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POSTER SESSION 2

POSTER SESSION 2: ALLOGENEIC TRANSPLANTS

338

Conditioning Therapy by TBI and Etoposid Causing High Rate of Acute Kidney Injury in all Allogenetic Stem Cell Transplantation in Children

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Results of children acute lymphoblastic leukemia (ALL) therapy improved dramatically in the past decades. Patients with very high risk leukemia may benefit from allogeneic hematopoieic stem cell transplantation (HSCT) after myeloablative conditioning regimen with expected overall survival of 70%. However such therapy could induce high toxicity such as acute kidney injury (AKI). In literature, up to 45% of children may experiment acute renal failure during HSCT. It could increase other toxicities and often leads to chronic kidney disease.

In this study we retrospectively reviewed medical files of patients treated at Robert Debré Hospital in Paris for very high risk ALL by allogenetic HSCT.

From March 2007 to January 2012, 57 consecutive patients were included. All patients received a myeloablative conditioning regimen followed by HSCT from either related or unrelated 9 and 10/10 HLA compatible donor or 4 to 6/6 cord blood. Patients received TBI in 6 fractions in 3 days from D-6 to D-3 and then etoposide (60mg/kg) at D-2 in 4 hour-infusion in central venous line. GvHD prophylaxis was cyclosporine A (CSA) 1.5mg/kg twice a day in 2-hour infusion alone for patients transplanted with sibling donor and CSA + short-course methotrexate and ATG for others.

From the 57 patients, seven patients (14%) developed AKI at day +1 from etoposid infusion (AKI group), defined by an increase of creatinine level of more than 2 fold of their own creatinine basis level and estimated glomerular filtration rate (EGFR) less than 90 ml/min/1.73m^2 the day after etoposide injection. Another group of 10 patients (17.5%) had a subclinical AKI with an increase between 1.5 and 2 fold (sAKI group). EGFR means before graft of the whole cohort was of 185.7ml/min/1.73m^2 [170-200]. At day +1 from etoposide infusion, AKI groupe patients eGFR mean was of 55.4 [33-79] ($P < .0001$) and 95.5 [72-118] ($P < .0155$) ml/min/1.73m^{2}respectively. Secondary to acute kidney injury, five patients among seven required a delay for stem cell injection. Two years overall survival at was of 84.4% [76.8-98] and was not statistically different between control, AKI and sAKI group. Relapse was similar in all groups (18.6% [42-3.8] for all patients). Transplanted related mortality was higher in AKI and sAKI groups versus control group. Indeed 3/17 patients with persistent complete remission died in those 2 groups (TRM of 17.6% [0.4-50.6]), while no patient died in control group ($P = .007$). Finally, GVH was of 62.8% [49.7;73.4] in control group, 85.7% [94.1;67.6] in AKI group and 80.6 [92.6;54.6] in sAKI group (p =NS).

Acute renal injury is frequent with TBI-VP16 based conditioning regimen for high risk ALL and occurs about 24 hours after etoposide injection. It is a major adverse effect, may impact mortality and delay transplantation. Long term consequence and chronic kidney disease should be evaluated among survivors. Further study are needed to specify these results.

339

Micafungin Followed by Posaconazole is Effective as Primary Antifungal Prophylaxis in First Three Months After Unrelated Donor Transplantation

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Introduction: Invasive fungal infections (IFI) contribute to morbidity and mortality of hematopoietic cell transplantation (HCT). We evaluated micafungin followed by posaconazole for primary IFI prophylaxis.

Methods: Consecutive patients who received unrelated HCT at PMH from July 2009 to Dec 2011 with antifungal prophylaxis of Micafungin (50 mg IV daily) during hospitalization followed by posaconazole (200 mg po tid) for three months were reviewed.

Results: 86 patients received HCT in above setting. Median age was 48.3(range 18.6-71.2) years. 71 were 10/10 matches (allele level) while 15 were 9/10 (allele or antigen mismatch) (Table 1).

72 (83.7%) developed acute GVHD (aGVHD). Median day of development of aGVHD was 28.5 (range 7-100) days. Overall 1 and 2 year survival were 81.2% and 64.1% respectively. Relapse rate was 11.63%.

Median day of start of posaconazole was 22.5 (range 14-64) days. All patients tolerated posaconazole and micafungin well.

3 (3.5%) of patients were diagnosed with IFI in first three months. Median day of diagnosis was 13(range11-81) days. Diagnosis was based on symptoms with abnormal imaging and BAL galactomannan positivity in one. Two cases were treated for symptoms with imaging abnormalities (Table 2). All patients were switched to voriconazole and improved which makes it less likely that they were IFI.

Table 1
Patient Characteristics

Characteristics	n (%)
Total patients	86(100)
Age, yrs	
Less than 50	48(56)
More than 50	38(44)
Diagnosis	
AML	34(39)
ALL	10(12)
MDS	16(19)
NHL/HD	8(9)
Others	18(21)
Graft source	
Bone marrow	6(7)
Peripheral blood stem cells	80(93)
Conditioning	
MA	55(64)
RIC	31(36)
GVHD prophylaxis	
CSA/Campath	49(57)
CSA/MMF	33(38)
Others	4(5)