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INTRODUCTION

Despite of advances in relapsed refractory multipl myeloma (RRMM) treatment, it is not satisfactory and more effective treatments are needed. Carfilzomib-lenalidomide-dexamethasone (KRd) regimen is the most effective treatment (except monoclonal antibodies) in patients with RRMM, so far (1). Pharmacologic Ascorbic acid at pharmacologic doses can be effective in advanced malignant disease. Ascorbic acid selectively kills myeloma cells at pharmacologic doses (2). We report the results of high-dose ascorbic acid therapy in addition to KRd regimen in patients with RRMM.

METHODS

Ascorbic acid with the dose of 7.5 gram/day, intravenously, with a 30 minute infusion time, during two days as weekly was given with standard KRd regimen after the second cycle in four patients with RRMM who progressed under treatment. The evaluation was performed after the 14 th day every two cycles. Antiviral (acyclovir) and antithrombotic (aspirin) prophylaxis were given to all patients. Permission was obtained from the ministry of health for all patients because of it is a non-indicative treatment.

RESULTS

The patiens were previously treated with 6-9 different regimens containing melphalan-bortezomib, ixazomib, thalidomide, cyclophosphamide, lenalidomide, pomalidomide and autologous stem cell transplantation. Complete remission was achieved in one patient. Very good partial remission was achieved in the other three patients. Second autologous stem cell transplantation was performed on a patient with CR. Treatment was continued to progression in other patients. Adverse effects related with ascorbic acid were not observed in any patient.

DISCUSSION

The available treatment options are consumed in patients who demonstrate progression under KRd treatment if monoclonal antibodies can not be used for treatment. Allogenic stem cell transplantation is usually not suitable due to age and performance status in these patients. Genarally, ascorbic acid is used in combination with alltransretinoic acid for RRMM treatment. Because of cytotoxic effects of ATO in myeloma, cell lines are markedly enhanced by the addition of ascorbic acid (3,4). Some authors suggest that antioxidants can be lower or higher in multipl myeloma. In addition there was antioxidant depletions and increase of pro-oxidant molecules in myeloma patients (5). Based of this idea, we added a pharmacological dose of ascorbic acide to KRd regimen. The response rates have increased with the addition in presented patients with RRMM who demonstrated this affect in the 2nd cycles of KRd regimen. Ascorbic acid is very attractive because of it is very cheap, there is no adverse effect and also the application is very easy. We obtained responses in 4 patients with KRd plus ascorbic acid treatment. Further studies with KRd plus ascorbic acid treatment can be useful in patients with RRMM.

CONCLUSION

The addition of pharmacologic dose ascorbic acid to KRd is effective tolerable and also an economic option in patients with RRMM. KRd plus pharmacologic dose ascorbic acide treatment can be an alternative approach in treatment of patients with RRMM if there is no chance of using monoclonal antiobies.

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Table 1: General properties of patients				
Factors	Case 1	Case 2	Case 3	Case 4
Age /genus	64/female	75/male	61/male	73/male
Previous treatment	VCD, VTD, SCT, VTD*, Rd, IRd, PomDex, PomCycDex, KRd,, SCT	VMP, Rd, IRd, VRD, PomDex, PomCycDex, KRd	VCD, VTD, SCT, VTD*, Rd, PomCycDex, IRd, KRd	VCD, VTD, SCT, VTD*, Rd, PomDex, IRd, SCT, KRd
KRD plus ascorbic acide cyclus n	4	4	5	5
Plasmacytomas	Yes, multip1	No	No	No
Response to KRd plus ascorbic acide	CR	VGPR	VGPR	VGPR

*Two cyclus consolidation treatment