358

OUTCOME OF HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA IN THIRD COMPLETE REMISSION (CR3): A VITAL ROLE FOR GRAFT-VERSUS-HOST-DISEASE/ GRAFT-VERSUS-LEUKEMIA EFFECT IN SURVIVAL

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Children with acute lymphoblastic leukemia (ALL) who suffer 2 relapses could be salvaged by hematopoietic stem cell transplantation (HSCT) provided they respond to the pre HSCT chemotherapy and enter remission. However, these patients are at very high risk for post HSCT relapse and also at a high risk for transplant related mortality (TRM). Our objective, herein, was to review the outcome of children (0-18years) with ALL who received allogeneic HSCT in third complete remission (CR3) at our institution. From January 1994 – August 2005, twenty-two consecutive children in CR3 received HSCT in our instituation. Conditioning regimens included single dose VP16 (60mg/kg IV over 4 hours) and fractionated total body irradiation (TBI; 1200cGy) in six fractions over 3 days (VP16/TBI) in 10 patients and cyclophosphamide 50mg/kg IV over 1 hour daily for 4 days followed by the same dose of TBI (CY/TBI) in 12 patients. Almost all children received cyclosporine A and a short course of methotrexate for graft-versus-host disease (GVHD) prophylaxis, and all patients were in complete morphological remission prior to HSCT. Median age was 8.4 years (range 3-15.4). Donor sources were as follows: matched sibling donor (MSD), 8; matched unrelated donor (MUD) 6; one antigen mismatch related donor (MMRD) 4; one antigen mismatched unrelated donor (MMUD) 3 and one patient received 1 antigen mismatched cord progenitor stem cells. White cell engraftment was successful at a median of 18 days (range 9-29). Ten patients died of TRM, seven relapsed, one died from other causes and four patients are long term survivors at a median follow up of 3.7 years (range 1-10.2). All patients who did not develop clinical acute or chronic GVHD relapsed and died. Event free survival was (EFS 19% ± 4%). Three out of the 4 survivors received MMUD and all 4 survivors had moderate to severe acute GVHD and three had chronic GVHD, limited in two and extensive in one. **Conclusion:** Children with ALL in CR3 receiving HSCT are extremely high risk for relapse and transplant related mortality. These children have already relapsed twice and demonstrated chemotherapy resistance and GVL/ GVHD plays a key role in leukemia eradication. Although, TRM is high in such patients and GVHD could potentially increase TRM, there are no survivors without GVHD and exploring means of inducing GVHD by reduction of immunosuppressive medications or other means of immunotherapy should be considered in these patients.

359

OUTCOME OF MATCHED SIBLING DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR STANDARD RISK PEDIATRIC ACUTE MYELOGENOUS LEUKEMIA IN FIRST COMPLETE REMISSION

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In recent years there has been a significant improvement in the outcome of children with standard risk acute myelogenous leukemia (AML) treated with chemotherapy only. In the MRC-UK trials 10 and 12, standard risk AML children were allowed to proceed to hematopoietic stem cell transplantation (HSCT) if there is a full matched family donor. However, with the excellent results of chemotherapy and the known risks and long term effects of HSCT, this decision remains controversial. Herein, our objective was to review the outcome of all children between 1995-2005 with standard risk AML who received a matched sibling donor (MSD) in CR1 in our institution and compare their outcome with the published MRC-UK results. Standard risk features were defined according to the MRC-UK criteria. Thirty-two consecutive children (16 males:16 females) received MSD HSCT between 1995-2005 at the Hospital for Sick Children, Toronto. Median age was 8.4 years (range 0.5-17.5 years). Conditioning regimens included; busulphan/cyclophosphamide (Bu/Cy) n=23; Cy/Total body irradiation (TBI) n=4, VP16/ TBI n=4 and Bu/Melphalan (Bu/Mel) n=1. Graft-versus-host disease (GVHD) prophylaxis was with cyclosporine A and a short course of methotrexate. All patients engrafted apart from one patient who was conditioned with VP16/TBI and suffered a primary graft failure. That patient was re-conditioned with Bu/Cy/ATG and successfully engraft and still alive 6 years post the second HSCT. Acute grade I-II and grade III-IV GVHD occurred in 6 and 1 patients, respectively. Chronic GVHD affected 3 patients, limited in 2 and extensive in 1. One patient died from transplant related mortality (TRM). Eight patients relapsed and six died from their disease. Two relapsed patients received a second HSCT and continue to be in remission for 8 and 55 months, respectively. For a median follow up of 52 months (range 6-104 months), the relapse free survival (RFS) is 75% and the event free survival (EFS) including the 2 patients who received the second HSCT is 81%. Larger studies such as the MRC-UK 10 and 12 reported 63% RFS. **Conclusion:** Outcome of children with standard risk AML transplanted from a MSD in CR1 is very encouraging with minimal toxicity. HSCT for standard risk patient with an available family donor should be recommended.

360

PEDIATRIC PATIENTS WITH MALIGNANCIES TRANSPLANTED WITH PLASMA DEPLETED CORD BLOOD (PD CB) – AN AUDITED ANALYSIS OF 91 PATIENTS

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Cell dosage has a critical effect on cord blood transplantation (CBT) outcome; therefore pediatric patients are ideal for CBT. Younger recipient age is associated with better survival and neutrophil (ANC500) engraftment. However, even in young patients, outcome may be improved by increasing cell dose of the transplanted CB. CB banks practice red cell depletion (RCD) techniques to save storage space, which incur significant nucleated cell loss after processing; therefore, one method to minimize cell loss and still reduce volume after processing is to deplete plasma (PD), but not the red blood cells. Not washing UCB (NW) after thawing also minimizes cell loss. A large racially diverse PD UCB inventory of over 25,000 units is now available. There were 39 ALL, 23 AML, 5 JMML, 4 CML, and 20 other pediatric patients transplanted for malignant indications. Patients were classified as pediatric in two different ways: by age (less than 16 years) and by weight (less than 50kg). If the age definition is used, there were 88 pediatric patients transplanted with 89 PD UCB units (8 double cords); and if classified by weight, there were 78 patients transplanted with 78 PD UCB units (4 double cords). A retrospective audited analysis was performed on all 91 pediatric patients with engraftment and/or survival information. Of these, 24 patients had standard risks (26%), 58 patients (64%) with advanced risks and 9 risk status unknown (10%). The median age of combined patients was 5.8 years old (range 0.5-34); median weight 22 kg (range 5-91.6); male 66%. Transplant characteristics indicated a median # HLA ABDR matches of 5.0; median pre-freeze TNC dose 6.1×10^7/kg; median post-thaw TNC dose as reported by TC 5.5×10^7/kg; median pre-freeze CD34 dose 2.0×10^5/kg; transplants outside of U.S. 25%; double unit transplant 10%; non-myeloablative 9%. 56.5% of the transplanted UCB were washed post-thaw (W), 33.7% were infused without post-thaw wash (NW), with 9.8% of the units without available post-thaw data. Median