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The Outcome of Pediatric Allogeneic Stem Cell Transplantation At King Abdullah Specialized Children's Hospital (KASCH)

Muath Abuhaimed[1], Batal Aldosari[1], Bassam Alduwaifiry[1], Turki A. Alqahtani[1], Mohammed Essa[2], Abdulrahman Alsultan[2]

[1] *College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.*
[2] *Department of Pediatric Hematology/Oncology, King Abdullah Specialized Children's Hospital, Riyadh, Saudi Arabia*

Abstract:
Allogeneic stem cell transplantation (SCT) is an important modality of therapy for children with cancer and inherited disorders such as thalassemia. In this study, we reviewed the allogeneic SCT experience of the Pediatric SCT program at King Abdullah Specialized Children's Hospital (KASCH) in Riyadh from January 2010 - December 2014. The following data were collected through chart reviews including patients' demographics (age and gender), diagnosis, degree of HLA matching, stem cell source, conditioning regimens, and treatment outcomes. A total of 51 patients were transplanted during this period, of those 27 were males and 24 females. The median age at transplantation was 5.1 (range, 0.2–13.4) years. A total of 45 patients were transplanted using matched related donors and 6 were transplant from unrelated cord blood transplant (UCBT). All patients engrafted successfully except 2 patients who had UCBT. The median time for neutrophils engraftment was 24 days (range, 9-58 days) and for platelets engraftment 25 days (range, 8-73). Transplant related mortality at day 100 was 5%. The frequency of acute GVHD grade (II-IV) was 7.8% and for grade (III-IV) was 2%. There was only 9% with chronic GVHD. The 1-year and 2-year event free survival was 83.7%. In addition, the 1-year overall survival was 89.4% and the 2-year overall survival was 86.7%. The events were two graft failure with the cord transplants and two late graft failure in match related (bone marrow), three of those underwent successful second transplant. The causes of death were pulmonary toxicity in 2 patients, sever GVHD in 1 patient and leukemia relapses in 2 patients. In conclusion, the survival outcome of pediatric allogeneic SCT at KASCH is comparable to those reported from other centers. We observed low rate of GVHD in our study, which is expected given that majority of cases were transplanted from matched related donors.

Keywords: *Allogeneic, stem cells, Transplant, Pediatric, Riyadh, Saudi Arabia*

Introduction

Hematopoietic stem cell is a pluripotent stem cell that can divide and give rise to different cell lineages and blood cells.[1] Although the quantities of hematopoietic stem cells is not that high (1 in every 20 million nucleated cell found in Bone Marrow), it has a major role in producing the various blood products including RBCs, platelets, monocytes, neutrophils, eosinophils, basophils, lymphocytes and NK cells. Hematopoietic stem cells can be found in pelvic bones, sternum, femur and umbilical cord blood. They can also be found in small numbers within the peripheral blood.[2]

In stem cell transplantation, the pathological hematopoietic stem cells and immune system of the patient will be destroyed by chemotherapy and or radiotherapy and will be replaced by normal hematopoietic stem cells.[3] These new hematopoietic stem cells could be either from the patient himself (Autologous stem cell transplantation) or from an HLA matched donor (Allogeneic stem cell transplantation). [4-5]

The outcome of pediatric allogeneic stem cell transplant has improved over the last two decades. The outcome of transplant varies depending on the nature of the disease, the type of transplant used (myeloablative versus non-myeloablative) and the source of the stem cells (bone marrow, peripheral blood or cord blood). [6] Indications of allogeneic stem cell transplantation in children include leukemia, aplastic anemia, hemoglobinopathies, immunodeficiency and metabolic disorders.[7]

In this study, we will review our institutional experience from 2010 to 2014 using allogeneic transplant to treat malignant and nonmalignant disorders in children. This analysis focuses on estimating event free survival and overall survival. Therefore, we hypothesize that the outcome of pediatric allogeneic stem cell transplant at King Abdullah Specialized Children's Hospital (KASCH) is comparable to the international literature.

Patients and Methods

This is a retrospective study with a non-probability purposive sampling in which all charts of children who underwent allogeneic stem cell transplant between September 2010 to December, 2014 was reviewed. The study was performed at KASCH, which is one of the tertiary centers in the kingdom. We included all male and female pediatric patients up to the age of 14 years at KASCH between the mentioned periods.

Baseline characteristics were described. Transplant-related mortality and survival was estimated. The medical records of these patients were pulled from the medical records department. A data collection sheet containing the various variables of interest was prepared. The variables include age, gender, indication, disease status pre-transplant, complication, transplant details, disease assessment at day 100, and follow up post-transplant. Data was retrospectively obtained from patient's records and entered on the data sheets. Collected data was analyzed using an appropriate statistical package (EXCEL) and the graphs using Prism.

Results

The clinical characteristics of 51 pediatric patients who underwent allogeneic stem cell transplantation in KASCH from the period of January, 2010 to December, 2015 is summarized in Table I. The average age was 5.1 at the time of the transplant (range: 0.2-13.4 years). There were 45 bone marrow transplants and 6 unrelated cord blood transplants. Out of the 51 patients, 8 underwent transplant from unrelated matched donors.

Table 1. Clinical Characteristics of The 51 Patients Undergoing allogeneic Stem Cell Transplantation

Age [mean]	5.1(0.2-13.4)
Gender (N (%))	

Male	27 (52.94)
Female	24 (47.05)
Diagnosis:	
Malignant	14
ALL	10
AML	3
JMML	1
Benign	31
HLH	3
Bone marrow failure	15
Hemoglubinopathy	8
Immunodeficiency	5
Cord: malignancies	
Relapsed ALL	1
CML	1
JMML	2
Cord: benign	
Fanconi anemia	1
HLH	1
Donor status (N (%))	
Related	43 (84.31)
Unrelated	8 (15.68)
Donor-recipient mismatch (N (%))	
Gender mismatch	25 (49.01)
Blood type mismatch	31 (60.78)
Conditioning (N (%))	
Busulfan-based	14 (27.45)
TBI-based	14 (27.45)
Others	23 (45.09)
GVHD prophylaxis (N (%))	
MTX/CSA	20 (39.21)
MMF/CSA	25 (49.01)
Others	6 (11.76)
Successful neutrophil engraftment	49 (96.1)
Median time to NE (days)	24 (9-58)
Successful platelets engraftment	48 (94.2)
Median time to PE (days)	25 (8-73)
GVHD Status (N (%))	
Acute GVHD (II-IV)	4 (7.8%)
Acute GVHD (III-IV)	1 (2%)
Chronic GVHD	5 (9%)
Event free survival (at 1 year)	43 (83.7%)
Event free survival (at 2 year)	43 (83.7%)
Overall survival (at 1 year)	46 (89.4%)
Overall survival (at 2 year)	44 (86.7%)
Transplant related mortality at day 100:	5 (10.6%)

The Bone marrow transplant group was 23 females and 22 males. The indications of the transplants were 14 malignancies, 10 relapses of ALL, 3 AML and 1 JMML and 31 benign, 3 HLH, 15 bone marrow failure, 8 hemoglubinopathy (SCA and thalassemia) and 5 immune deficiencies. The cord transplant group was 5 males and 1 female. The causes of the transplants were CML, HLH, 2 JMML, fanconi anemia and relapsed ALL.

The donor-recipient mismatch was 25 gender mismatches, and 31 blood type mismatches. The conditioning regimen consisted of busulfan based in 14 patients, total body irradiation (TBI) in 14 patients and other regimen in 23 patients. The GVHD prophylaxis that was given included, methotrexate (MTX)/cyclosporine (CSA) in 20 patients, mycopheolate mofetil (MMF)/CSA in 25 patients and 6 were given other prophylaxes. Successful neutrophils engraftment was seen in 96.1% of patients with 2 grafts rejection in the cord transplant group. In addition, there were 94.2% successful platelets engraftments with 3 graft rejections in the cord transplant group.

One of the complications we see in stem cell transplantation is GVHD. In our study, the acute GVHD (II-IV) was 7.8% and for acute GVHD (III-IV) was 2%. In addition, the chronic GVHD was 9%. The 1-year and 2-year event free survival was 83.7. The events were 2 graft failure with the cord transplants and 2 late graft failure in match related (bone marrow). Furthermore, The 1-year overall survival was 89.4% and the 2-year overall survival was 86.7%. Transplant related mortality at day 100 was 10.6%. The causes of death were pulmonary toxicity in 2 patients, sever GVHD in 1 patient and leukemia relapses in 2 patients.

Discussion

This study aimed to measure the outcome of pediatric allogeneic HSCT at KASCH and compare it to the international figures. The most important finding of this study was an overall survival of 89.4% at 1 year (Figure 1). In addition, the 1-year event free survival was 83.7% (Figure 2). In comparison to a study that was conducted in Europe, which reported an overall survival at 1 year reached up to 77, and 1-year event free survival of 70%.[8] Another study in the United state reported that the overall survival at 1 year was 88% (80%-92%).[9]

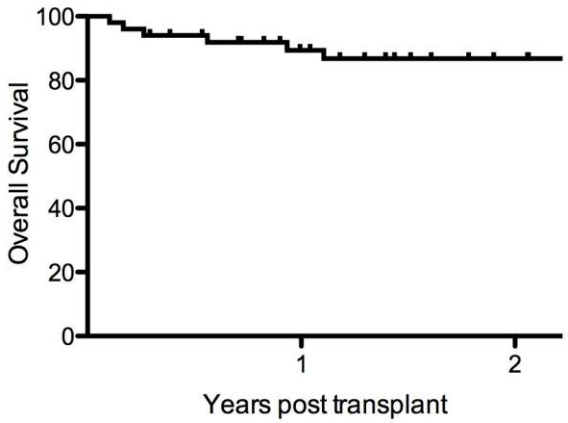

Figure 1: Overall survival (OS) among patients post transplantation

Figure 2: Event free survival (EFS) among patients post transplantation

In our study, the frequency of acute GVHD grade (II-IV) was 7.8%, for grade (III-IV) was 2% and 9% with chronic GVHD. In comparison to the American study, which acute GVHD grade (II-IV) was 46%, for grade (III-IV) was 24% and 37% with chronic GVHD. We observed lower rates of GVHD in our study, which is expected given that majority of the cases were transplanted from matched related donors.[8] We conclude that the survival outcome of pediatric allogeneic SCT at KASCH is comparable to those reported from other centers.

One of the limitations of this study was the small sample size. Since the program of stem cell transplantation at our center was launched in January 2010, only 51 pediatric patients have underwent allogeneic HSCT by the end of December 2014, which made it difficult to compare to international studies in which the sample size was much higher. Another limitation was the short time of follow up. While the follow up duration of most of the studies was 5 or even up to 10 years, we followed up our patients for only two years, taking the novelty of our program into account. In addition, most of the conducted researches in this field estimated the outcome in specific diseases such as leukemia, which somehow limited the comparison given that our study was not disease specific.

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