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Review / Revisão

Advances in the treatment of aplastic anemia

Avanços no tratamento da aplasia medular

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*Over the last 2 decades, there have been changes in the treatment strategy for patients with acquired severe aplastic anemia (SAA). Immunosuppressive therapy (IST) is still based on the combination of anti-thymocyte globulin (ATG) and cyclosporin, with or without growth factor (G-CSF). Age used to be a significant predictor only in transplantation: it is now also very significant in patients receiving IST. Currently survival after BMT from HLA identical siblings in young patients exceeds 90% after conventional cyclophosphamide conditioning, and unmanipulated bone marrow, which is still preferred over peripheral blood as a stem cell source. Two final important messages: a short interval between diagnosis and treatment will improve results, and patients should be entered on well-designed prospective clinical trials in order to attempt to further improve outcomes. Rev. Bras. Hematol. Hemoter. 2009;**31**(Supl. 2):61-62.*

Key words:*Severe plastic anemia, anti-thymocyte globulin, hematopoietic stem cell transplantation*

Introduction

Over the last 2 decades, there have been changes in treatment strategy for patients with acquired severe aplastic anemia (SAA).

Immunosuppressive therapy (IST) is still based on the combination of anti-thymocyte globulin (ATG) and cyclosporin, with or without growth factor (G-CSF). This combination is very effective in patients with very severe aplastic anemia (vSAA), but less so in patients with non-severe anemia (nSAA). As a result, severity, as identified by neutrophil counts (<200, 2-500, >500), is no longer a predictor of outcome. Age used to be a significant predictor only in transplantation: it is now also very significant in patients receiving IST. Overall survival has not improved in the last decade for patients given IST.

On the other hand, the outcomes of bone marrow transplantation (BMT) have improved overall, significantly in the last decade. This is mostly true for young patients and for patients receiving an unrelated donor transplant. Age remains a very significant predictor. Currently survival after BMT from HLA identical siblings in young patients exceeds 90% after conventional cyclophosphamide conditioning, and unmanipulated bone marrow, which is still preferred over peripheral blood as a stem cell source. In some countries patients come to transplant with a heavy transfusion burden, and highly sensitized: the conditioning regimen may need to be modified in this situation, with the addition of low dose total body irradiation (TBI) or low dose busulfan. The combination of fludarabine and cyclophosphamide (FLU-CY) is now being successfully explored instead of the conventional CY 200 regimen in older patients. This combination, together with low dose TBI has become the standard regimen for unrelated donor transplants in Europe and Japan and is being tested in the USA: 3 year survival close to 80% can now be achieved with unrelated donor transplants, both in children and adults. These results suggest an unrelated donor search should be considered, early in the course of the disease.

Two final important messages: a short interval between diagnosis and treatment will improve results, whatever the first line therapy used: this should call for immediate referral

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of these rare patients to an experienced center. In addition, because AA is a rare disease, patients should be entered on well-designed prospective clinical trials in order to attempt to further improve outcomes.

Resumo

*Modificações na estratégia terapêutica da AAS ocorreram nas últimas décadas. Terapêutica imunossupressora (TIS) mantém-se baseada na combinação de globulina antitimocitária e ciclosporina com ou sem G-CSF. A idade, importante preditor no transplante é também significante na TIS. Atualmente a sobrevida no transplante com doadores irmãos HLA idênticos é superior a 90% utilizando preferentemente a medula óssea como fonte de células. Finalmente duas mensagens: o menor intervalo entre o diagnóstico e o tratamento melhora os resultados, e pacientes devem entrar em estudos prospectivos bem desenhados para possibilitar melhor evolução. Rev. Bras. Hematol. Hemoter. 2009;**31**(Supl. 2):61-62.*

***Palavras-chave**: Aplasia medular severa; globulina antitimocitária; transplante de célula-tronco hematopoética.*

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