Allogeneic Bone Marrow Transplantation for Malignant Haematological Disorders

Editorial commentary on Olle Ringdén: Allogeneic bone marrow transplantation for haematological malignancies—Controversies and recent advances

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Allogeneic bone marrow transplantation, as applied in the treatment of malignant haematological disorders, is among the most intensive treatments given to man. The justification for such an aggressive and toxic treatment is the poor prognosis of the disease treated. For some diseases, bone marrow transplantation is the only curative treatment, while in some other diseases it gives the best outcome. However, for many disorders treated with bone marrow transplantation there are alternative therapies, and as different treatment modalities develop, the indications for different treatments including bone marrow transplantation must be constantly reviewed. During the past few years new indications for allogeneic bone marrow transplantation, e.g. chronic lymphatic leukaemia, have appeared, but some disease states which earlier were indications for bone marrow transplantation are no longer regarded as such. A good example is acute myeloid leukaemia in first remission, which was widely regarded as a clear indication for transplantation. Now the choice between transplantation and chemotherapy is based on the karyotype and other prognostic factors.

As described by Ringdén in this issue (1), comparing the results of allogeneic bone marrow transplantation with those obtained using other forms of treatment is not always easy. A typical example is the treatment of acute leukaemia, where a proportion of patients can be cured with chemotherapy only. There are some prospective trials comparing different forms of treatment as described by Ringdén (1), but most of the available information comes from retrospective analyses where the transplantation data originate from bone marrow transplantation registries. The interpretation of registry data can be problematic. Transplanted patients, allogeneic or autologous, are likely to be more selective compared with patients treated with chemotherapy only. On the other hand, registry results are often compiled over a long period of time, and do not take into account that considerable improvements in transplantation techniques have taken place during the intervening years. Although an effort is made to match the patient material, for example when comparing data from transplantation registries and national chemotherapy trials, true matching is difficult to achieve. It is also important to realize that allogeneic bone marrow transplantation is a more complicated treatment than intensive chemotherapy because of immunological problems. Therefore much more experience is needed in allogeneic transplantation than in chemotherapy in order to achieve optimal results. Registry materials consist of pooled materials from all kinds of centres, experienced and inexperienced. For these reasons available registry data probably give too pessimistic a picture of what can be achieved with allogeneic transplantation in skilful and experienced hands today. The relative merits of various forms of treatments may depend on the institution that is giving the treatment.

Allogeneic bone marrow transplantation has become an increasingly widely used treatment modality during the past few years (2). This is mainly due to the rapid growth of volunteer donor registries, and it is now possible to find a donor for about 70% of Caucasian patients. However, transplantations from registry donors are more complicated than sibling transplantations because of greater immunological differences, even though the main tissue types

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are identical. The development of typing technologies has shown that a significant proportion of registry donors who were typed just some years ago are mismatches according to today's criteria (3). With the refinements in tissue-typing, it is now increasingly possible to find more suitable donors for patients, but 'complete' matches are becoming more rare. Therefore it is important to learn which mismatches are 'permissible'. With the improvement in tissue-typing, the clinical results of unrelated donor transplantation have already improved, and this development will undoubtedly continue.

One of the big issues in allogeneic transplantation at the moment is the source of stem cells. Stem cells harvested from the blood have largely replaced bone marrow as the source of graft in autologous transplantation, and there is a similar trend in allogeneic transplantation. However, the situation is more complex in the allogeneic setting (4). While there are obvious advantages in using blood stem cells for both the donor and the patient, the avoidance of anaesthesia and multiple bone punctures as well as a somewhat faster engraftment, some uncertainties remain. Because of the much higher number of lymphocytes transfused with a blood stem cell graft as opposed to bone marrow, there might be more graft-versus-host disease after blood stem cell transplantation. The graft versus leukaemia effect might also be different depending on the source of the graft. The, thus far, rather limited experience has not yet resolved these issues, but ongoing studies will probably give the answers. The donor has to be given a growth factor to mobilize stem cells into the blood, and some concern about possible, although unlikely, long-term effects of the growth factor has been the most important single factor restricting the increased use of blood stem cells. At the moment only a few bone marrow donor registries allow the use of blood stem cells as the primary source of the graft. However, it seems likely, although not at all certain, that blood stem cell transplantation will to a great extent replace bone marrow transplantation also in the allogeneic setting.

Umbilical cord blood is another new source of stem cells. Cord blood transplantation shows great promise, but many uncertainties about the indications as well as optimal use still remain, and this form of transplantation in the treatment of malignant haematological diseases will only be seen after some years.

In addition to improving tissue-typing, other developments of the transplantation procedure will probably lead to further improved results. Viral infections, especially the common and problematic cytomegalovirus infections, can now be prevented and treated much more effectively than a few years ago. There are also some improvements in the treatment of fungal infections, but these are still a big problem. Immune modulation with cytokines and antibodies directed against cytokines will probably be applied to an increasing extent. By these means it will most likely be possible to further reduce transplantation-related morbidity and mortality. The problem of recurrent malignancy has been more difficult to tackle than transplantation-related mortality, but a more sophisticated utilization of the graft versus leukaemia effect and biological response modifiers may lead to a reduction in relapse rate.

Although the ultimate goal must be to develop less toxic forms of treatment in the management of malignant blood diseases, allogeneic bone marrow and blood stem cell transplantation will remain a widely used treatment modality for many years to come, and its use may even widen with new applications such as gene therapy.

REFERENCES

1. Ringdén O. Allogeneic bone marrow transplantation for hematological malignancies—Controversies and recent advances. Acta Oncol 1997; 36: 549–64.
2. Gratwohl A, Hermans J, Baldomero H. Blood and marrow transplantation activity in Europe 1995. Bone Marrow Transplant 1997; 19: 407–19.
3. Rufer N, Tiercy J-M, Breur-Vriesendorp B, et al. Histoincompatibilities in ABDR-matched unrelated donor recipient combinations. Bone Marrow Transplant 1995; 16: 641–6.
4. Schmitz N, Bacigalupo A, Labopin M, et al. Transplantation of peripheral blood progenitor cells from HLA-identical sibling donors, European Group for Blood and Marrow Transplantation. Br J Haematol 1996; 95: 715–23.