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THE EFFECT OF MODERATE EXERCISE ON ERYTHROCYTE BLOOD PARAMETERS IN ALLOGENIC BONE MARROW TRANSPLANT PATIENTS

UČINEK ZMERNE VADBE NA PARAMETRE ERITROCITOV V KRVI PRI BOLNIKIH Z ALOGENSKO PRESADITVIJO KOSTNEGA MOZGA

ABSTRACT

In this study, we investigated the effects of moderate exercise on the erythrocyte blood parameters in patients receiving the treatment of allogeneic bone marrow transplant. 20 patients attended the study voluntarily during the period of allogeneic bone marrow transplant. The volunteers were divided into two groups (treatment and control group). The treatment group was given moderate exercise program five days a week for eight weeks under the supervision of a doctor in charge. Subjects in the control group did not participate in any exercise program. By using Siemens advia 2120 blood count device at Hematology Central Laboratory, erythrocyte (RBC; Red Blood Cell) blood cell analysis was done. In comparing groups statistically, two-way analysis of variance was used in iterative measurements. In comparing the groups according to the measurements within themselves, one-way analysis of variance was used in iterative measurements. According to results of our study, there is no significant difference in comparisons of the variables belonging to erythrocyte parameters between-groups when the group effect is thought as independent ($p>0.05$). After the exercise given to the control and treatment groups, when the effect of time was taken into consideration, a statistically significant difference occurred according to the result of the comparison of iterative measurements of the variables of RBC, HGB, HCT, MCV, MCHC, RDW and HDW. As a result, it was seen that exercises had a positive effect on erythrocyte blood parameters. It is thought that this effect arose from the exercise program.

Key Words: Exercise, Erythrocyte, Allogenic Bone Marrow, Patients

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IZVLEČEK

V tej raziskavi smo preučili učinke zmerne vadbe na parametre eritrocitov v krvi pri bolnikih z alogensko presaditvijo kostnega mozga. 20 bolnikov je prostovoljno sodelovalo v raziskavi v obdobju po alogenski presaditvi kostnega mozga. Raziskovance smo razdelili v dve skupini (zdravljena skupina in kontrolna skupina). Zdravljena skupina je pod nadzorom lečečega zdravnika petkrat na dan v obdobju osmih tednov izvajala program zmerne vadbe. Člani kontrolne skupine niso sodelovali v nobenem vadbenem programu. S pomočjo naprave za ugotavljanje krvne slike Siemens advia 2120 je bila v osrednjem hematološkem laboratoriju izvedena analiza eritrocitov (Red Blood Cell – RBC). V statistični primerjavi obeh skupin smo v ponovljenih meritvah uporabili dvosmerno analizo variance. Enosmerno analizo variance pa smo uporabili, ko smo primerjali skupine glede na ponovljene meritve sprememb pri posameznih članih skupine. V skladu z rezultati naše raziskave med skupinama ni značilnih razlik v primerjavi spremenljivk, povezanih s parametri eritrocitov, kadar je bil skupinski učinek obravnavan kot neodvisen ($p > 0,05$). Po vadbi, ki sta jo izvajali tako kontrolna kot zdravljena skupina, se je v primeru, ko se je upošteval učinek časa, pojavila statistično značilna razlika v skladu z rezultatom primerjave ponavljajočih se meritev spremenljivk RBC, HGB, HCT, MCV, MCHC, RDW in HDW. Rezultati so pokazali, da je vadba pozitivno vplivala na parametre eritrocitov v krvi. Menimo, da je ta učinek posledica vadbenega programa.

Ključne besede: vadba, eritrocit, alogenska presaditev kostnega mozga, bolniki

INTRODUCTION

Cancer is a disease showing increase around the world depending on several variables in recent years. It is in the second place after the heart diseases in the ranking of the diseases having death risk, and it is also one of the most important health problems since it is frequent and has negative effects on the quality of life.[1] According to the data of World Health Organization and the Agency for Research on Cancer, 12 million people were diagnosed cancer in 2008, and it is predicted that this number will exceed 27 million in 2030.[2] As a cancer type, hematological malignancies create a negative effect on the large part of the body, and they cause a negative effect on the patients' physical function and the quality of life.[3] Hematological malignancies are treated by using methods such as chemotherapy, radiotherapy and hematopoietic stem cell transplantation (HSCT) that have an early or late side effect on the body systems. Hematopoietic stem cell transplantation, which is one of these implementations, is a method that is used on a lot of malignant or benign diseases to improve the clinical conditions and extend the length of life. Stem cell transplantation is the only treatment choice that maintains its validity today on high risk leucaemia or lymphomas resistant to chemotherapy. As concordant with the increase in the efficiency and usability of the implementations of the stem cell transplantation, the number of the implementations has been also increasing fast.[4-6]

In spite of the improvements in the treatments, stem cell transplantation causes important complications. The adverse effects of high-dose chemotherapy or radiotherapy, variable clinical conditions and hematologic and immunological differences increase the problems related to the treatment. Individuals' quality of life is affected negatively as a result of infection, prostration, immune reactions and decrease in physical performance and functions.[4]

As concordant with the data obtained from the studies conducted in recent years, it is predicted that, for the success of the treatment, the patients should be handled in detail and their quality of life should be increased. There are a great number of studies that searches the effects of the exercise programs in the treatment of in-patients with cancer and that reveals that they have positive results. Exercise programs are important for patients having hematologic cancer since they have positive effects on the physical performance, fatigue and quality of life for the treatment of the disease. It is stated that on such cases exercise improves the quality of life and it has psychological, physical and physiologic benefits.[7]

The objective of the study is to assess the effects of therapeutic exercises on hematological malignancies, to prevent or minimize the loss of physical and physiological functions of the hematopoietic stem cell transplantation patients during the treatment and to reveal the therapeutic effect of the exercise on the all negative situations affecting the quality of life of the patients during the long treatment process.

MATERIAL AND METHOD

20 patients who would have allogeneic bone marrow transplant at the Hematology Department of the Medical Faculty, Erciyes University participated the study voluntarily. The age of the patients in the treatment group was 31, 30±**13**.60, and in control group the patients were 45.50±15.90 years old. Initially, the volunteers were made written and oral explanations related to the research and measurements. Volunteers who accepted to participate in the study were made to sign an

"Informed Consent Form." Participants were divided into two groups randomly as treatment group and control group. The treatment group was given an exercise program under the supervision of a doctor in charge five days a week for eight weeks. The subjects in the control group were not included in any exercise program. The study was conducted in the hospital recreation room in the Hematology Department of the Medical Faculty, Erciyes University which was assigned by the hospital management. The volunteers were made to have endurance and strength training in the recreation room five days a week for eight weeks. During the exercise programs of the patients, One-repetition maximum (1RM) rule was used for strength exercises and Karvonen method was used for endurance trainings. Also, by taking into consideration the potential problems in the measurements that would be used to determine the physical conditions and exercise programs of the patients, the Borg Scale that is used in such studies was the determiner of the intensity of the exercise. For the intensity of the exercise, Borg Scale 24 was used. 14-16 score was taken as the measurement for strength exercises and 12-14 score for endurance exercises.

The patients who would have Allogenic HSCT were included in the exercise program at least two weeks ago. The patients having arthralgias, uncontrolled cardiovascular diseases and metastatic bone disease were not included in the study. The exercise programs of the patients were delayed in the cases such as infection findings (above 38.0°C), anemia (Hb <5 g / dL), neutropenia (absolute neutrophil counts <0.5 x 109 / L) or thrombocytopenia (thrombocyte count <10.000).

To determine the ages of the volunteers, credentials were used. The statures of the subjects were measured in cm by using a wall scale of which degree of accuracy was 0.1 cm. The bodyweights of the volunteers were scaled by using Tanita brand scale. Body mass indexes were calculated by the formula of body weight (kg) / height (m). Blood samples were taken at Hematology Laboratory of the Medical Faculty, Erciyes University between 7:00 am and 8:00 am. Blood samples of 5 ml each which were taken from forearm antecubital area by a catheter in accordance with the hygienic measures were taken to the tubes with EDTA. Erythrocyte (RBC) blood cell analysis was made by using Siemens advia 2120 blood count device at the Hematology Central Laboratory.

Statistical Evaluation

The data were evaluated by using IBM SPSS 22 statistics package. The control of the normal distribution of the variables was made by Shapiro-Wilk. It was determined that variables revealed normal distribution. Parametric tests were used to determine the distribution. For statistical arithmetic mean and the comparison of the groups, two-way analysis of variance was used in iterative measurements. In comparing the groups according to the measurements within themselves, one-way analysis of variance was used in iterative measurements. For determination of the difference between groups, t test was used in independent groups, and for the equality of the variance-covariance matrixes, Box-M test was used. Wilks lambda value was taken into consideration in replicate test table. Mauchly test for sphericity was used to control whether sphericity hypothesis was provided or not. In the cases that sphericity hypothesis was not provided, one of the Greenhouse-Geisser, Huynh-Feild, or Lower-Bound fixes was used. Significance level was taken as $p<0.05$.

RESULTS

As shown in table 1 there is a significant difference between the values of age, height and bmi when the results obtained from exercise and practice group are examined ($p<0.05$). It is seen that there isn't a significant difference between the control and treatment groups for value of body weight ($p>0.05$).

Table 1. Distribution of the Volunteers in terms of Their Physical Characteristics

Control Group (N=10)			**Treatment Group (N=10)**			
Variables	Mean	SD	Variables	Mean	SD	p
Age (year)	45,50	15,90	Age (year)	31.30	13.60	0.046*
Height (cm)	165,40	4,97	Height (cm)	173.50	8.52	0.018*
Body Weight (kg)	81,23	17,95	Body Weight (kg)	69.50	21.92	0.217
BMI (Kg/m^2)	28,52	7,00	BMI (Kg/m^2)	22.60	5.75	0.017*

p<0.05;p<0.01;***p<0.001*

It is seen that there isn't a significant difference between the control and treatment groups after the exercises ($p>0.05$). After the exercise, when control and treatment groups are compared by taking into consideration of the time effect, a statistical difference occurs according to the comparison results of the iterative measurements of the variances of RBC (red blood cell) , HGB (hemoglobin), HCT (hematocrit), MCV (mean corpuscular volume), MCHC (mean corpuscular hemoglobin concentration), RDW (red cell distribution witdth), HDW (hemoglobin distribution witdth). A difference in the direction of decline difference ($p<0.001$) occurs between the 1st and 3rd and between the 2nd and 3rd measurements of the RBC variable of the control group. When the variables of the treatment group are examined, it is seen that there is a statistical difference ($p<0.001$) between the 1st and 3rd measurements in the direction of decline. When HGB variable is examined, it is seen that there is a statistical difference ($p<0.001$) between the 1st and 3rd measurements and the 2nd and 3rd measurements of the control group in the direction of decline. In the results of the treatment group, a statistical difference ($p<0.001$) is found between the 1st and 3rd measurements in the direction of decline. In terms of HCT variable, there is a statistical difference ($p<0.001$) between the 1st and 3rd and between the 2nd and 3rd measurements of the control group in the direction of decline. In the treatment group's results, there is a statistical difference ($p<0.001$) between the 1st and 3rd measurements in the direction of decline. When MCV variable is examined, it is seen that there is a statistical difference($p<0.001$) between the 1st and 3rd measurements of the control group in the direction of decline, and between the 3rd and 4th measurements ($p<0.001$) in up direction. MCHC variable measurement results reveal a difference ($p<0.05$) between the 1st and 3rd measurements of the control group in up direction. When RDW variable is evaluated, a statistically significant difference ($p<0.01$) is found between the 2nd and the 4th measurement results of the control group in up direction. According to HDW variable measurement results, there is a statistically significant difference ($p<0.01$) between the 2nd and 3rd measurement results and between the 2nd and 4th measurement results of the control group in up direction. When time x group interaction after the exercises given to the control and treatment groups is taken into consideration, there is an interaction between the measurements of the RBC ($p<0.032$) and HGB ($p<0.014$) variables of the control and treatment groups (Table 2).

Table 2. The Distribution of the Volunteers in terms of Erythrocyte Parameters

		Measurements				Group		Time Effect		Time x Group Interaction	
		1 Mean ±SD	2 Mean ±SD	3 Mean ±SD	4 Mean ±SD	*F*	*P*	*F*	*P*	*F*	*P*
RBC	**C**	3.66±0.80[a]	4.34±0.67[a]	2.96±0.35[b]	3.31±0.64[a,b]	0.322	0.578	14.767	**<0.001*****	3.150	**0.032***
	T	3.72±1.03[a]	3.51±1.20[a,b]	2.95±0.64[b]	3.37±1.13[a,b]						
HGB	**C**	10.78 ± 2.29[a]	12.79 ± 1.86[a]	8.57 ± 1.17[b]	9.98 ±2.04[a,b]	0.181	0.676	25.494	**<0.001*****	2.98	**0.014****
	T	11.13 ± 2.55[a]	10.37 ±3.26[a,b]	8.91 ±1.83[b]	10.33 ± 2.54[a,b]						
HCT	**C**	33.47±8.41[a]	38.65±5.79[a]	25.56±3.60[b]	29.95±5.91[a,b]	0.111	0.743	19.926	**<0.001*****	2.738	0.052
	T	34.39±8.45[a]	32.13±10.69[a,b]	26.13±5.27[b]	31.30±9.71[a,b]						
MCV	**C**	90.79±5.00[a]	89.13±3.52[a,b]	85.92±3.13[b]	90.56±3.85[a]	2.195	0.156	24.437	**<0.001*****	0.092	0.963
	T	93.37±7.57	92.68±8.69	88.69±4.08	93.55±3.92						
NCH	**C**	29.69±1.78	29.42±1.64	28.92±1.53	30.22±1.38	0.931	0.347	1.496	0.240	0.311	0.622
	T	30.34±2.74	30.18±3.04	30.20±1.37	32.46±9.34						
MCHC	**C**	32.81±2.25	33.00±0.76	33.65±1.54	33.34±0.77	0.59	0.811	0.940	0.364	0.258	0.669
	T	32.53±1.86	32.60±1.75	34.07±1.32	34.44±8.27						
CHCM	**C**	31.75±1.58	32.39±1.38	33.22±1.40	32.11±0.57	0.375	0.548	4.101	**0.025***	0.55	0.655
	T	31.71±1.96	32.26±1.87	32.39±1.22	31.85±1.36						
CH	**C**	28.61±1.48	28.71±2.11	28.41±1.51	28.82±1.21	0.711	0.410	3.022	0.060	0.627	0.608
	T	29.34±2.31	29.68±3.13	28.53±1.48	29.46±1.18						
RDW	**C**	15.78±1.75[a,b]	14.81±1.24[b]	15.95±1.87[a,b]	19.47±3.08[a]	2.047	0.170	10.993	**0.001****	0.507	0.565
	T	17.02±2.80	16.95±3.71	16.53±2.79	19.95±3.39						
HDW	**C**	3.26±0.40[a,b]	2.96±0.30[a]	3.48±0.36[b]	3.40±0.35[b]	1.953	0.179	7.442	**0.002****	0.518	0.676
	T	3.08±0.32	2.90±0.44	3.20±0.38	3.20±0.48						

p<0.05;p<0.01;***p<0.001*
C: Control Group, T: Treatment Group
a,b,c,: *There is no difference between the groups in the same line having the same letters.*

DISCUSSION AND CONCLUSION

As a result of this study with the aim of determining the effects of moderate exercise on erythrocyte blood parameters in allogeneic patients, it is seen that there are differences and similarities when obtained findings are compared with the findings of the studies on this field. While the rarity of parallel studies increases the importance our research, it limits the discussion.

Given the findings of our study, it is seen that there are declining and increasing changes in the erythrocyte parameters of the volunteers. These changes are between the normal reference range in some subjects but not between the normal reference range in others. It is thought that these different values arise from the diseases of the subjects.

In this study, when the values of erythrocyte parameters are evaluated after the training given to the control and treatment groups by considering the group effect independently, it is seen that the difference in the comparison of the variables between groups is not significant (p>0.05). When

the time effect is taken into consideration, it is seen that the difference between the measurements is statistically significant as a result of the comparison of the iterative measurements of RBC, HGB, HCT, MCV, MCHC, RDW, and HDW after the exercises given to the control and treatment groups.

In this research, the values of the erythrocyte parameters are high in the training group. Ercan et al. (1996) state that there is an increase in the erythrocyte number after long term enduring exercises when compared to before the exercises.[8] Regular exercises are of great importance in ensuring proper blood flow and oxygenation of tissues. Deformability and aggregation characteristics of erythrocyte are very important in providing oxygen to capillary fields and tissues.[9] The studies in this field have determined that long term regular exercises have an important effect on the levels of erythrocyte and erythrocyte parameters in a positive way.[10,11] Ünal determined that after an 8-week aerobic exercise, there was a significant increase in the hemoglobin values of the subjects.[12] This literature knowledge supports our findings. As a result of the study conducted by Koç et al. (2012) it was determined that the change in MCV and MCH values was significant but the changes in other variables were not significant.[13] Characteristically, hemoglobin and hematocrit values decrease in those having intense exercise program, which is also regarded as sportsman anemia.[14] A slight decrease in blood volume may occur due to fluid loss.[15] Magazanik et al. (1998) investigated the chronic effects of the exercise and they determined that erythrocyte parameters decreased.[16] In the study conducted by Ricci et al. (1988) it was stated that hematologic parameters decreased as a result of chronic exercises.[17] As a result of the study conducted by Dimeo et al. (2003) it was determined that hemoglobin levels decreased when the pretest-posttest measurements of the 30-day endurance exercise given to the voluntary patients.[18]

There are studies stating that erythrocyte values did not change after the exercise.[19] They stated that there was no statistically significant increase in hematocrit value and erythrocyte number by submaximal exercise.[20] According to the literature and obtained findings, although erythrocyte blood cells are not in the reference range in most volunteers, they reveal difference in a positive way in the volunteers having the exercise program, and it is thought that this depends on the level of the training. In their study, Dimeo et al. (1997) investigated the effect of aerobic exercise in the rehabilitation of cancer patients after high-dose chemotherapy and autologous peripheric stem cell transplantation. When the hemoglobin concentrations of the control and exercise groups in their discharge period after treatment were evaluated, no difference was determined between two groups in the first measurements. When the measurements after a 7-week exercise were compared, it was stated that hemoglobin concentration was significantly higher in exercise group when compared to the control group.[21] Marchese et al. (2004) specified the participants as exercise and control groups in their study. They gave the exercise group aerobic and strength training on certain days for four months. Afterwards, when they compared the pretest and posttest values of both groups, they stated that no difference was found in their hemoglobin levels.[22]

In their study, Özdal et al. (2014) specified 11 healthy male sportsmen between the ages of 12 and 14 who do regular training as the treatment group, and 11 healthy sedantry male doing no sports as the control group. Both groups were given aerobic training three days a week for 8 weeks. When the pretest and posttest hemoglobin values of the exercises were compared, it was seen that the values after the exercise were in the direction of increase.[23] It was determined that, in healthy individuals who did not do exercise, short term exercise led increase in hemoglobin and leucocyte values, long term exercise led a significant increase in HGB, MCV, WBC and MHC values and a decrease in MPV levels.[24]

During the exercise, a certain amount of fluid leaves the veins, transfers through tissues and it leads an increase in the intensity of hemoglobin and plasma proteins.[25, 26]

During the exercise, depending on the intensity of the exercise, erythrocyte amount in the circulation, velocity of circulation, oxygen amount left in the active muscle and metabolic rate increases. This leads an increase in the free radical production and can affect the functional characteristics of the erythrocytes.[27,28]

When we look at the studies in this field, we see that there is no consensus on how exercise affects erythrocyte and erythrocyte parameters. While there are studies stating that there is an increase and decrease in erythrocyte parameter levels as a result of exercise, there are also studies that indicate there is no change in erythrocyte parameter levels. This difference is thought to be due to the training program carried out. In addition, it is also thought that the difference is due to the methods used in the researches, the time of the experiments, the subjects' quality of lives, the intensity, duration and frequency of the exercises, physical, physiological and condition states of the subjects, and most importantly, it is thought that it occurs because of that volunteers' having a serious health problem and the employed treatment methods.

It is predicted that the homogeneity between groups should be increased by conducting such researches on the groups having similar ages, the variables of gender of the volunteers should be grouped within themselves, the exercises to be employed should be started long before the transplantation, and, to create a standard, they should be conducted with a large number of repetitions and subjects. It is thought that the data obtained without this study will shed light on hematologic cancer-exercise studies in the future.

Authors' contributions

MKKUS conceived of the study and conducted the systematic review process. HK also conceived of the study, and participated in its design and coordination. All authors drafted the manuscript, read and approved the final version of the manuscript, and agreed with the order of presentation of authors.

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