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The effect of treatment of acute lymphoblastic leukemia on mean erythroyte volume in children

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Summary

Aim: Mean cell volume (MCV) is an easily obtained parameter with the use of automatic blood counters and is mainly evaluated in the classification of anemias. Treatment protocols including folic acid antagonists, DNA synthesis inhibitors and cyclophosfamide may increase MCV. Our aim was to evaluate MCV changes in children with acute lymphoblastic leukemia (ALL) under chemotherapy and to compare pre- and post-treatment MCV values in relation to prognosis and relapse.

Material and Method: One hundred-twenty-five children with ALL were included in this retrospective study. The MCV values of the patients (age 1-15 years, 83 boys, 42 girls) at diagnosis, at induction/consolidation chemotherapy and after maintenance treatment were evaluated.

Results: The MCV values of the patients at diagnosis, at induction/consolidation chemotherapy and after maintenance treatment were 78,5+3,9 fl; 89,1+6,8 fl and 95,6+3,8 fl, respectively. On follow-up, MCV values were found to decrease with a mean of 1 fl per month after chemotherapy. The results of 15 relapsed patients were compared with results of 110 patients without relapse; there was no statistically significant difference in MCV values (p>0.05).

Conclusions: MCV was not found to be a significant parameter in relation to prognosis and relapse in children with ALL. *(Turk Arch Ped 2011; 46: 126-9)*

Key words: Acute lymphoblastic leukemia, mean cell volume, children, relapse

Introduction

The most common malign disease in childhood is acute leukemia. Among acute leukemias, acute lymphoblastic leukemia (ALL) is the most commonly seen leukemia (85%). With intensive chemotherapy, success rates in ALL treatment have increased and 5-year event-free survival rate in children has reached up to 80%. However, relapse still occurs in 20% of the patients. Currently, one of the targets of ALL treatment is to know which patients have a high risk for relapse and to give them intensive treatment (1).

In recent years, technological improvements have been reflected to hematology laboratories and electronic blood counting devices have become indispensable equipment. Our notion about blood cells have increased due to these devices which provide more accurate results in a short time. Mean erythrocyte volume (MCV) is an easily evaluated blood variable used in classification of anemias (2). It shows variability by age. Generally, '7+age' formula is used for determining MCV lower limit and '84+ age x 0,6' formula is used for determining upper limit in children (1-12 years of age). In children, MCV levels are more frequently found to be low than high. MCV increases because of the mechanisms of action in patients receiving chemotherapy (purin, primidin analogs and ribonucleotid reductase inhibitors). In daily practice, a MCV value of >100 fL in children and a MCV value of >90 fL in adults is investigated further (Breedveld >105 (3) fL, Kenan >100 fL (4), Wyner>98.5 fL (5), Davidson>100 fL (6), Pappo (7) 6 months -12 years >90 fl) (7). MCV variance in terms of prognosis, relapse and secondary leukemia has

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been examined in cancer patients (8,9). In addition, the importance of MCV in diagnosis has been investigated in different studies (10).

The aim of this study was to investigate if MCV was related to prognosis and relapse in follow-up in children with ALL.

Material and Method

201 children were treated with a diagnosis of ALL in Cerrahpaşa Medical Faculty, Division of Pediatric Hematology-Oncology between January 1995 and December 2005. 125 of these patients with adequate file data were included in the study (ages 1-15 years, mean 5.99±3.94, 42 female, 83 male) and their files were examined retrospectively.

Results

Blood samples of all the subjects were placed in EDTA tubes for hematologic evaluation and tested with Coulter MD2. The MCV values of the patients were obtained from blood counts performed at diagnosis, after intensive chemotherapy, at the end of maintenance treatment and 3 and 6 months after maintenance treatment ended (Table 1). The highest values each patient achieved were recorded and the difference between these values and the values at diagnosis was found (Table 2). The patients were divided into groups by MCV values at diagnosis (Table 3). MCV values at diagnosis, at induction and after maintenance were compared in patients with relapse and in patients in remission (Table 4). The mean time (months)

Table 1. MCV values of the patients by period of treatment

MCV	N	Mean	<70fL Number of subjects	70-75 fL Number of subjects	75-80 fL Number of subjects	80-85 fL Number of subjects	85-90 fL Number of subjects	>90 fL Number of subjects	>100 fL Number of subjects
At diagnosis	125	78.5±3.9	2	15	25	59	20	4	0
At the end of induction treatment	125	89.1±6.8	0	1	21	40	45	18	0
At the end of maintenance treatment	125	95.6±3.8	0	1	0	4	48	54	13
3 months after the maintenance treatment	125	91±3.2	0	1	3	13	85	23	0
6 months after the maintenance treatment	125	86.2±2.6	1	2	5	54	52	11	0

Table 2. The highest MCV values achieved

	The highest MCV achieved (fL)	Difference of highest MCV	Mean difference of MCV
At diagnosis	93.2		
At the end of induction treatment	98.6	28.5	9.36±12.28
At the end of maintenance treatment	117.6	36.7	13.8 ±14.7

Table 3. MCV values at diagnosis

Mean MCV (diagnosis)	N	Microcytes N(%)	Normocytes N(%)	Macrocytes N(%)
6 months -2 years	7	< 70 fL 2 (% 29)	70-86 5 (%71)	>86 0
2-6 years	77	<75 fL 13 (% 17)	75-87 61 (%79)	>87 3 (% 4)7
6-12 years	34	<77 fL 3 (% 8.8)	77-92 28 (%82)	>92 3 (%8.8)
>12 years male	4	<78 fL 1 (% 25)	78-96 2 (%50)	>96 1 (%25)
>12 years female	3	<78 fL 2 (% 67)	78-96 1 (%33)	>96 0
Total	125	21 (%17)	97 (% 78)	7 (%6)

Table 4: MCV values in the patients with relapse and without relapse

Mean MCV	Subjects with relapse n=15	Subjects without relapse n=110	p
At diagnosis	81.2	78.4	>0.05
At the end of induction treatment	88.6	89.4	>0.05
At the end of maintenance treatment	93.8	94.7	>0.05

from the end of treatment to the achievement of normal MCV values was found to be 14.2+3.1 months (8-19 months).

Discussion

Leukemias constitute 25-30% of childhood cancers and ALL constitutes 75-85% of leukemias. In cancer treatment, treatment of childhood ALL has made a breakthrough. While all cases of ALL were being lost 40-50 years ago, currently 5-year survival rate has reached 80%. Contemporary treatment protocols classify the patients as low, standard and high-risk patients according to the risk they carry. The aim of this classification is to give more intensive treatment to patients who are expected to relapse and to protect low-risk patients from late side effects of the treatment. Although ALL treatment is gradually being developed in certain patterns, it is being tried to be individualized (1).

In recent years, technological improvements have been reflected to hematology laboratories and electronic blood counter devices have become indispensable equipment. In this study, we examined the variance of MCV value in ALL at diagnosis, at intensive chemotherapy and in the later period which is one of the variables obtained from these devices providing more accurate results in a short time compared to manual methods. We specifically evaluated the effect of increase and decrease rates in MCV values and peak values of MCV after chemotherapy on prognosis.

Generally, MCV values are found normocytic in children with leukemia. Our findings supported these results. MCV values were found to be macrocytic in 6% of our children and microcytic in 17%. As expected, microcytic values were found to be more frequent in the age group of <2 years and >12 years (29% and 25%) in whom iron deficiency anemia is more common (Table 3).

In our clinic, BFM (Berlin-Frankfurt-Munich) protocols are used for ALL treatment. In these protocols, intensive chemotherapy is given specifically during the first 6 months and later antimetabolites including 6-mercaptopurin and methotrexate are used for a mean period of 1,5 years. After these treatments, we observed that the highest MCV values were achieved at the end of the maintenance treatment. Mean MVC value was found to be 78 fL at diagnosis, 89 fL after chemotherapy and 95 fL at the end of maintenance treatment. A mean increase of 9,36±12,28 was found during the induction treatment in MCV values of the patients and the highest difference was found to be 28.5 fL. During the maintenance treatment, mean increase in MCV was found to be 13.8±4.7 and the highest difference was found to be 36.7 fL. It may be concluded that relapses will be observed more frequently in patients with the lowest MCV increase, considering that increase in MCV value as a good response to chemotherapy. However, our data did nor support this conclusion. When we divided our 125 subjects comprising our group into two sugbgroups in whom relapse was found and who were still in remission, we found no difference between values (Table 4). It is thought that associating effects and side effects of chemotherapeuticals with being adequate at cellular level is not so correct. Similarly, in our clinical observations, a decrease in rates of relapse could not be shown in cases in whom mucositis which is a side effect of methotrexate had a severe prognosis. Recently, White et al.(11) investigated if increased MCV was a marker for hematologic toxicity in patients receiving methotrexate treatment with a diagnosis of rheumatic arthritis, but they could not find a relation . In another study, the relation of MCV values with cytogenetic response and prognosis was investigated in patients with a diagnosis of chronic myeloid leukemia receiving imatinib treatment (13). In patients in whom early and continious increase in MCV was shown (independent of the degree of anemia), a higher cytogenetic response was found after imatinib treatment for 12 months. As a result of the study, high MCV was found to be an independent marker for complete cytogenetic response .

As a result of evaluation of our study, we found a mean decrease of 1 fL during the period when the patients recover from the effect of chemotherapy after chemotherapy is completed.

MCV values are found to be low in patients with thalassemia minor. We found no information about MCV variance with chemotherapy in patients with thalassemia in the literature. In our subject, we found the highest MCV value to be 73 fL in spite of chemotherapy. The pre-treatment MCV value of this subject was 55.3 fL.

Consequently, MCV was not found to be a significant indicator in terms of prognosis and relapse in the follow-up of ALL, although it is an easily evaluated variable and has an important role in classifying anemia.

Conflict of interest: None declared.

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