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Original Article

The effect of vitamin d and parathyroid hormone level on the number of cd 34 stem cells after mobilization regime in patients with multiple myelom and non hodgkin lymphoma

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Abstract

Background: Multiple myeloma (MM) and Non-hodgkin lymphoma (NHL) are frequently seen among hematological malignancies. Autologous hematopoietic stem cell transplantation is a treatment approach that is frequently used in patients with MM who develop consolidation therapy and in patients with non-hodgkin lymphoma who develop recurrence after standard treatments.

Materials and Methods: After the approval of the scientific research projects coordination unit (BAP) of İnönü University in 2017, the study data were collected. Project ID: 698. CD34+ cells were harvested from patients undergoing autologue stem cell transplantation after the mobilization regimen. Before mobilization, parathyroid hormone and vitamin D levels were measured in the patients. The relationship between the SPSS statistical program and the current data of the patients was examined.

Result: A total of 77 patients with 28 non-hodgkin lymphoma and 49 multiple myeloma were included in the study. The mean age of the patients was 55±11 and 55 were male and 22 were female. Parathormone level of lymphoma patients was identified as 68.8 ± 43.6 pg/mL, Vitamin D level was 7. 68±5.85 ng/mL and CD34+ cell number was 9.08x106/kg. The relationship between PTH and vitamin D levels or CD34 stem cell number in lymphoma patients was not statistically significant. Parathormone level of multiple myeloma patients was identified as 88.36±76.3 pg/mL, Vitamin D level was 68±ng/mL, and CD34+ cell count was 10.28x106/kg. The relationship between PTH and vitamin D levels or CD34 stem cell number in MM patients was not statistically significant.In our study, it was found that parathyroid hormone and vitamin D levels with CD34+ cell count were negatively correlated in non-hodgkin lymphoma and multiple myeloma patients. However, this relationship was not identified statistically significant.

Introduction

Multiple Myeloma (MM) and Non hodgkin lymphoma are among the most common types of cancer. MM is characterized by neoplastic proliferation of plasma cells originating from a single clone producing monoclonal immunoglobulin. Autologous stem cell transplantation in MM, it is the standard treatment approach for patients after induction therapy [1]. Lymphomas are widely distributed cancer types that can show an indolet and aggressive course of the lymphatic system. The World Health Organization (WHO) classifies lymphoid neoplasms according to morphology, immunophenotype, genetic findings, and cell of origin of the tumor. After initial response with chemotherapy and/or radiotherapy in non-hodgkin lymphoma, autologous stem cell transplantation is the appropriate treatment option in aggressive lymphomas (T-cell and Mantle-cell), first line in diffuse large B cell lymphomas, in chemotherapy sensitive cases after relapse, and in refractory/relapsed cases in Hodgkin's patients [1].

Autologous stem cell transplantation is reintroduction of stem cells previously collected from a patient to the patient after high dose chemotherapy. Hematopoietic stem cells are at fairly low levels in the peripheral blood [2]. With chemotherapy and/or G-CSF, mobilization can be done by increasing the number of stem cells that are normally found in very small amounts in the peripheral blood [2]. Vitamin D and its metabolites, calcium homeostasis and bone metabolism play an important clinical role. Some autoimmune diseases have been associated with vitamin D deficiency and are thought to have an important role in the immune system [3]. The main task of parathyroid hormone is to maintain calcium concentration at normal levels in the extracellular fluid. It has important effects on kidney and bones. Most immunological cells have parathyroid hormone receptors. Parathyroid hormone is thought to have a possible role as an immunomodulatory [4].

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Material and Method

Between January 2017 and May 2018, cases older than 18 years who were diagnosed with non-hodgkin lymphoma and multiple myeloma and planned autologous stem cell transplantation in our hospital were included in the study. A total of 49 MM and 28 non-hodgkin lymphoma patients were included in the study. After the decision of autologous stem cell transplantation for the patients, blood samples were taken for parathyroid and vitamin D levels before the mobilization regimen was applied. The samples taken were studied with the Roche e411 model immunoassay device in the biochemistry laboratory. After applying the mobilization regimen, when the target CD34+ stem cell level is reached, "Caridian BCT Inc. Spectra Optia Apheresis System" CD34+ stem cells were collected by using continuous current apheresis devices. The level of CD34+ stem cells in per kilogram of the collected product was calculated. Spearman correlation test of SPSS 18.0 data analysis program was used for statistical calculations.

Result

A total of 77 patients with 28 non-hodgkin lymphoma and 49 MM were included in the study. The mean age of the patients was 55±11, the mean vitamin D level was 16.09±12.32, the mean parathyroid hormone level was 80.41±64.5, and the mean stem cell level was found 9.06±6.42. The patients was 55 male and 22 female. Parathormone level of non-hodgkin lymphoma patients was identified as 68.8 ± 43.6 pg/mL, Vitamin D level was 7. 68±5.85 ng/mL and CD34+ cell number was 9.08x106/kg (Table 1). The relationship between PTH and vitamin D levels or CD34 stem cell number in non-hodgkin lymphoma patients was not statistically significant. Parathormone level of multiple myeloma patients was identified as 88.36±76.3 pg/mL, Vitamin D level was 68±ng/mL, and CD34+ cell count was 10.28x106/kg. The relationship between PTH and vitamin D levels or CD34 stem cell number in MM patients was not statistically significant.

Table 1: Distributions of age, hormone and stem cell level of the patients.

N (E/K)	77 (55/22)
Median Age	55±11
Vıtamın D (ng/mL)	16.09±12.32
Parathyroid Hormone (pg/mL)	80.41±64.5
CD34+ Stem Cell (x10^6/kg)	9.06±6.42
Multiple Myelom	49
Vıtamın D (ng/mL)	16.82±14.15
Parathyroid Hormone (pg/mL)	88.36±76.3
CD34+ Stem Cell (x10^6/kg)	10.28
Non Hodgkin Lymphoma	28
Vıtamın D (ng/mL)	7.68±5.85
Parathyroid Hormone (pg/mL)	68.8 ± 43.6
CD34+ Stem Cell (x10^6/kg)	9.08±4.78

Discussion

It prolongs event-free and overall survival in patients with MM who are eligible for autologous hematopoietic stem cell transplantation. At the same time, high dose chemotherapy + autologous hematopoietic stem cell transplantation has an important place in the relapse treatment of non-Hodgkin lymphoma patients. Under normal conditions, hematopoietic stem cells and progenitor cells are constantly released into the circulation. Stem cell mobilization can be achieved experimentally and in animal models or clinically with a wide variety of substances such as cytokines and small molecular [5]. For stem cell mobilization, G-CSF, cyclophosphamide is widely used.

There are studies showing that the use of PTH and vitamin D significantly mobilizes progenitor cells from the bone marrow into the peripheral blood, similar to G-CSF [6]. The use of parathyroid hormone and vitamin D in combination with G-CSF in mobilization does not cause depletion of bone marrow Lin/Sca-1, C-kit and CD34+ stem cells [7]. When vitamin D receptor knocked-out rats are mobilized with active vitamin D, they result in increased monocyte/macrophage differentiation, normal hematopoietic stem cell lines, leukemic cell lines and mature cell numbers [7]. In a review study by Aric C. Hall, Mark B. Juckett et al. entitled "The Role of Vitamin D in Hematological Disease and Stem Cell Transplantation", it was shown that the VDR is mediated by vitamin D activity and is due to a receptor in a family of steroid/thyroid hormone activated transcription factors. However, there are studies with knock-out animals support that vitamin D signaling is not required for the differentiation of normal hematopoietic cells of the repertoire for the vitamin D receptors damaged mice due to the normal production of blood cells [8, 9, 10, 11].

Stefan Brunnera et al. used G-CSF and parathyroid hormone together in their study and showed that progenitor cells were significantly mobilized into the peripheral blood [6]. Stefan Brunnera et al. used G-CSF and parathyroid hormone together in their study and showed that progenitor cells were significantly mobilized into the peripheral blood.

In our study, basal PTH and vitamin D levels were checked before mobilization and mobilization was performed by applying G-CSF. The mean PTH level was found above the normal value of 68.8±43.6 pg/mL and the mean Vitamin D level was found below the normal value of 7.68±5.85 ng/mL. A negative relationship was found between PTH and vitamin D levels and CD34+ stem cell levels, and this relationship was not statistically significant. Although there is evidence in the literature that PTH may have positive effects on stem cell mobilization, also there was a negative correlation between PTH and vitamin D levels or CD34+ cell levels, it was not found statistically significant (P=0.531, P=0.869) in our study.

As a result, although there are data in the literature showing that PTH may have positive effects on stem cell mobilization, this issue is still controversial. The inability to reveal a positive effect of parathyroid hormone and vitamin D levels with CD34+ stem cell number in our study may be associated with the low number of cases. Extensive studies are needed to determine the effects of parathyroid hormone and vitamin D on mobilization.

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