Original Article

Evaluate the Response Rate of Acute Lymphocytic Leukemia Patients to Hyper Cyclophosphamide, Vincristine, Adriamycin, and Dexamethasone Regimen and Remission Rate to Stay Until the End of the Arbitrary Treatment

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Abstract

Background: This study aimed to determine the effect of Hyper-Cyclophosphamide, Vincristine, Adriamycin, and Dexamethasone (CVAD) in the treatment of acute lymphoblastic leukemia (ALL) patients and remission duration. **Materials and Methods:** During a cross-sectional study in the Seyed Al-Shohada Hospital in Isfahan, patients with ALL who were admitted and treated from 2011 to 2015 because of the risk of ALL were selected and through the records investigation, demographic information, disease information, treatment, remission duration, current status, and duration of survival were collected in the form of data and are sick after going into remission, including the duration and recurrence remission survival time in treatment were analyzed and consequence, whether the patient is going into remission, remission and relapse and survival time based on the duration of treatment were analyzed. **Results:** Of the 62 patients, 13 patients after starting of treatment did not go to remission and died, but 49 patients (79%) went into complete remission. 21 of them of Hyper-CVAD group and 28 patients of classical treatment group (75/7% vs. 84%), but the difference was not significant (P = 0.43). Of the 48 patients who had a complete remission with the treatment regimen, ten patients relapsed after treatment with two of them of Hyper-CVAD group and eight patients were in the classical treatment group (9/5% vs. 29/6%), and the difference between the two groups was significant (P = 0.015). **Conclusion:** Hyper-CVAD regimen resulted in increased survival time of patients with ALL and less disease recurrence and therefore contraindications for use if the existing rules, and under the supervision of treatment, can be used.

Keywords: *Acute lymphoblastic leukemia, Hyper Cyclophosphamide, Vincristine, Adriamycin, and Dexamethasone, recurrence, survival*

Introduction

In recent years, with the adoption of more effective anticancer drugs, survival of patients with leukemia has been increased.[1-3] These drugs are causing symptoms subside so that during treatment with these drugs the symptoms is not worse and even to some extent patients were treated.[4,5] Leukemia treatment depends on the type of leukemia, the disease status at baseline, age, general health, and how patients are responding to treatment and status of Philadelphia chromosome, which sometimes leads to the patient's completely health.[6] Of the most important factor in improving the patient's disease is having high spirits to deal with the disease. Treatment methods include chemotherapy, radiotherapy, bone marrow, and stem cell transplantation.[7] One of the things that has always been considered in chemotherapy and radiotherapy acute lymphoblastic leukemia (ALL) was the impact of treatment on the remission duration that some studies also have been done in this direction.[8,9] Along with the new anti-cancer drugs, a lot of efforts are taken to minimize the effects of treatment and increased survival and prolong the period of remission.[10] In adults, the use of analog current regime with rather little small cases used in the cure rate (complete remission) is almost 75% and long-term disease-free survival rate is 20%–35%.[9] Treatment consists of dose-intensive treatment and preservatives. Complete response refers to cases where the blood count (granulocyte more than 109/L, the absence of blasts in peripheral blood and no more than 5% bone marrow blasts which

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considered to be normal. The survival rate from the start of treatment and duration of complete remission of the CR until relapse of leukemic evidence (≥10% lymphoblasts in the bone marrow) are calculated. In some studies of acute lymphocytic leukemia remission with Hyper-CVAD regime were 91%[10,11] and 91/6%.[12] At the same time, there is no consensus hypothesis about the efficacy of the treatment regimen in acute lymphocytic leukemia, therefore, this study aimed to determine the effect of the Hyper-CVAD treatment and the duration of remission in ALL patients.

Materials and Methods

This study was performed in the Seyed Al-Shohada Hospital in Isfahan. The study population was patients with ALL who presented to the institution from 2011 to 2015 and has been treated. Inclusion criteria included suffer to ALL, the age range of 15–60 years and their existing enough information in the patient records to contact a patient family to solve the defects. Furthermore, HIV-positive, other active malignancy, and the lack of cooperation or lack of family consent of the patient to provide information were considered as exclusion criteria.

In this study, sampling was census and during this, all patients with ALL over the past 5 years who have been treated at the center were enrolled.

By referring researcher at the unit of the medical records of Sayyid Al-Shuhada Hospital, patients with a diagnosis of ALL (based on the morphology of lymphoblasts or blasts with <3% by light microscopy and positive myeloperoxidase positivity test or periodic acid–Schiff and immune phenotypic studies) were examined and demographic data, data sent and received information about the disease and the treatment remission time, duration of survival, and the patient's current condition and were recorded in the form of data collection. In the case, the uncertainty of the current state of the patient or any of the required information, contact has been made with the patient's family and urged them to cooperate to complete the information, and in some cases, a family unwillingness to cooperate were excluded from this study.

Data from the study finally entered into SPSS version 23 (SPSS Inc., Chicago, IL) and analyzed by Chi-square test, *t*-test, and analysis of Kaplan–Meier survival analysis. Data from patients in terms of receiving and not receiving Hyper-CVAD regimen and in terms of survival time after diagnosis, remission, time and other variables were analyzed.

Results

In this study, 62 patients with ALL during the beginning of 2011 until the end of 2015 who have been treated in Sayyid Al-Shuhada Hospital of Isfahan were studied. The mean age of these patients were 19.7 ± 6.5 years (range 15–42). Forty (64.5%) of the patients were male and 22 (35/5%) were female. Eight patients with ALL were with T-cell origin, and 54 of patients (87.1%) were B-cell origin. The average age at diagnosis was 13.6 ± 9.4 years. Of the 62 patients, 25 patients (40/3%) were under the Hyper-CVAD regimen. In Table 1, the distribution of demographic and clinical characteristics of two groups of Hyper-CVAD regimen and classical treatment is shown. Based on the results, the average age and age at diagnosis depending on the treatment regimen has a significant difference, but there was no significant difference in sex and type of disease between the two groups. Of the 62 patients, 13 patients after starting treatment did not go to remission and died, and 49 patients (79%) went into complete remission, 21 cases of Hyper-CVAD and 28 of the classical treatment group (84% vs. 75/7%), but this difference was not significant ($P = 0.43$). Of the 48 patients who had a complete remission with treatment regimen, ten patients relapsed after treatment with two of them of Hyper-CVAD and eight patients in the classical treatment group (9.5% vs. 29.6%) and recurrence between the two groups was significant ($P = 0.015$). Finally, 62 patients with ALL, 23 cases (37.1%) died during the study, 6 of them of Hyper-CVAD and 17 of the classical treatment group (24% vs. 45/9%), but the incidence of death was insignificant in terms of the type of hormone replacement therapy [Figure 1] ($P = 0.11$). The mean duration of treatment for patient complete remission in Hyper-CVAD and classical treatment groups were respectively 7.95 ± 3.4 and 6.3 ± 3.8 months and based on the test *t*-test, there was no significant difference between the two groups ($P = 0.12$).

The average duration of survival in the two groups treated with Hyper-CVAD regimen and classical treatment were 56.64 ± 5.51 and 33.74 ± 4.68 months respectively and based on the log-rank test (log rank test) there was a significant difference between the two groups ($P = 0.041$). Figure 2 shows Kaplan–Meier survival curves of the two treatment groups. Based on the curve, Hyper-CVAD regimen patients had higher survival rates. The median survival time in the group treated classic was 17 months and in the Hyper-CVAD with was 27 months.

Table 1: Distribution of demographic and clinical characteristics

Variables	Regimen		*P*
	Classic	Hyper-CVAD	
Age (year), mean±SD	22.4±8.6	10.7±3.9	<0.001
Diagnosis (year), mean±SD	21.9±9	7.9±3.9	<0.001
Sex, *n* (%)			
Male	16 (64)	24 (64.9)	0.94
Female	9 (36)	13 (35.1)	
Origin of disease, *n* (%)			
B-cell	4 (16)	4 (10.8)	0.55
T-cell	21 (84)	33 (89.2)	

SD: Standard deviation, CVAD: Cyclophosphamide, Vincristine, Adriamycin, and Dexamethasone

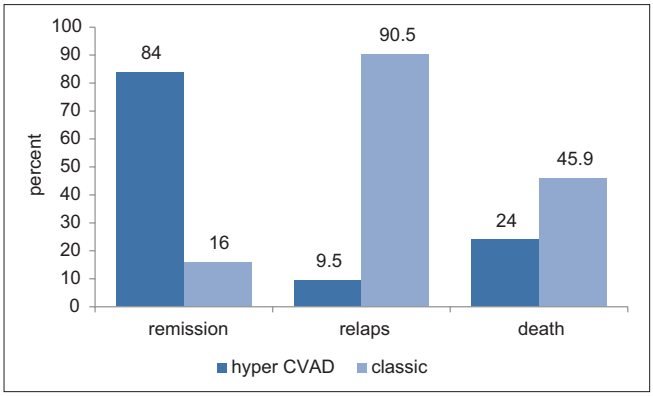

Figure 1: Percentage of remission, relapse, and death in both groups

Cox regression analysis of data showed that there was no significant difference in terms of age, sex, type of disease, duration of treatment and patient remission, cell and platelet count, and number of cyclic PAC chemotherapy.

Discussion

ALL is the most common malignant disease which is associated with high morbidity and mortality rates in children and adults. To increase the survival of patients with ALL several therapeutic approaches have been applied for this disease and recently new drugs for the disease is presented but research on their effectiveness is limited[13-15]. Hyper-CVAD regimen is one of the treatment regimens that were considered by many experts in oncology and blood and had a higher efficacy compared with other studies.[16,21] The results of our study showed that 84% of Hyper-CVAD and 75.7% of the classical treatment group underwent remission, but this difference was not significant. On the other hand, based on the results of the study, the recurrence rate was significantly lower in patients on Hyper-CVAD, but in the term of the overall mortality, there was no significant difference in the two treatment groups. The evaluation of survival time of two groups showed that those who were treated with Hyper-CVAD regimen had higher survival rate; in other words, the regimen was more effective in the treatment of ALL. Some previous studies have shown the Hyper-CVAD regimen excellence rather than other treatment regimens.[17-20] For example, in one study, patients with lymphoblastic lymphoma with 80% immune phenotype at diagnosis T-cell, 70% stage 4–3 disease, central nervous system disease 70% and 9% mediastinal involvement, which was treated with chemotherapy regimen Hyper-CVAD achieved full recovery in 91 cases and partial response in 9% of cases.[21] In another study, Hyper-CVAD regimen was evaluated in acute lymphocytic leukemia in adults. In 204 cases, 91% had complete remission, and the 5-year survival was 39%.[22] In a study which was conducted at on 36 patients with ALL treated with 4-cycle Hyper-CVAD regimen and high-dose methotrexate (MTX) and alternatively cytarabine, intrathecal injection of

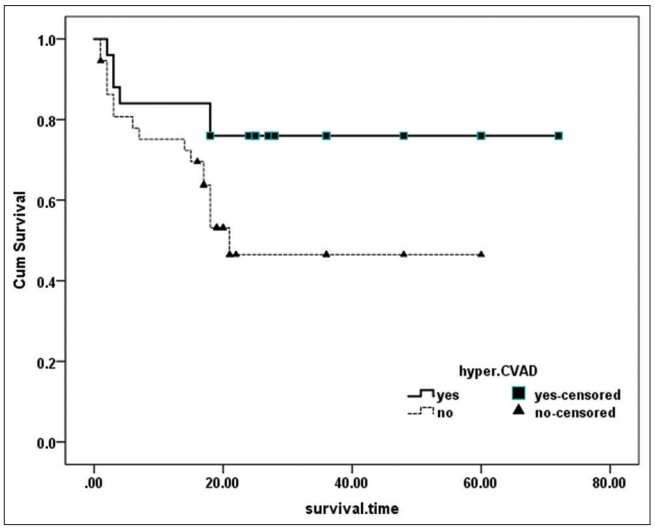

Figure 2: Survival time in both groups

antibiotics and prophylactic granulocyte-colony stimulating factor. Maintenance therapy consisted of mercaptopurine, MTX, vincristine, and prednisone since 2 years. Results of treatment on complete remission and survival were evaluated.[23]

Conclusion

According to the results of this study and comparison with the general conclusion of the other studies, Hyper-CVAD regimen resulted in increased survival time of patients with ALL and less disease recurrence and therefore, in the absence of contraindications to use, and according to treatment group, it can be used for as the treatment regimen.

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Conflicts of interest

There are no conflicts of interest.

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