THE OUTCOME OF ATG ON THE STEM CELL TRANSPLANTS FROM MATCHED UNRELATED DONOR, A SINGLE INSTITUTE EXPERIENCE

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Abstract

BACKGROUND: Antithymocyte globulin (ATG) was found to decrease the morbidity of stem cell transplant (SCT) from matched unrelated donor (MUD) by decreasing the incidence of chronic graft vs host disease cGvHD, and at high doses, acute GvHD. We reviewed our results of MUD transplants where ATG was incorporated into the preparative regimen, and compared the results to patients prior to September 2006 where ATG was not used. The primary endpoints were the effect on GvHD and lethal infectious complications.

Method: All stem cell transplants from MUD performed after 2000 at IU hospital for treatment of hematological malignancies using a myelo-ablative regimen were retrospectively reviewed.

Result: between 1/2000 and 3/2009 seventy nine stem cell transplants were conducted using stem cells from MUD. 28 patients received ATG at a total dose of 7.5mg/kg vs 51 patients who did not receive ATG. Both groups were matched in term of age, sex, underline malignancies, degree of HLA-match, CMV serology, and conditioning regimens. Ninety-six percent of patient in ATG group received prophylaxis for GvHD using FK506/Sirolimus vs 14% in the no ATG group where a methotrexate based treatment was used ($P<0.0001$). The rate of Grade II-VI acute GVHD at day 100 was significantly lower in the ATG group compare to no ATG (14% vs 39%, $P =0.011$). Although however, the rate of chronic GVHD at 1 year was higher in ATG group than in the no ATG group, this was statistically not significant (43% and 23%; $P=0.2$). The rates of overall fungal infections and lethal fungal infections were comparable (14% and 10%) for ATG vs (17% and 11%) for no ATG ($p =0.70$). The rate of primary CMV infection (i.e., in patient not receiving corticosteroid treatment for GVHD) was higher in ATG group, although not statistically significant (31% vs 17%, $P=0.27$). Day 100 mortality was 15% and 25% in ATG and no ATG group respectively, overall survival at 1 and 2 years was 47% and 31% for ATG group vs 49% and 36% for no ATG group ($P>0.05$), Median time to death was 8.6 months (CI95%, 1.8-15.4) and 11.9 months (CI95%, 8-15.7) with $P=0.7$. The mortality from GVHD at 4 months was 0% in ATG group vs 12% in no ATG group ($P =0.08$).While the mortality rate from bacterial infection and sepsis were equivalent, more patients in the ATG group who did not receiving corticosteroid treatment for aGVHD died from viral and fungal infection (15% vs 0% at 8 months, $P=0.013$).

Summary: While ATG was associated with a trend toward lower mortality rate at day 100 due to statistically significant decrease in incidence and mortality of aGVHD, it was associated with increase rate of delayed-onset acute GVHD and statistically significant high rate of lethal viral and fungal infection leading to similar overall survival at 1 and 2 years. This study demonstrates the lack of overall benefit of ATG at dose of 7.5mg/kg. Further study to investigate the outcome of using lower doses of ATG to lower the rate of lethal infections while still reducing the risk of GvHD is recommended.