

Hematopoietic Stem Cell Transplantation

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During the past 50 years, the use of hematopoietic stem cell transplantation (HSCT) for pediatric cancer and non-malignant hematologic disease has progressed from empirical trials to standard therapy. Continued research by transplant teams worldwide is likely to sustain this progress toward the development of novel improved treatment modalities and the wider application of pluripotent hematopoietic stem cells in the treatment of human disease.

In recent years, the availabilities of peripheral and cord blood as sources of stem cells, in addition to bone marrow, have expanded the applicability of hematopoietic stem cell transplantation. Besides differences in stem cell content, immune cells in the grafts from these three sources differ in quality and quantity. As a consequence, transplants from different sources have different hematologic recovery kinetics. Stem cell sources also influence the risks of developing graft-versus-host disease.

HSCTs utilizing bone marrow as a stem cell sources, have become an accepted treatment modality for a variety of immunologic, hematologic, and malignant disorders. However, the widespread use of this modality has made it apparent that BM donation is inconvenient, uncomfortable, and not without risk. These observations led to a search for more easily and safely acquired hematopoietic stem cell sources. Recent experience suggests that peripheral blood may serve as an alternative to marrow. Indeed if the current trend continues peripheral blood stem cells (PBSCs) will soon replace BM in adults as a preferred stem cell source for both HLA-matched and unrelated HSCTs. Furthermore, adults who have experienced both seem to prefer PBSCs to BM donation.

Recently a number of small trials have supported the feasibility of using PBSCs harvest from HLA-matched minor sibling donors. With regard to the recipient, data indicate more rapid engraftment, an acceptable incidence of acute and chronic graft versus host disease (GVHD), decreased infection, and increased survival for patients with malignancies when PBSCs are utilized. These observations are based almost entirely on adult experience and are far from definitive in children. The relatively lower risk and severity of acute and chronic GVHD, the more frequent use of HSCTs for non-malignant disorders, and the diminished role of graft versus tumor/leukemia (GVT/L) in the treatment of typical malignancies are factors particular to pediatric HSCT. In addition the sense that mobilization and harvesting of PBSCs may pose unique and significant risks for the young donor, suggests to some that PBSCs may not possess the properties required to warrant their use in a pediatric transplant setting. Thus both available adult-derived data and experience suggest clinical equipoise with regard to the choice of a stem cell product, under certain circumstances for children. This circumstance strongly supports the need for a comprehensive study to evaluate the safety and efficacy of PBSCs vs. BM HSCs in children.

Umbilical cord blood was rapidly established as an alternative source of stem cells to bone marrow for allogeneic-related and unrelated hematopoietic transplantation. To date, almost 70,000 CB units are available for transplantation and more than 2,000 CB transplants (CBT) have been performed, mostly in children, to treat a variety of malignant and nonmalignant conditions. Considerable experience has been rapidly accumulated in this field and many aspects

of CBT have been elucidated, though other questions remain unresolved. A concise review of the clinical results achieved after related and unrelated CBT is presented and discussed.

Long-term sequelae of stem cell transplantation, such as impaired intellectual and psychomotor functioning, neuroendocrine abnormalities, impaired reproductive capacity, cardiotoxicity, and second malignant neoplasms, are now being reported with increasing frequency in the growing cohort of survivors. Moreover, knowledge of the late-effects of stem cell transplantation for cancer in children and adolescents continues to increase through ongoing research efforts. However, much of the available information relates to outcomes within the first post-treatment decade, but information about longer-term outcomes in adulthood is emerging as a result of well-conducted large cohort studies. Through a multi-disciplinary approach to the diagnosis, treatment, and long-term follow-up of pediatric leukemia patients, we can achieve the goal of cure while minimizing the occurrence of long-term adverse outcomes.

The Korean Society of Pediatric Hematology-Oncology surveyed pediatric allogeneic hematopoietic stem cell transplantation in Korea. Over 400 children underwent allogeneic hematopoietic stem cell transplantation for acute myelogenous leukemia (AML), severe aplastic anemia (SAA), acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia/myelodysplastic syndrome (CML/MDS), and nonmalignant rare disease, in decreasing order. It was found that the estimated event-free survival (EFS) of patients with SAA that underwent HLA-matched sibling transplants was 89%; estimated EFS of ALL in CR1 and CR2 were 77% and 67%, respectively; estimated EFS of AML in CR1 and CR2 were 73% and 60%; estimated EFS of AML in CR1 prepared with Bu/Cy was 82%; and the estimated EFS of CML/MDS was 71%. About eighty of these patients underwent cord blood transplantation. The outcomes of patients that received alternative stem cell sources were not estimated due to short median follow-up. These data shows that allogeneic hematopoietic stem cell transplantation is a

curative method in children with hematopoietic stem cell disorders, and thus, we wish to share these results.