Allogeneic hematopoietic stem cell transplantation in chronic myeloid leukemia - Current concepts and Brazilian experience

Transplante de célula-tronco hematopoética na leucemia mielóide crônica - Conceitos atuais e experiência brasileira

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Allogeneic Stem Cell Transplantation (ASCT) remains the unique curative therapy for CML in all clinical phases of the disease. However, the results of Imatinib Mesylate (IM) therapy are sufficiently impressive to have displaced ASCT to second- or third-line treatment depending on the availability of newly developed tyrosine kinase inhibitors. The decision for transplantation depends on a variety of clinical and biological situations. The Leukemia Net recommendations as well the NCCN guidelines help us to choose the best moment to perform ASCT. In 1998, Gratwohl and colleagues published a score in order to establish the risk of ASCT before the procedure. In 2005, the Brazilian group, studying more than 1000 patients in an independent population, validated the risk score previously proposed by the EBMT Group. In this paper we discuss the position of ASCT in a country such as Brazil that presents resource limitations. In 2006, the EBMT published an activity survey about ASCT in CML and discussed the changes in treatment indications over the past 15 years and presented differences in medical conduct in West versus East Europe concerning ASCT indication. Despite of risks, ASCT remains a valid curative treatment. To delay or to perform the ASCT in advanced phases (accelerated- or blastic-phase) increases procedure-related mortality rates and reduces the probability of cure. Rev. bras. hematol. hemoter. 2008; 30(Supl. 2):30-32.

Key words: Chronic myeloid leukemia (CML); allogeneic hematopoietic stem cell transplantation (AHSCT); tyrosine kinase inhibitors.
patients receiving allogeneic HSCT. In the IM era and in situations with limited resources we need information regarding the best chance to benefit from HSCT.

More and more data have been published in recent years regarding the use of IM as front line therapy for CML as well as the newly developed TK inhibitor as Nilotinib and Dasatinib. The high level of hematological and cytogenetics responses associated to safety of the drugs created a new and important paradigm in the treatment of CML. However, the possibility of progression, are the most important concerns to be analyzed in order to choose the most effective and less toxic approach. Allogeneic HSCT has demonstrated to be able to cure CML in all clinical phases. However, the risks of high morbidity and TRM associated with acute and chronic GVHD must be considered against the benefit of HSCT. The present challenge is to identify subsets of patients which would benefit from HSCT. Based on our observation and in important papers published by Gratwohl and then by Passweg, patients presenting low risk scores (0 to 2) proposed by the EBMT, may be the best subgroup to be treated with HSCT. In contrast, patients treated with HSCT and presenting risk score 3 or beyond, showed low OS and DFS and high TRM and relapse rate. In addition, the status of disease had showed a high power to predict outcome.

The Brazilian paper report previously had the aim to present the results of CML patient in developing country treated with HSCT, and tried to validate the EBMT risk score. The patients in the study represent the evolution and the history of 20 years of HSCT in CML in Brazil. Our data, in an independent population, get to demonstrate that the EBMT risk score is reliable, and represents a useful guide for clinical decision making. Our data present slight differences compared with the original Gratwohl study. Disease status and recipient male/donor female presented the worst prognostic impact factors, whereas patients’ age and time from diagnosis to transplant were not significant either in univariate or in multivariate analysis. These differences can be related to differences in patients’ characteristics between the two populations: we had fewer patients in blast crisis compared to the original study (4% vs. 14%), our patients were much younger, as assessed by the proportion of patients younger than 20 years (14% on our study vs. 8% in the original study), and the time from diagnosis to transplantation was much longer (79% of our patients >12 months from diagnosis to transplantation, compared to 51% in the study by Gratwohl et al). Regarding the time from diagnosis to transplant, we speculate that in our country there is a delay in making the diagnosis and referring to a bone marrow transplant center. Concerning the results of OS and TRM according to periods of time they showed a progressive improvement which could be predictable with the improving of the support treatment, modern typing, GVHD and CMV control. EBMT activity survey published in 2004 showed the changes in disease indication over the past 15 years. This paper demonstrated a dramatically reduction of HSCT in the west Europe. However, in the east Europe the number of transplants increased in the same period. HSCT remains as an important alternative and countries presenting reduced resources may consider this procedure in an early phase of disease using patient' and transplant' risks. The EBMT score remains as an important instrument to decision making. Despite these slight differences, the Brazilian study validates the EBMT risk score and confirms its usefulness for point-decision in a development country, especially in choosing the best treatment in the IM era.

Resumo

O transplante alogênico de célula-tronco hematopoética permanece como a única terapêutica com potencial terapêutico para a LMC in todas as fases da doença. Entretanto, os resultados com a utilização do mesilato de imatinibe são suficientemente impressionantes para deslocar a utilização do transplante para segunda ou mesmo terceira linha de tratamento dependendo da disponibilidade dos novos inibidores de tirosino quinases. A decisão para a indicação do transplante depende da fase clínica e dos achados biológicos. As recomendações da Leukemia Net e as diretrizes da NCCN nos auxiliam a escolher o melhor momento para a elaboração do transplante. Em 1998, Gratwohl e colaboradores publicaram um escore no sentido de estabelecer o risco do transplante antes de sua realização. Em 2005, um grupo brasileiro estudando mais de 1.000 pacientes em uma população independente validou o escore de risco proposto pelo grupo europeu. Neste manuscrito o autor discutirá a posição do transplante em países com limitações de recursos como o Brasil. Em 2006, a mesma escola europeia publicou um estudo de monitoramento do transplante e discutiu as mudanças desta modalidade de tratamento nos últimos 15 anos e apresentou as diferenças no comportamento médico na Europa do oeste (mais rica) versus do leste (mais pobre) na indicação e utilização do transplante. A despeito dos riscos, o transplante permanece como uma terapêutica curativa válida. Atrasar a indicação ou realizar o procedimento em fases avançadas, como a fase acelerada ou blástica, aumenta o risco de mortalidade relacionada ao procedimento e reduz a probabilidade de cura. Rev. bras. hematol. hemoter. 2008; 30(Supl. 2):30-32.

Palavras-chave: Leucemia mielóide crônica (LMC); transplante alogênico de célula-tronco hematopoética (TACTH); inibidores de tirosino quinases.
References