Original Article

Effects Of Ethnicity On Allogenic Stem Cell Mobilization

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Abstract

Purpose: In our study, we compared the stem cell levels collected after the mobilization regimen and the engraftment levels after allogeneic stem cell transplantation in Syrian patients and Turkish patients who received stem cell transplantation in our center. We aimed to reveal the differences in allogeneic stem cell transplantation between two ethnicities.

Methods: The data of Syrian patients and Turkish patients in our bone marrow transplant centre were analysed retrospectively. Ten patients with Aplastic Anemia, 2 with Thalassemia, 6 with Acute Myeloid Leukemia, 20 with Acute Lymphocytic Leukemia, 4 with Chronic Myeloid Leukemia, a total of 21 patients with Syrian origin and 21 patients with Turkish origin as the group were included in the study.

Results: A total of 42 people, 21 (50%) Turkish and 21 (50%) Syrian, with a mean age of 32.33±13,083 were included in the study. There is a statistically significant difference between Turkish and Syrian in terms of stem cell level. (p value: 0.01). When the effect size for the stem cell level is examined, this detected difference is clinically quite large. (effect size: 0.867).

Conclusion: The stem cell mobilization of level of Turks is significantly higher compared to Syrian so Mobilization of patients with syrian and platelet engraftment were more difficult. Like many factors, ethnicity can be effective in stem cell mobilization

Keywords: Ethnicity, Allogenic, Stem cells, Mobilization

INTRODUCTION

Allogeneic stem cell transplant (ASCT) is a treatment method for various malignant and non-malignant hematologic disorders. The pluripotent hematopoietic stem cells are usually obtained from the bone marrow or peripheral blood of a donor. The results of allogeneic bone marrow transplantation from the human leukocyte antigen (HLA) compatible sibling are much better. (1). Hematopoietic cell transplantation is a general term that covers a number of procedures in which the patient is treated with chemotherapy, radiation therapy, or both. Various strategies for hematopoietic cell transplantation have been developed and implemented depending on the patient's disease and disease stage, the hematopoietic cell donor and the source of the hematopoietic progenitor cells (2). ASCT is increasingly used to treat a variety of hematologic neoplasms and non-malignant bone marrow disorders (acquired and inherited) including inborn errors of metabolism (3). Many centers consider 55 years the limit for myeloablative ASCT, but allow lower-intensity ASCT in physically fit patients up to 75 years of age (4). The degree of myelosuppression and the duration of hematopoietic recovery differ according to many factors, including the regimen of preparation and the source of the graft (5). When infused hematopoietic stem cells begin to produce normal blood cells in the bone marrow, it is called engraftment. By definition, it is defined as the recipient's peripheral blood absolute neutrophil count of 1000 micro/L or greater than 500 for three consecutive days after hematopoietic cell transplantation. Depending on the donor, graft composition and type of preparation regimen, on average it is about 30 days after transplant (6). Aggressiveness of the underlying disease, disease status has a significant impact on the long-term survival of ASCT patients (7). Eligibility for ASCT differs between countries and institutions, and there are few strict rules about who is a suitable candidate and who is not. Instead, a decision must be made on whether the long-term and short-term risks of the transplant outweigh its benefits. Risk factors include the state of performance, comorbidity, age, adaptation, prevalence and condition of the disease, as well as the sensitivity of the tumor to standard therapy. It cannot be predicted that the patient will develop chronic graft-versus-host disease or other complications before hematopoietic cell transplantation. Patients should be informed of the possibilities and their impact on quality of life. All of these factors should be taken into account when determining the appropriateness of ASCT for an individual. The final decision on transplant eligibility should be made based on the risk-benefit assessment and the patient's needs and wishes (8). Following ASCT, patients are immunocompromised and therefore at high risk for infectious complications, especially when exposed to large crowds (9). Low socioeconomic status is considered

to have a negative impact on the success of hematopoietic cell transplantation based on a retrospective analysis (10). Studie investigating this relationship suggest that race consists of a complex social, cultural and political structure rather than a biological concept. It has been observed that black patients are less likely to have hematopoietic cell transplantation for leukemia or lymphoma than white patients (11). In our study, stem cell levels of Syria ethnicity patients who had underwent ASCT in our center were compared with those of Turkish ethnicity patients.

MATERIALS AND METHODS

Our study was approved by the Inonu University Ethics Committee with the approval number 2021/2715. After the ethics committee approval, the patients who applied to İnönü University Turgut Özal Medical Center between the years 2018-2021 were analyzed retrospectively. Mobilization protocols, neutrophil and platelet engraftment time, collected CD34(+) stem cell level, and chemotherapy protocols before allogeneic stem cell transplantation were obtained from patient records. The collected stem cell levels of 21 Syrian and 21 Turkish patients were recorded. The donors of the allogeneic transplantation patients with stem cell levels in the study had the same ethnic structure. Neutrophil engraftment was considered the when the absolute neutrophil count was >0.5 × 109/L without G-CSF supplementation. Platelet engraftment was accepted when the platelet count was >20×109/L without platelet apheresis support.The patients were divided into two groups (Syrian and Turkish patients). Allogeneic stem cell apheresis forms of 42 patients were analyzed retrospectively whit ASCT at İnönü University Turgut Özal Medical Center bone marrow transplant unit. Ten patients with Aplastic Anemia(AA), 2 with Thalassemia, 6 with Acute Myeloid Leukemia(AML), 20 with Acute Lymphocytic Leukemia(ALL), 4 with Chronic Myeloid Leukemia(CML), a total of 21 patients with Syrian origin and 21 patients with Turkish origin as the control group were included in the study(table 1).The distribution of patients according to diagnoses and ages is available in Table 1.Each stem cell number was obtained by collecting CD34(+) stem cells with the help of the Spectra optia device after the patients received a mobilization regimen, and calculating the number of CD34(+) cells per kilogram.

RESULTS

Data analysis

Missing values in the PLT ENG (platelet engraftment) and NE ENG (neutrophıl engraftment)variables were assigned according to the mean. Normally distributed quantitative data were summarized as mean ± standard deviation and non-normally distributed quantitative data were summarized as median (minimum-maximum). Qualitative data were summarized by number (percentage). Independent samples t-test and Mann-Whitney U test were used where appropriate for statistical analysis. In this study, in addition to basic comparisons, effect sizes were calculated to evaluate the effects of each variables on Syrıan and Turkish groups. Effect size is defined as the size of the difference between groups (13). The general interpretation of the effect size in the literature; between 0.01-0.06 values, there is a small effect, between 0.06-0.14 a medium effect, and a value above 0.14 a large effect. p<0.05

was considered statistically significant. Python 3.9 Version and SPSS 26.0 programming languages were used for data analysis.

Basic Properties of Data

A total of 42 people, 21 (50%) Turkish with a mean age of 39.09 ± 15.07 and 21 (50%) Syrıans with a mean age of 28 ± 12.84, were included in the study (Table 1). Descriptive statistics and effect sizes of Turkish and Syrıan groups according to SCL (stem cell level), PLT ENG and NE ENG variables of the data set are given in Table 2. There is a statistically significant difference in terms of SCL (p: 0.01) and NE ENG (p: 0.034) variables of Turkish and Syrian patients. When the effect size is analyzed for SCL (effect size: 0.867) and NE ENG (effect size: 0.685) This difference is clinically quite large. While the SCL values of the Turks were significantly higher than those of the Syrıans, their NE ENG values were significantly lower.

Table 1: Distribution of Patients Diagnoses.

		Nationality		p
		Syrıan	Turkish	
Age	Mean ± SD	28 ± 12.84	39.09 ± 15.07	0.014
DIAGNOSIS	AA n (%)	5 (23.8)	5 (23.8)	-
	ALL n (%)	10 (47.61)	10 (47.61)	
	AML n (%)	3 (14.28)	3 (14.28)	
	CML n (%)	2 (9.52)	2 (9.52)	
	TALESEMİ n (%)	1 (4.76)	1 (4.76)	

Abbreviations: Aplastic Anemia (AA), Thalassemia, Acute Myeloid Leukemia (AML), Acute Lymphocytic Leukemia (ALL), Chronic Myeloid Leukemia (CML)
SD: Standart deviation

Table 2: Stem cell level and Engraftment Distribution

	Nationality		p	effect size
	Syrıan	Turkish		
	Median(Min-Max)	Median(Min-Max)		
SCL	8.13 (5-15)	10.4 (4.95-20.4)	0.01	0.867
PLT ENG	19 (10-40)	16 (9-29)	0.071	-
NE ENG	18 (11-28)	15 (7-23)	0.034	0.685

Abbreviations: PLT ENG(platelet engraftment), NE ENG (neutrophıl engraftment),SCL(stem cell level).

DISCUSSION

Allogeneic hematopoietic cell transplantation is a treatment method for various malignant and non-malignant hematologic disorders. The necessary pluripotent hematopoietic stem cells are usually obtained from the bone marrow or peripheral blood of a donor. Hematopoietic cell transplantation is a general term that covers a number of procedures in which the patient is treated with chemotherapy, radiation therapy, or both.

Studies investigating this relationship suggest that race consists of a complex social, cultural and political structure rather than a biological concept. It has been observed that black patients are less likely to have hematopoietic cell transplantation for leukemia or lymphoma than white patients. Hematopoietic cell transplantation is an effec-

tive treatment for high-risk hematological disease. HLA compatibility between donor and patient limitations (13). After HLA matched unrelated donor, African Americans showed lower survival compared to Caucasians with hematologic malignancies, which was linked to higher transplant-related mortality (13). Increasing use of HLA-haploidentical relatives has expanded access to transplantation, especially for minorities (14).

In a recent unicenter report, survival after HLA haploidentic transplantation with cyclophosphamide after transplantation was found to be better for African-American patients than for patients of Caucasian origin (15). After fusion of mobilized stem cells, hematopoietic rearrangement is rapid and requires approximately 8-10 days for neutrophil recovery and 10-12 days for platelets. Since patients receiving a CD34 (+) cell dose / kg, more than 2 x 106 CD34(+) cells / kg, usually have rapid and continuous hematopoietic recovery, this value has proven to be a useful value. Thus, this cell dose is usually defined as the adequate dose of stem cells that allows rapid re-hematopoietic recovery. However, there is no set minimum dose. Most centers accepted doses of 2 x 10 6 CD34(+) cells (16). Factors affecting the level of bone marrow stem cells include a low level of circulating CD34(+) cells, a more advanced age of the donor, and a decrease in the total volume of blood. However, the effect of age is not clear (17). Ethnic differences in patients with solid tumors are well documented. Less is known about the impact of ethnic differences in hematological malignancies. New chemotherapeutics, targeted molecular, cellular and immunological treatments may lead to different results in treatment. Overall survival is not evenly distributed across different racial and ethnic groups (18,19). In our study, stem cell levels were higher and neutrophil engraftment time was shorter in patients of Turkish ethnicity after mobilization allogeneic stem cell transplant than in syrian patients. opposite it was difficult to provide sufficient stem cell level and platelet engraftment in Syrian patients.Biological factors such as drug metabolism, sensitivity to chemotherapy, cytogenetic profiles, and non-biological factors such as social support, financial status, treatment compliance or access to treatment may contribute to the stem cell level. It is unclear whether the stem cell level and engraftment time are the result of a more aggressive disease or are due to non-biological factors. Some studies have hypothesized the differential metabolism of chemotherapy drugs as a possible cause of different treatment results in hematologic malignancies (20,21). Chemotherapy drugs administered before allogeneic stem cells can be thought to effect of the genetic polymorphism number of stem cells between possible ethnicities. Pre-existing or comorbid conditions of patients that occur during transplantation can be blamed as a potential cause of racial disparities in ASCT. There are ethnic differences in incidence and survival in patients with hematological malignancies. (22). As ethnic diversity continues to increase in ASCT, improving treatment results for all ethnic groups is of great importance. In our study, in parallel with the literature, it was observed that there were differences between ethnic structures in allogeneic bone marrow transplantation. The collected stem cell level of Turkish patients is significantly higher than Syrian patients. Social determinants and biological hypotheses should be systematically evaluated in randomized trials with wide data in hematological malignancies. To clarify hypotheses, focus should be on increasing the participation of minority groups with hematological malignancies in clinical trials and bone marrow transplantation.

CONCLUSİON

In our study, in parallel with the literature, it was observed that there were differences between ethnic structures in allogeneic bone marrow transplantation. The level of stem cells collected from Turkish patients was significantly higher than that of Syrian patients.

CONFLİCT OF İNTEREST:

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL:

Our study was approved by the Inonu University Ethics Committee with the approval number 2021/2715.

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