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Editorial and Views

Outpatient programs of myeloablative chemotherapy, autologous and allogeneic bone marrow transplantation

Stimulated by the economic constraints in developing countries, we have been interested in changes in the therapeutic approaches to hematologic malignancies that may result in both simplification and reduction of costs.[1-4] One of the changes that has been shown to result in diminished costs of the modern effective therapeutic regimens is the completion of the procedures on an outpatient basis. Accordingly, we have engaged in studies to analyze the effectiveness of outpatient treatments for hematologic malignancies in three areas: outpatient delivery of myeloablative chemotherapy in acute myelogenous leukemia (AML), outpatient autologous bone marrow transplantation (BMT) and outpatient allogeneic BMT.

Outpatient delivery of myeloablative chemotherapy in AML

The cytarabine/anthracycline (7+3) chemotherapeutic schedule employed in the treatment of AML induces a myelosuppression which may be fatal if adequate platelet transfusion support and antibiotic treatment are not available. We have shown, in México, that the most important prognostic factor in the treatment of patients with AML using the 7+3 schedule is the availability of adequate platelet transfusion.[5] AML patients can be given the chemotherapy in hospital for 7 days, then discharged once the infusion of cytabarine is completed, to be transfused and given oral antibiotics on an outpatient basis.[6] A median of 1,700 US$ per patient were saved using outpatient support of the iatrogenic pancytopenia. Fundamental to the success of the outpatient approach is the availability of a 7 day-a-week clinic where medications and transfusions can be provided rapidly and efficiently for cytopenias, when needed. These data were later confirmed in Israel.[7] In the case of promyelocytic leukemia, which is unusually frequent in Latin America,[8] all trans-retinoic acid (ATRA) can be given to the patients successfully on an outpatient basis to diminish costs[9] and the simultaneous administration of oral steroids, also on an oupatient basis, seems to be related to a lower incidence of the ATRA-syndrome.[9]

Outpatient autologous BMT

After showing that the chemotherapy-induced hypoplasia of the 7+3 chemotherapeutic schedule could be supported safely in outpatients, we studied the possibility of supporting also the autologous BMT-induced pancytopenia in the outpatient setting. Initial data showed not only that this could be done,[10] but that it resulted in a substantial decrease in the costs of the autologous BMT procedure, since the median cost of an outpatient BMT procedure was 7,500 US$.[10,11] In a prospective study we showed that 75% of patients needing an autologous BMT can undergo the transplant fully as outpatients, obtaining similar results to those treated in hospital, with a transplant-related mortality of 3.4%.[11] The rational use of hematopoietic growth factors and the selection of myeloablative drugs that do not induce severe mucositis are factors that enable the outpatient autologous BMT procedures to be accomplished. It must be stressed that the outpatient autotransplant program cannot be offered to all patients needing an autograft: only patients who are asymptomatic, fully active, able to stay at home, with relatives or friends or in nearby hotels, and who have a fair educational level are eligible for this program; again, fundamental to the success of this approach is the availability of a permanent clinic where medications and transfusions can be provided rapidly and efficiently for cytopenias.[12] Other authors have also shown that outpatient-based autologous BMT is cheaper and possibly associated with a better post-transplant survival.[13,14]

Outpatient allogeneic BMT

Complications stemming from allogeneic BMT have traditionally obliged inpatient delivery of care, with lengthy inpatient stays; however, novel allotransplant approaches are based on the concept that current intensive and toxic cytoreductive conditioning therapy can be replaced by non-myelotoxic immunosuppression and that stem cell allografts create their own marrow space through graft-versus-host disease reactions which, furthermore, are responsible for the control of certain hematologic malignancies. To exploit the graft-versus-malignancy effect, non-myeloablative regimens may be used to promote engraftment of allogeneic progenitor cells; these procedures, known as mini-transplants or non-myeloablative transplants, induce short-term cytopenias similar to or even less severe than those caused by autologous transplants. In a

pilot study, we showed that non-myeloablative transplants can be completed fully on an outpatient basis, resulting in a substantial decrease of the cost of the procedure[15,16] with a median cost of 18,000 US$ per patient, a figure obviously lower than that of its counterpart using in-hospital myeloablative conditioning regimens. Later on, we conducted allogeneic peripheral blood stem cell mini-transplants in 26 patients; in 21 individuals (81%) the procedure was completed fully on an outpatient basis, the 100-day mortality being 3.8%.[17] Other authors have also shown that mini-transplants can be completed safely on an outpatient basis using low-dose radiotherapy.[18] In summary, the carrying out modern, intensive therapeutic procedures on an outpatient basis is feasible provided that certain requirements are fulfilled. These changes have resulted in simplification of the treatments, reduction of costs and, in consequence, availability to a larger number of patients. These observations may be critical in developing countries, where very few individuals can afford the regular costs of some modern therapeutic procedures.[1-4,19]

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