Hematologic Adverse Effects of 2 Different Polyclonal Antilymphocyte Preparations in De Novo Kidney Transplant Patients

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Abstract

Objectives: **To evaluate the hematologic adverse effects of polyclonal antilymphocyte globulins within the first month after surgery in kidney transplant recipients.**

Materials and Methods: **In this prospective, randomized trial, we included 16 adult-sensitized (panel-reactive antibodies > 30%) recipients of a kidney from a deceased donor. Eight patients received therapy with Genzyme (Thymoglobulin: ATG-G; 6.2 ± 2.9 mg/kg for 7 days), and 8 patients received Fresenius (Lymphoglobulin: ATG-F; 22.6 ± 7.9 mg/kg for 6 days). Other immunosuppressants included mycophenolate mofetil, tacrolimus, and steroids.**

Results: **Platelet counts were normal before transplant and significantly reduced after transplant; however, this was more pronounced in ATG-F patients, and had normalized by day 7 in the ATG-G and by day 10 in the ATG-F groups. Mean leukocyte/polymorphonuclear cell counts remained within the normal range in both groups through follow-up. Hemoglobin levels were similar at ~10 g/dL for both groups, up to day 10. However, erythropoietin-stimulating–agent therapy had been given to more patients in the ATG-F group than patients in the ATG-G group. Reticulocyte counts were significantly lower in ATG-F patients by days 3, 5, 7, and 10. From day 14 onwards, reticulocyte counts were similar in both groups. With regard to lymphocyte counts, these were normal in both groups before transplant and then significantly decreased afterward. No patient presented with acute rejection or serum-sickness disease.**

Conclusions: **Reduced platelet and reticulocyte counts occur more frequently immediately after transplant when using ATG-F compared with ATG-G therapy. Consequently, erythropoietin-stimulating agent therapy was needed more often for ATG-F patients.**

Key words: *Thymoglulin, Lymphoglobulin, Antilymphocyte globulins, Anemia, Thrombocytopenia, Kidney transplantation.*

Induction therapies based on polyclonal antilymphocyte preparations are frequently used in de novo kidney transplant patients (1-6), but harbor potential adverse effects, such as reactivation of *cytomegalovirus*, cytopenia, eg, leucopenia, and thrombopenia (2-5). However, anemia rarely occurs.

Within the European Union there are 2 licensed polyclonal antilymphocyte preparations: antithymocyte globulins (ATG-G; genzyme [Thymoglobulin]) and antilymphocyte globulins (ATG-F; fresenius [Lymphoglobulin]).

This prospective, randomized trial assessed the polyclonal antilymphocyte preparation-related adverse effects within the first month after transplant in 16 adult sensitized (panel-reactive antibodies > 30%) recipients of a kidney from a deceased donor. Eight patients were allocated to receive ATG-G (6.2 ± 2.9 mg/kg over 7 days) and 8 patients were to recieve ATG-F therapy (22.6 ± 7.9 mg/kg over 6 days). Other immunosuppressants included mycophenolate mofetil (2.5 g/d), tacrolimus (aiming at trough levels of 8 to 12 ng/mL), and steroids (1 mg/kg/d until day 7, then gradual reduction to 0.25 mg/kg/d by day 30). All patients received anticytomegalovirus and *Pneumocystis jiroveci* prophylaxis. Baseline

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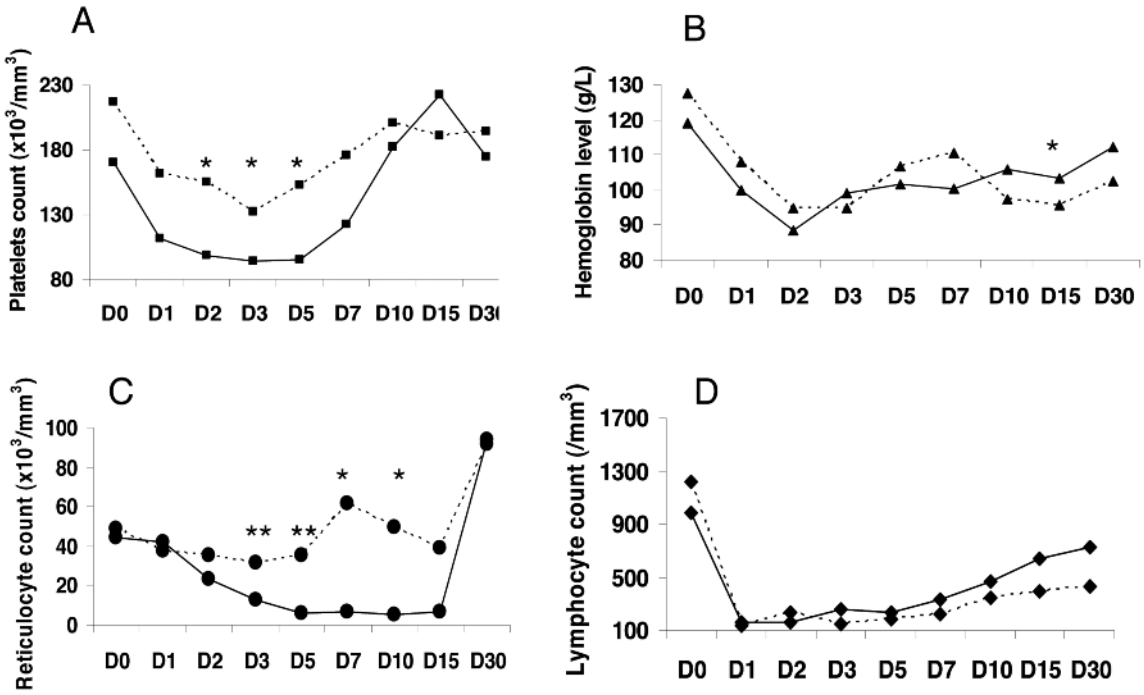

Figure 1. One-month posttransplant outcome of platelet counts (panel A), hemoglobin levels (panel B), reticulocyte counts (panel C), and total lymphocyte counts (panel D), with respect to induction therapy with either antilymphocyte globulins from Fresenius (full lines) or antithymocyte globulins from Genzyme (dotted lines). *Denotes *P* value < .05; **denotes *P* value < .01.

demographic data were similar in both groups. Prior to the study, the study protocol, which conforms with the ethical guidelines of the 1975 Helsinki Declaration, was approved by our local institutional ethics committee. Written informed consent was obtained from all of the subjects

Platelet counts were normal before transplant and significantly reduced after transplant; however, this was more pronounced by days 2 ($P = .03$), 3 ($P = .05$), and 5 ($P = .02$) in ATG-F patients (Figure 1A) and had normalized by day 7 in the ATG-G and by day 10 in the ATG-F groups. Mean leukocyte/polymorphonuclear cell counts remained within the normal range in both groups through follow-up, except for 1 ATG-G patient, who presented with mild leucopenia/neutropenia (1000/mm^3 and 900/mm^3) on day 5. Hemoglobin levels were similar at ~10 g/dL for both groups up to day 10 (Figure 1B). However, erythropoietin-stimulating agent therapy had been given to more patients in the ATG-F group compared with patients in the ATG-G group: (7/8 by day 7 for the ATG-F group vs 2/8 for the ATG-G group, and 7/8 by day 14 for the ATG-F vs 6/8 for ATG-G patients). Similar numbers of red blood cell transfusions were given in both groups.

It was striking that reticulocyte counts were significantly lower in ATG-F patients by day 3 ($P = .004$), day 5 ($P = .003$), day 7 ($P = .004$), and day 10 ($P = .02$) (Figure 1C). At no time point were there any differences between the 2 groups regarding haptoglobin and lactate dehydrogenase levels or schizocyte counts. From day 14 onwards, reticulocyte counts were similar in both groups. With regard to lymphocyte counts, these were normal in both groups before transplant and then significantly decreased afterward (Figure 1D). Although they were always lower in the ATG-G group, this difference was not statistically significant. One patient in the ATG-G group, and 2 from the ATG-F group, presented with delayed graft function.

Serum creatinine at every time point was similar in both groups. No patient presented with acute rejection or serum-sickness disease. With regards to infections, within the first month, the incidence was similar, that is, 1 patient from the ATG-F group presented with urinary tract infection, 1 with pneumonia, and 1 with peritonitis. In the ATG-G group, 3 patients had urinary tract infections, and 2 had pyelonephritis.

We conclude that reduced platelet and reticulocyte counts occur more frequently immediately after transplant when using ATG-F compared with ATG-G therapy. Consequently, erythropoietin-stimulating agent therapy was needed more frequently for the ATG-F patients.

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