

## **ABDIC REGIMEN IN RELAPSED OR REFRACTORY HODGKIN'S DISEASE: RESULTS OF GULHANE MILITARY MEDICAL ACADEMY HAYDARPAŞA TRAINING HOSPITAL**

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### **ABSTRACT**

**Objective:** The aim of this study is to present the results of ABDIC regimen in patients with relapsed or refractory Hodgkin's disease treated at the Department of Hematology of Gülhane Military Medical Academy Haydarpaşa Training Hospital.

**Methods:** Twelve patients with relapsed or refractory Hodgkin's disease, who had been heavily pretreated, received Doxorubicine, Bleomycin, Dacarbazine, CCNU and Prednisone (ABDIC) regimen. There were 10 men, 2 women and mean age was 31.

**Results:** Complete response was achieved in one patient and 5 patients had partial response. Total response rate was 50%. The patient who achieved complete response with ABDIC is alive and free of disease at 13 months. High dose chemotherapy with stem cell transplantation was performed in two patients with partial response and these patients are alive and free of disease at 6 and 11 months respectively. Remaining three partial responders died at 8, 10 and 13 months respectively.

**Conclusion:** ABDIC regimen is a well tolerated and effective regimen for relapsed or refractory Hodgkin's disease patients who received MOPP and ABVD regimen before.

**Key Words:** Hodgkin's disease, ABDIC regimen.

### **INTRODUCTION**

High rates of complete remission can be achieved for Hodgkin's disease (HD) with recent advances in radiotherapy and chemotherapy. Prolonged complete remission rates are as high as 90% in the early stage, 70-90% in advanced stage of HD and 55-65% long-term remission can be obtained in state III-IV of HD with various regimens (1-5). Prolonged disease-free survival can be achieved in additional 10-15% of patients with appropriate salvage chemotherapy (6). For patients with refractory disease or a disease-free interval of less than 12 months, virtually no chance of durable disease-free survival exists with standard chemotherapy. High-dose chemotherapy with bone marrow transplantation (BMT) or peripheral stem cell transplantation is considered for these patients and those with relapse more than 12 months after initial therapy are considered for salvage chemotherapy (7,8).

A regimen of doxorubicin, bleomycin, vinblastin and dacarbazine (ABVD) and other regimens including doxorubicine, bleomycin, dacarbazine, lomustine and prednisone (ABDIC) are used for patients resistant to mechlorethamine, vincristine, procarbazine and prednisone (MOPP) (1,3). The overall response rate reported for ABDIC was 70% with complete remission in 35% (9). This regimen was later modified to include continuous infusion of doxorubicine for 2 days and dacarbazine for 5 days (10). We report our results of ABDIC regimen in 12 patients with refractory or relapsing HD.

## MATERIALS AND METHODS

Twelve patients who were relapsed, or refractory to, MOPP, ABVD or MOPP/ABVD alternating regimens were included in this study between 1993-1996.

Chemotherapy regimen: Doxorubicin 25 mg/m<sup>2</sup> by continuous infusion daily for 2 days, bleomycin 5 U/m<sup>2</sup> intravenous bolus on days 1 and 5, dacarbazine 200 mg/m<sup>2</sup> by continuous infusion daily for 5 days, CCNU 40 mg/m<sup>2</sup> orally on day 1, and prednisone 40 mg/m<sup>2</sup> orally for 5 days.

Treatment was repeated every 28 days if leucocyte count was more than 3000/mm<sup>3</sup> and the platelet count at least 100000/mm<sup>3</sup>. Hemopoietic growth factor (G-CSF) was used in those patients whose leucocyte count was below 3000/mm<sup>3</sup> on the 28th day of chemotherapy.

Response was assessed before each course of chemotherapy. Complete response was defined as no evidence of disease by physical examination, radiological evaluation and screening chemistry profile. Partial response was defined as more than 50% reduction in all measurable lesions and the absence of new lesions. No response was defined as stable and progressive disease. There were 10 men and 2 women. The mean age of the patients was 31 years (range, 20-50). The characteristics of the patients are presented in Table-I. All of the patients had received multiple previous regimens. Recurrence of the disease within 12 months of their first treatment was observed in 7 patients.

## RESULTS

Complete response was observed in one patient and 5 patients had partial response of the 12 patients. Total response rate was 50%. The mean number of

**Table I.** The characteristics of the patients

Number of patients	12
Female/Male	2/10
Mean age	31 (20-50)
Histological type	
Nodular sclerosing	4
Mixed cellular	7
Lymphocyte depletion	1
Initial stage	
IIB	2
IIIB	3
*IV	7
Time to recurrence	
>12 months	5
<12 months	7

regimens before ABDIC was comparable in responders and non-responders. Remission duration was more than 12 months after initial regimens in the patient who achieved complete response. Of the 5 partial responders, 2 patients' remission duration was less than 12 months and 3 patients' remission duration was more than 12 months after the initial regimens. The patient who achieved complete response with ABDIC is alive and free of disease at 13 months. High dose chemotherapy (ifosfamide, carboplatin, vepesid -ICE) with peripheral stem cell transplantation was performed in two partial responding patients and these patients are alive and free of disease at 6 and 11 months, respectively. Two of the remaining three partial responding patients died in 8th and 10th months due to multiple organ dysfunction, secondary progressive disease and the third patient died at 13 months due to acute fulminant hepatitis.

## DISCUSSION

Patients who do not achieve complete remission with initial chemotherapy and those whose initial duration of remission is less than 1 year are usually considered to have resistant Hodgkin's disease (HD). Long term disease free survival is 10% in patients with short initial remission. The age at diagnosis and the duration of initial remission have significant correlation with survival (11). Three risk factors were identified in patients at first relapse, time from primary treatment to relapse of less than 1 year or stage IV disease at primary diagnosis and B symptoms at relapse (12). There are various conventional dose combination regimens that have activity in relapsing patients (13-17). It was reported that 70% response rate with complete remission in 35% of patients with ABDIC were considered to have MOPP resistant HD (9). In another study, a response rate of 63% was achieved in patients with relapsed or refractory HD (8). In our study, complete response was observed in one patient and partial response in five patients. Overall response was 50% and this result was in accordance with the literature. High dose combination chemotherapy with autologous bone marrow (BMT) or peripheral stem cell transplantation (PSCT) or both have become the standard salvage approach for most patients relapsing after initial chemotherapy (18-22). Results of this treatment reveal complete response rates of 34-80% with median progression-free survival for all patients for 12-24 months. The results of BMT are improved in patients with chemotherapy sensitive disease and minimal tumor burden. Thus patient usually receives cytoreductive therapy before BMT. Although the optimal therapy in this situation must be individualised, it was reported that the results of ABDIC are found to be active and well tolerated (8). Moreover, ABDIC offers the

possibility of palliation in patients with refractory or relapsed HD. ABDIC as a cytoreductive therapy followed by intensive therapy with BMT or PSCT offers the possibility of long term disease-free survival in these heavily pretreated patients. We performed high dose chemotherapy with stem cell transplantation on two patients who were relapsed less than 12 months. They are alive at 6 and 11 months after PSCT.

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