Leukopenia Management in Thymoglobulin Treated Renal Transplant Recipients

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Leukopenia Management in Thymoglobulin Treated Renal Transplant Recipients

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Abstract:

Leukopenia is common following renal transplantation, though it is infrequently reported and lacks well-defined management. We retrospectively reviewed 228 consecutive renal transplant recipients at a single center for leukopenia in the first year following transplant. Leukopenic patients were evaluated for treatment strategies, efficacy, and complications including CMV infection, rejection, graft failure, and death. Leukopenia was observed in 43 of 228 (19%) transplants with median onset and duration of 95 days. Ninety-three percent of patients received treatment for leukopenia including Neupogen®, dose reduction of mycophenolic acid (MPA) or valganciclovir, and initiation of prednisone. Grade 2 neutropenia, defined as ANC≤1000 cells/mm^3, had statistically significant increased incidence of CMV ($p<0.0001$), defined as positive serum PCR, and rejection ($p=0.013$) compared to non-leukopenic patients. MPA dose reductions >50% were associated with higher rates of both CMV (60% v 42%) and rejection (60% v 33%). Conclusions: 1. Leukopenic patients experience significantly increased CMV and rejection. 2. MPA and valganciclovir dose reductions are associated with increased risk of rejection and CMV. 3. Neupogen® is an effective treatment for leukopenia.

Background:

While lymphocyte depleting induction immunosuppression agents are responsible for much of the early post-transplant leukopenia, MPA and valganciclovir have also been linked to a decrease in WBC count and ANC.[1-3]

Methods:

This retrospective, single-center study included all patients undergoing kidney and/or pancreas transplantation between January 2009 and May 2012. All recipients received thymoglobulin 4-6mg/kg in 3-4 doses and maintenance MPA/tacrolimus. All leukopenic episodes occurring between one month and one year post-transplant were analyzed. Successful treatment of leukopenia was defined as a WBC count of greater than 3500 cells/mm^3 for 30 days.

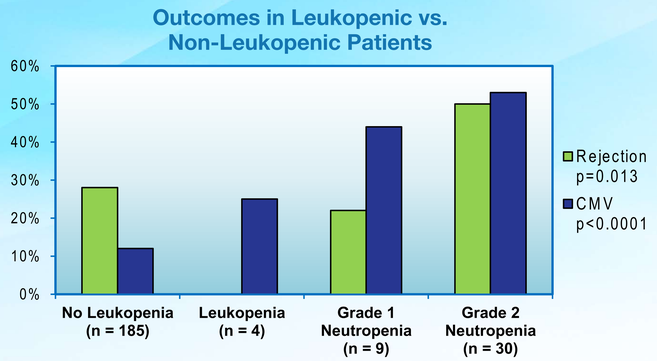
Results:

Leukopenic patients had significantly lower BMI ($p=0.0152$) than non-leukopenic patients, but matched in age, gender, transplant type, and PRA. Interventions for leukopenia were not standardized.

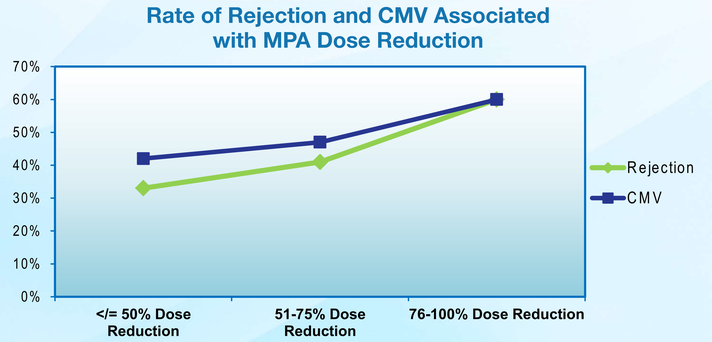
Severely neutropenic patients had a statistically significant increased incidence of CMV ($p<0.0001$) compared with non-leukopenic patients. Of the 20 leukopenic patients who developed CMV, 10/20 (50%) developed CMV prior to leukopenia. Compared with full dose valganciclovir, dose reduction was associated with a higher rate of CMV (77% v 37%) $p=0.021$. Only 4 of 10 had dose reduction prior to the CMV infection.

Neutropenic patients also had a statistically significant increase in rejection ($p=0.013$) compared with non-leukopenic patients. 11/17 (65%) leukopenic patients experienced rejection after treatment of leukopenia.

While greater degrees of MPA dose reduction resulted in a shorter median duration of leukopenia (110 v 74 days), greater MPA dose reductions were also associated with higher rates of CMV and rejection (see graph).



Grade 1 Neutropenia (1000 cells/mm^3<ANC≤1500 cells/mm^3), and ***Grade 2*** Neutropenia (ANC≤1000 cells/mm^3).



Of the 4 patients who received Neupogen® without any medication dose reductions, only 1 experienced rejection and CMV. Neupogen® took the shortest amount of time to recover WBC count (29 days) compared to prednisone (71 days), MPA dose reductions (55 days), and valganciclovir dose reduction (35 days). It is difficult to attribute improvement in leukopenia to one treatment given the multifactorial treatment process.

Conclusions:

1. Leukopenic patients experience significantly increased CMV and rejection.
2. MPA and valganciclovir dose reductions are associated with an increased risk of rejection and CMV.
3. Neupogen® is an effective treatment for leukopenia.

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