VAD Regimen as Initial Treatment for Multiple Myeloma

Mohammad Ali Mashhadi1,[1] Mehdi Hashemi,[1] Negin Khosravi[1]

[1]Hematology- Oncology Department, Ali Ebne Abitaleb Hospital, Zahedan University of Medical Sciences, Zahedan, Iran

Correspondig author: Mohammad Ali Mashhadi1, MD; Hematologist-Oncologist
Hematology- Oncology Department, Ali Ebne Abitaleb Hospital, Zahedan University of Medical Sciences, Zahedan, Iran
Tel. Number: 09153411445
E-mail: dralimashhadi@yahoo.com

Abstract

Introduction: The aim of our study is evaluation of response rate of VAD (Vincristin, Adriamycin and Dexamethason) regimen as initial treatment in 40 new cases of multiple myeloma. This is the first systemic and classic report of VAD regimen in Iranian population.

Methods: All patients with at least stage 2 multiple myeloma or progressive disease after physical examination, para- clinical profile such as (Imaging, CBC, BUN, Creatinine, Ca, P, Alk Phos, protein eletrophoresis, immuno electrophoresis and B_2 Microglobuline) entered to this study and investigation. All patients received VAD regimen (Vincristin 0.4mg/day 1-→4 days, Adriamycin 9mg/m2 1-→4 days and Dexamethasone 40 mg/day/1→4 (days), 9→12 (days), 17→20 (days)/cycle in outpatient therapy (24mg/morning and 16 mg evening) and repeated every 28 days for 4 cycles. The evaluation of response rate was with: decreased clinical manifestation, changes in para clinical profile and M- component and B_2 microglubuline.

Results: Fourty (40) patients enrolled, 24 cases (60%) were female, 16 (40%) male, the mean age was 48 (25-64), IgG myeloma was 80% (32), IgA myeloma 15% (6), and IgM myeloma 5% (2). 9 cases had thrombocytopenia in initiation of treatment and 7 cases during treatment protocol, and in the end of treatment, thrombocytopenia remained in 3 cases (total 16 cases) with mild thrombocytopenia (PLT= 100,000- 120,000), azotemia detected in 7 cases and in 2 cases resolved during treatment protocol. The over all response rate was 85%, median survival to now was 44.3 months. Toxicity was mild and acceptable.

Conclusion: Our result revealed the high response rate of VAD regimen as initial therapy and good survival rate with minor and acceptable toxicity.

Key words: VAD regimen, Initial therapy, Multiple myeloma

Introduction

Multiple myeloma is the most common second hematologic malignancy and is approximately 1% of all cancers and 2 % of all cancers death. In the past decade the usage of melphalan and prednisone was the standard treatment protocol.(1) From 30 years ago to now, various combination chemotherapeutic agents such as VBMCP or VMCP/VBAP used and all of them had similar response rate and survival effect like to melphalan/prednisone regimen.(2) The usage of high dose dexamethasone and Vincristine and Adriamycin (VAD regimen) as front line therapy described 1990.(3) In other study the usage of VAD regimen showed: 50% rapid response in refractory myeloma and 75% cytoreduction, this regimen was with quick response and without mjor toxicity or stem cell defect and more effective in emergency state such as hyper calcemia, renal failure, rapid effect on bone pain relief.(4)

The aim of this study is to evaluate the response rate, tolerability and toxicity of classic VAD regimen in Iranian population for first time.

Methods and materials

All Patients with multiple myeloma (at least stage 2) entered. In pre treatment evaluation all patients after full physical examination, laboratory profile (CBC, ESR, total protein, Alb, Globulin, BUN, Creatinin, Ca, Phosphor, Uric acid, LDH, Alk Phosphates, protein electrophoresis, Immuno electrophoresis assessed. All patients received: Vincristin .4 mg/day/civ 1→4, Adriamycin

Table- 1. Patients characteristics (n=40).

Characteristics	Number (%)
Age (years)	
Range	55-64
Median	48
Sex	
Male	16(40%)
Female	24(60%)
Clinical stage	
IIIA	33 (82.5 %)
IIIB	7 (17.5%)
Myeloma type:	
IgG myeloma	32 (80 %)
IgA myeloma	6 (15 %)
IgM myeloma	2 (5%)

9 mg/m2/day/civ 1→4 and Dexamethasone 40 mg/day 1→4 (days IV 10 mg/6h), 9→12 (days), 17→20 (days) in outpatient therapy (24mg/morning and 16 mg evening). When we used dexamethasone all patients received Famotidin for prevents of peptic ulcer. This protocol repeated every 28 days for 4 cycles. Prior to every cycle necessary laboratory profile re checked. After the end of treatment all patients reevaluated and the major criteria for response was M- component.(5)

Results

40 cases with multiple myeloma entered and evaluated. The most common myeloma were: IgG myeloma 32 cases (80%), IgA myeloma 15% (6 cases) and 2 cases with rising in IgM antibody in immunoelectrophoresis (initial presentation was acrocyanosis and headache and every 2 cases had renal failure at presentation), 60 % were female and 40 % male, the mean age was 48 (25- 64), 87.5% had anemia (35 cases) at presentation and mean hemoglobin level was 7.5± 1.3 gr/dl, 9 cases had thrombocytopenia (22.5%), rising in BUN and creatinin detected in 7 cases (17.5%). In the end of treatment 2 cases had normalized BUN and creatinin and 5 cases remain in presenting status, all patients had significant rising in ESR (> or = 90). Failure to treatment was 15%, and over all response rate was 85% and median survival was 44.3 months. Majority of cases experienced the relief of their symptoms.

The over all toxicity was mild and included: Alopecia, weight gain (Corticosteroid toxicity), fever and infective illness. We didn't see any cases with major end organ damage and toxicity. 2 cases had cord compression due to vertebral damage and resolved with radiotherapy. Treatment related mortality was 0%, fungal infection such as candidiasis and viral infection such as herpes zoster and bacterial infection with positive culture were 0%, but fever without culture positive or site specific observed and resolved with oral antibiotic therapy in 8 cases (20%).

Discussion

The evaluation and report of this classic regimen is the first study in Iranian population. We reported 40 cases with stage 3 multiple myeloma that treated only with VAD regimen without stem cell support.

In our study the sex prodominancy was female (60%) and 40% was male patients, and median age was 48 years but in other studies the mean age were older than 55 and this finding revealed the earlier and early age presentation of multiple myeloma in Iranian populations.(6, 7) In our study 35 cases (87.5%) had anemia and in all of them the cause of anemia was bone marrow replacement, although in other study, increased in plasma volume was one of the causes of anemia.(8) and this date showed and revealed advance stage and more aggressive disease in our study. In our study the most common myeloma was IgG myeloma (80%) but in other study the most common myeloma was IgG with 57.1% prevalence and in another study this parameter was very varied, this result documented the minimal presentation and frequency of renal involvement in our study, although renal failure observed in 7 cases.(9, 10) The over all response rate in our study was 85% and this result was similar to other studies,(10, 11) but in our study the majority of cases had complete response (60%) and differ to other studies. Toxicities were mild and acceptable and 2 cases had cord compression and usage of radiotherapy was mandatory, every 2 cases are normal to now (one case from 2 years ago and other case from 60 months ago). In Anderson study,(7) after initial treatment with VAD regimen, used of stem cell support but in our study the solely treatment protocol was VAD regimen. In our study treatment related mortality was 0% and minimum survivor had a duration of response without any evidence of primary disease, but in other study with

this regimen (VAD regimen),(7) 6% (9 cases) of patients died in 30 days of the initiation of treatment. Of these 9 cases, 5 cases died of progressive myeloma, 3 cases of infection and myeloma and 1 cases related to progressive leucoencephalapathy. In this study,(7) 54% of patients needed antibiotic therapy during VAD regimen therapy, but this requirement in our study during VAD therapy was 0%. In Anderson study,(7) despite Ketoconazole therapy, Candidiasis was 13% and herpes zoster infection was 4%, but in our study these infective disease were 0%. The bacterial infective disease with positive culture was 0% but fever without any specific site or culture positive observed and resolved with oral antibiotic therapy. Only major toxicity of our patient was corticosteroid toxicity and this toxicity didn't need to change our treatment protocol, that same to Anderson study.

In other study,(9) the median age was 58 years old and in our study was the mean age was 48, sex prodominancy was males (62.8%) and in our study was females prodominancy (60%). In this study(9) 3 cases had primary treatment failure and 2 cases died in their condition, but we didn't experience this refractoriness to treatment protocol. The median follow up in this study,(9) was 26 months, but in our study was 44.3 months. In this study,(9) the most common treatment related toxicity was corticosteroid toxicity but other toxicities included: infection in 18 cases, myopathy in 3 cases, treatment modification in 12 of 30 cases secondary to corticosteroid related toxicity, but in our study the most common toxicity was corticosteroid toxicity with mild effect and without the cause of change in treatment protocol. In this study,(9) like to our study myelotoxicity or cardiac toxicity was not observed.

Conclusion

Our study revealed the efficacy of VAD regimen as first line therapy without stem cell support in multiple myeloma patients with significant response rate, and with minor and acceptable toxicity.

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