 10 ng/mL during the first 15 days and thereafter 5 to 10 ng/mL; mycophenolate mofetil at a pretransplant dose of 1 g per os and maintenance dose of 1 g/d; and corticosteroids with a pretransplant dose of 500 mg IV of 6-methylprednisolone, 125 mg the first posttransplant day, and thereafter 20 to 25 mg/d of oral prednisone, according to their weight. The dose of corticosteroids was gradually tapered over the 2nd and 3rd posttransplant months to 5 mg/d.

During the 3rd month, the patients who were not hyperimmunized (PRA >50%), who had not suffered an episode of acute rejection (>1A, Banff 97), and whose kidney function remained stable, were randomized into two treatment groups following a 1:1 sequence. In the steroid withdrawal group (SW), the corticosteroid therapy was gradually withdrawn over 3 weeks, and the other maintenance group (M) continued receiving prednisone 5 mg/d.

**RESULTS**

Of the 120 patients, 92 fulfilled the conditions for randomization, resulting in 46 patients in each group. There were no significant differences between the two groups in the cause of the primary disease, hemodialysis time, number of HLA mismatches, cold ischemia time, donor age, cause of the donor’s death (cranial trauma or cerebral stroke), or plasma levels of tacrolimus.

The incidence of acute rejection prior to randomization was 13.3% SW vs 8.7% M (P = NS), and after randomization it was 6% SW vs 3% M (P = NS). All patients responded to corticosteroid treatment. No patient in the SW group required reintroduction of the corticosteroids. There were no intergroup differences in plasma creatinine (1.5 vs 1.58 mg/dL); creatinine clearance (Fig 1) calculated according to the formula of Cockcroft-Gault (66.9 vs 63.0 mL/min); requirement for hypotensive agents (55.1 vs...
66.6%); treatment with statins (10.2 vs 13.1%), or levels of total cholesterol, HDL and LDL cholesterol, and triglycerides. Posttransplant diabetes mellitus developed in 4% of the patients in each group. The remainder underwent measurements of the glucose curve, C peptide, and insulin after an oral glucose tolerance test with 75 g of glucose, there being no significant differences between the two groups. Two-year graft survival after randomization was 96.7% SW vs 97% M, patient survival being 100% in each group.

CONCLUSIONS
Withdrawal of corticosteroids in a selected group of patients with a low immunological risk did not significantly increase their risk of acute rejection or influence the kidney function in patients treated with tacrolimus and mycophenolate mofetil during the study period. Studies with a greater number of patients and a longer follow-up are necessary in order to determine any possible effect of corticosteroid suppression on cardiovascular risk factors and graft survival.

REFERENCES

Fig. 1. Creatinine clearance (Cockcroft-Gault formula).