LETTERS

Combination of low-dose cyclophosphamide and etoposide to mobilize peripheral stem cells before autologous transplantation in patients with multiple myeloma

Dear Editor,

After primary chemotherapy, the standard of care for eligible patients with multiple myeloma (MM) remains high-dose chemotherapy followed by autologous stem cell transplantation (ASCT). A minimum of 2 x 10^6 CD34+ cells/kg is required for a single transplant. Collecting 4 x 10^6 CD34+ cells/kg is recommended because some patients may benefit from a tandem transplant.

Granulocyte-colony stimulating factor (G-CSF) alone or an intermediate dose of cyclophosphamide (3-4 g/m^2) plus G-CSF is most often utilized in MM patients to mobilize peripheral blood stem cells. G-CSF alone is not so effective and may bear a risk of tumor cell contamination. An intermediate dose of cyclophosphamide causes frequent adverse effects, such as neutropenic fever. Therefore, an optimal regimen with high mobilization efficiency and moderate toxicity needs to be explored.

We conducted a study to explore the mobilization efficacy and safety of a low-dose CE regimen (cyclophosphamide 30 mg/kg d1-2, etoposide 5 mg/kg d1-2). We retrospectively analyzed the medical records of 53 MM patients who underwent mobilization with a low-dose CE regimen, followed by G-CSF 10 ug/kg between November 2013 and May 2018 at Naval Medical University Changhai Hospital. The patients had a median age of 51 (range: 35-66) years. The median time from diagnosis to mobilization was six (3-37) months. Thirty-seven patients (69.8 %) had received one line of prior therapy, 13 patients (24.5 %) two lines, and three patients (5.7 %) three lines.

Patients were mobilized with cyclophosphamide 60 mg/kg and etoposide 10 mg/kg, divided into two days, followed by G-CSF 10 ug/kg/d started from the onset of neutropenia (absolute neutrophil count <2 x 10^9/L) and continued until the final day of apheresis. Apheresis was commenced when white blood cells reached 8 x 10^9/L at a median of 13 (11-15) days, and the median time of apheresis was one (1-2) day. The median CD34+ cells collected on d1 was 6.9 x 10^6/kg (0.64-41.89). By the first apheresis, five patients failed to achieve 2 x 10^6 CD34+ cells/kg, and another ten did not achieve 4 x 10^6 CD34+ cells/kg. Among the 15 patients, 13 underwent a second apheresis. The median number of CD34+ cells collected was 6.9 x 10^6/kg (1.76-41.89). Finally, one patient (1.9 %) did not achieve the threshold of 2 x 10^6 CD34+ cells/kg, and nine (17 %) failed to achieve the target of 4 x 10^6 CD34+ cells/kg.

As this regimen has been used for more than ten years at our center, few patients only presented with severe adverse effects. Most patients were discharged after CE regimen administration and re-hospitalized before the injection of G-CSF. Among the 53 patients, six were hospitalized from chemo-mobilization onset until the collection of stem cells. One patient experienced grade 3 neutropenia, one grade 4 neutropenia lasting for one day, and one grade 3 thrombocytopenia. There was no grade 3-4 anemia or non-hematological adverse effects. The other 47 patients who were discharged reported no severe adverse effects when re-hospitalized.

Among the 53 patients, in terms of body surface area, the median dose of cyclophosphamide was 2.25 g/m^2 (1.93-2.96) and of etoposide 370mg/m^2 (199-491). Previous studies with cyclophosphamide at 3 g/m^2 reported a median of 9.6 x 10^6 CD34+ cells/kg collected. Of their patients, 10.8 % failed to collect 2 x 10^6 CD34+ cells/kg, and 18.5 % collected less than 4 x 10^6 CD34+ cells/kg[1]. Another study demonstrated that 4 g/m^2 cyclophosphamide mobilized a median of 8.91 x 10^6 CD34+ cells/kg[2]. This suggests that the efficacy of our CE regimen was comparable to that of 3-4 g/m^2 cyclophosphamide. Moreover, our study implied that the CE regimen was very safe. According to previous trials, however, 18.5 % of patients experienced severe infection, and 37.7 % showed febrile neutropenia with cyclophosphamide 3 g/m^2 and 4 g/m^2, respectively[1,2].

In conclusion, we showed that a low-dose CE regimen allowed for efficient stem cell mobilization with limited toxicity before ASCT in MM patients.

Conflict of interest
None.

Keywords: cyclophosphamide, etoposide, multiple myeloma, hematopoietic stem cell mobilization

References

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