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Brief Report

Stem Cell Transplantation; Iranian Experience

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From March 1991 through 31st December 2007, 2042 patients underwent stem cell transplantation at the Hematology-Oncology and Stem Cell Transplantation Research Center, affiliated to Tehran University of Medical Sciences. These transplantations included 1405 allogeneic stem cell transplantation, 624 autologous stem cell transplantation, and 13 syngeneic stem cell transplantation. Stem cell transplantation was performed for various diseases including acute myelogenous leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, chronic lymphoblastic leukemia, thalassemia major, sickle cell thalassemia, sickle cell disease, multiple myeloma, myelodysplasia, mucopolysaccharidosis, paroxysmal nocturnal hemoglobinuria, non-Hodgkin's lymphoma, Hodgkin's disease, severe aplastic anemia, plasma cell leukemia, Niemann-Pick disease, Fanconi anemia, severe combine immunodeficiency, congenital neutropenia, leukocyte adhesion deficiencies, Chediak-Higashi syndrome, osteopetrosis, histiocytosis X, Hurler syndrome, amyloidosis, systemic sclerosis, breast cancer, Ewing's sarcoma, testicular cancer, germ cell tumors, neuroblastoma, medulloblastoma, renal cell carcinoma, nasopharyngeal carcinoma, ovarian cancer, Wilms' tumor, rhabdomyosarcoma, pancreatoblastoma, and multiple sclerosis. We had 105 cellular therapies for postmyocardial infarction, multiple sclerosis, cirrhosis, head of femur necrosis, and renal cell carcinoma. About 30 patients were retransplanted in this center. About 74.9% of the patients (1530 of 2042) remained alive between one to 168 months after stem cell transplantation. Nearly 25.1% (512 of 2042) of our patients died after stem cell transplantation. The causes of deaths were relapse, infections, hemorrhagic cystitis, graft versus host disease, and others.

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Introduction

Bone marrow transplantation was the original term used to describe the collection and transplantation of hematopoietic stem cells, but with the recent demonstration that the peripheral blood and umbilical cord blood are also useful sources of stem cells, hematopoietic cell transplantation has become the preferred generic term for this process.[1]

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Iran has a population about 70 million. The incidence of transplantable disease is estimated at about two per 100,000 or 1400 patients per year. The cost of transplant procedures is borne by insurance companies and private sources.

Hematology-Oncology and Stem Cell Transplantation Research Center is affiliated to Tehran University of Medical Sciences located in Shariati Hospital, Tehran, Iran. Our center's activities have started in 1991 in order to help needful patients and augment new data to reach new aspects of therapeutic trials.[2]

Patients and Methods

From Mach 1991 through 31st December 2007,

1405 patients were treated by myeloablative and nonmyeloablative chemotherapy followed by allogeneic stem cell transplantation (SCT),[3] at the Hematology-Oncology and Stem Cell Transplantation Research Center, affiliated to Tehran University of Medical Sciences. Their diseases in order of frequency included acute myelogenous leukemia (AML, n=354), thalassemia major (n=335), acute lymphoblastic leukemia (ALL, n=244), chronic myelogenous leukemia (CML, n=222), severe aplastic anemia (SAA, n=120), myelodysplasia (MDS)/mucopolysaccharidosis(MPS)/paroxysmal nocturnal hemoglobinuria(PNH) (n=35), non-Hodgkin's lymphoma (NHL, n=27), Fanconi anemia (n=27), chronic lymphoblastic leukemia (CLL, n=7), Hodgkin's disease (HD, n=5), severe combine immune-deficiency (SCID, n=5), leukocyte adhesion deficiencies (LADs, n=4), multiple myeloma (n=3), Chediak-Higashi syndrome (n=3), breast cancer (n=2), renal cell carcinoma (n=2), sickle cell thalassemia (n=1), neuroblastoma (n=1), plasma cell leukemia (n=1), Niemann-Pick disease (n=1), osteopetrosis (n=1), histiocytosis X (n=1), Hurler syndrome (n=1), rhabdomyosarcoma (n=1), congenital neutropenia (n=1), and sickle cell disease (n=1).

The donor types of SCTs were histocompatible siblings (n=1367), HLA-mismatch siblings (n=29), HLA-match other relatives (n=5), and HLA-mismatch unrelated (n=4).[4] The patients who were treated by allogeneic SCT received a median of 9.44×10^8/kg nucleated cells (range: 0.93 – 33.29×10^8/kg).

From March 1991 through 31st December 2007, 624 patients were treated by intensive chemotherapy followed by reinfusion of non-cryopreserved autologous stem cells. These patients had the following diseases: AML (n=190), multiple myeloma (n=158), NHL (n=107), HD (n=98), ALL (n=25), germ cell tumor (n=5), breast cancer (n=6), Ewing's sarcoma (n=6), plasma cell leukemia (n=2), systemic sclerosis (n=3), neuroblastoma (n=3), medulloblastoma (n=3), ovarian cancer (n=2), amyloidosis (n=3), nasopharyngeal carcinoma (n=1), Wilms' tumor (n=1), pancreatoblastoma (n=1), multiple sclerosis (n=1), testicular cancer (n=7), and plasma cell disorders (n=2). The patients who were treated by autologous SCT received a median of 6.96×10^8/kg (0. 1 – 33.25×10^8/kg) nucleated marrow cells.

During this period, 13 patients were treated by syngeneic SCT. Their diseases were ALL (n=6), AML (n=4), severe aplastic anemia (n=2), and NHL (n=1). They received a median of 6.26×10^8/kg (3.8 – 9.22×10^8/kg) nucleated marrow cells.

Stem cells were obtained and kept at 4°C for one to four days before reinfusion. The stem cells were reinfused without purging. All the patients were treated in reverse barrier isolation in single rooms but without air filtration or laminar airflow protection. They received intestinal decontamination and low-bacteria content food.[5–7]

Results

The median age at the time of transplantation for allogeneic, autologous, and syngeneic patients was 20 years (range:0 – 63), 31 years (range:2 – 95), and 21 years (range:16 – 36), respectively. The male:female ratio was 835:570 in allogeneic, 369:255 in autologous, and 10:3 in syngeneic groups. Sources of stem cells were peripheral blood (82%), bone marrow (17%), and cord blood (1%). Acute graft versus host disease (GVHD) developed in 44.7% (grade I=29.5%, grade II=34.1%, grade III=26.3%, and grade IV=10.1%). Chronic GVHD developed in 20.6% of the patients with allogeneic SCT (limited=62.3%, extensive=37.7%, and the severity was mild in 57%, moderate in 28%, and severe in 15%).

At present, 1054 (74.7%) patients with allogeneic SCT are alive and 355 (25.3%) patients died. The causes of death were relapse (25.9%), GVHD (28.2%), infection (11.8%), veno-occlusive diseases (VOD, 2%), and others (32.1%).

About 471 of the 624 (75.5%) patients with autologous SCT are alive and 153 (24.5%) patients died. The causes of death were reject/relapse (77.8%), infections (5.9%), VOD and cardiac toxicity (1.3%), and other causes (15%).

Of the 13 patients with syngeneic SCT, eight (61.5%) patients are alive and five (38.5%) patients died. The causes of death were reject/relapse (60%), infections (20%), and GVHD (20%).

The median duration of follow-up for all the patients was 19 (range≤1 to 195) months (median of 21 months for allogeneic SCT, 15 months for autologous SCT, and 18 months for syngeneic SCT).

We had 105 cellular therapy for post-myocardial infarction, multiple sclerosis, cirrhosis, head of femur necrosis, and renal cell carcinoma. Of the 513 deaths, 185 (36.1%) were occurred

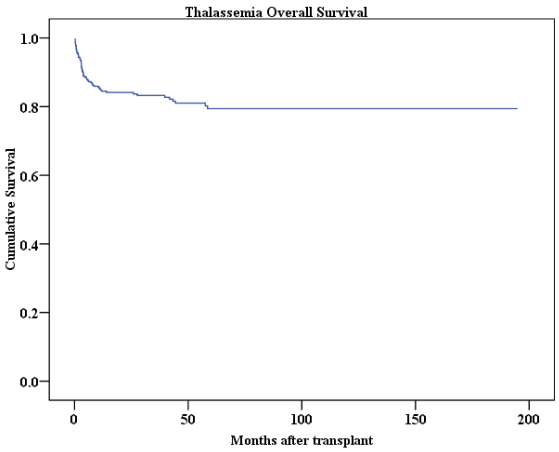

Figure 1. Overall survival of patients with thalassemia.

during the first 100 days of SCT. The common causes of death during the first 100 days were relapse/rejection, infection, GVHD, VOD, and others.

Our thalassemic patients have an overall survival (OS) of 79.4% (SE=3%) and disease free survival (DFS) of 68.4% (SE=3%) at 12 years after SCT (Figure 1).

In patients with AML and ALL the allogeneic SCT was performed more than autologous SCT. In AML patients with allogeneic SCT, DFS, and OS were significantly more than the patients with autologous SCT (P<0.0001, Figure 2). But there was no significant difference in DFS and OS between the ALL patients with allogeneic or autologous SCT (P= 0.07 and 0.06, respectively) (Figure 3).

We found that DFS and OS in CML patients were higher in those who received peripheral blood SCT compared with those who received bone marrow transplantation (P=0.012 and 0.002, respectively).

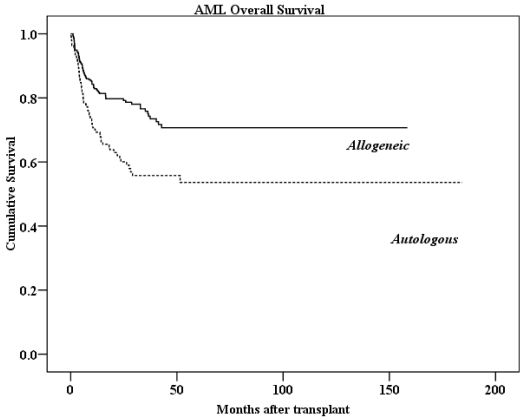

Figure 2. Overall survival of acute myelogenous leukemia (allogeneic versus autologous).

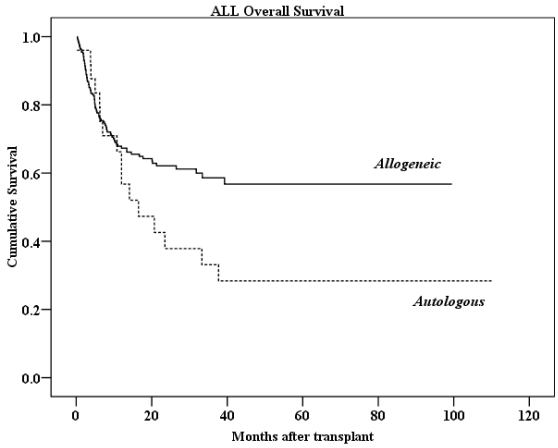

Figure 3. Overall survival of acute lymphoblastic leukemia (allogeneic versus autologous).

The patients with aplastic anemia who received SCT had an eight-year DFS of 66% and OS of 78%. The nine-year DFS and OS in patients with multiple myeloma who received autologous SCT was 24.1% and 57.7%, respectively.

In patients with NHL who received autologous SCT, the five-year DFS and OS was 52.4 % and 63.7%, respectively. The four-year DFS and Os in patients with HD was 65.3% and 75.8%, respectively. The patients with Fanconi anemia who received allogeneic SCT had a three- year DFS and OS of 41%.

Discussion

Hematopoietic SCT is a choice treatment of many malignant, nonmalignant, and genetic diseases. According to statistical reviewing during the past 17 years in Hematology-Oncology and Stem Cell Transplantation Research Center, we found that our thalassemic patients have an OS of 79.4% (SE=3%) and DFS of 68.4% (SE=3%) at 12 years after SCT. The DFS of thalassemia in our center is close to the result of thalassemia in Italy.[8] The number of hematopoietic SCT for AML and ALL was more frequent amongst all disorders. In patients with AML and ALL the allogeneic SCT is more than autologous SCT that is similar to the results of European Group for Blood and Marrow Transplantation (EBMT) Survey.[9]

SCT is the treatment of choice for many neoplastic, non-neoplastic, and genetic diseases. We found that allogeneic SCT is an effective treatment for patients with AML. The actual survival at 12 years exceeds 50%.

The allogeneic SCT has been used in the

treatment of thalassemia major with 80% survival. The cure rate for patients with severe aplastic anemia following SCT was 70 – 80%.

References

1 Frederick R. Hematopoietic cell transplantation. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, eds. *Harrison's Principles of Internal Medicine*. Section 2, Chapter 100, 16th ed. Appelbaum; 2008: 668 – 673.

2 Ghavamzadeh A, Jahani M, Baybordi I. Bone marrow transplantation in Iran. *Bone Marrow Transplant*. 1994; **13:** 743 – 744.

3 Ghavamzadeh A, Nasseri P, Eshraghian MR, Jahani M, Baybordi I, Nateghi J, et al. Prognostic factors in bone marrow transplantation for beta -thalassemia major: experiences from Iran. *Bone Marrow Transplant*. 1998; **22:** 1167 – 1169.

4 Ghavamzadeh A, Bahar B, Jahani M, Khodabandeh A, Shahriari A. Bone Marrow Transplantation of Thalassemia, the Experience in Tehran, Iran. Third International Symposium on Bone Marrow Transplantation in Thalassemia; 1997.

5 Ghavamzadeh A, Bahar B. Communication with the cancer patient in Iran. Information and truth. *Ann N Y Acad Sci*. 1997; **809:** 261 – 265.

6 Iravani M, Evazi MR, Mousavi SA, Shamshiri AR, Tavakoli M, Ashouri A, et al. Fludarabine and busulfan as a myeloablative conditioning regimen for allogeneic stem cell transplantation in high- and standard-risk leukemic patients. *Bone Marrow Transplant*. 2007; **40:** 105 – 110.

7 Ghavamzadeh A, Iravani M, Ashouri A, Mousavi SA, Mahdavi N, Shamshiri A, et al. Peripheral blood versus bone marrow as a source of hematopoietic stem cells for allogeneic transplantation in children with class I and II beta- thalassemia major. *Biol Blood Marrow Transplant*. 2008; **14:** 301 – 308.

8 Lucarelli G, Andreani M, Angelucci E. The cure of thalassemia by bone marrow transplantation. *Blood Rev*. 2002; **16:** 81 – 85.

9 Gratwohl A, Baldomero H, Horisberger B, Schmid C, Passweg J, Urbano-Ispizua A ,et al. Current trends in hematopoietic stem cell transplantation in Europe. *Blood*. 2002; **100:** 2374 – 2386.