Format: Abstract

Srp Arh Celok Lek. 1996 Nov-Dec;124(11-12):292-6.

[Results of treatment of patients with advanced multiple myeloma with the vincristine-adriamycin-dexamethasone protocol].

[Article in Serbian]

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Abstract

A very few treatment regimens have shown a benefit in patients with multiple myeloma resistant to conventional melphalan/prednosone therapy or similar combinations. The first "biologically designed" protocol for the treatment of advanced, refractory myeloma was a combination of vincristine, doxorubicin and intermittent high-dose dexamethasone, so called VAD regimen. This report summarizes our experience in VAD regimen in the treatment of advanced, refractory myeloma patients, initially treated with melphalan-based chemotherapy.

METHODS: Between July 1989 and July 1995, 27 patients with high-tumour-mass stage (Durie Salmon staging system) of the disease were treated with VAD combination. Clinical characteristics of patients are shown in Table 1. There were 17 pts who never responded (9 pts) of who progressed during induction therapy (8 pts). The second group of 10 pts responded to induction therapy and relapsed. Five pts (four with progressive and one with resistant myeloma) were treated with VAD therapy particularly due to significant extramedullary infiltrates. All pts in this study were initially treated with VMCP induction therapy. Seven of them were additionally treated with ABP combination, and this subgroup of pts was characterized as "resistant to melphalan and doxorubicin". The VAD regimen consisted of four-day continuous infusions of vincristine (0.4 mg per day) and doxorubicin (9 mg/m2 per day) in addition to dexamethasone in a dose of 40 mg for four days, beginning od days 1.9 and 17 of each cycle. The response was defined as a reduction of serum myeloma-protein concentration exceeding 75 per cent, with disappearance of Bence-Jones protein excretion.

RESULTS: "Good" response to VAD regimen was achieved in 12 of 27 pts (44 per cent), mainly after three cycles of chemotherapy (Table 2). The tumour reduction occurred rapidly (Table 3), without significant myelosuppression. Response-rate was significantly higher in relapsing myeloma pts than in pts with progressive or resistant disease (chi 2 = 4.2; $p < 0.05$). Neither previous treatment (Table 2) nor the type or paraprotein concentration, degree of marrow infiltration and cytologic type of plasma cells affected the response to VAD. Among 15 pts with "bad" response to VAD, seven died during first four months of treatment. All pts with significant extramedullary infiltrates failed to respond to VAD (chi 2 = 4.91; $p < 0.05$). Median survival of all pts was 16 months. In responsive pts remissions were of good quality and survival was significantly longer that that in whom treatment failed (Figure 1, left). In responsive pts the median duration of "plateau-phase" was 11 months

the "plateau-phase". The most important complications of treatment with VAD combination were infections (8 pts) but, fortunately, serious forms (i.e. pneumonia) were observed only in two pts.

DISCUSSION: The antitumour effect of VAD regimen originates from a combined effect of doxorubicin and vincristine continuous infusions and intermittent pulses of high-dose corticosteroids. The rationale for protracted administration of vincristine and doxorubicin was based on long generation time and low growth fraction of plasma cells in most patients, while the use of high-dose dexamethasone was based on well-known dose-depend antimyeloma effect of corticosteroids. Using this chemotherapy schedule, significant prolongation of survival was achieved in our responding patients comparing to patients with VAD-resistant myeloma. The major toxic effect of treatment was infection, which was attributed in part to intensive steroid program. Relapse of the disease could be expected about one year after completion of VAD therapy. Nevertheless, the second "plateau-phase" can be obtained upon reinitiation of VAD (ABSTRACT TRUNCATED).

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