IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Stem cell transplantation in acquired severe aplastic anaemia[1]

Executive Summary

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Research question

The aim of this review was the evaluation of studies on allogeneic stem cell transplantation with an unrelated donor vs. immunosuppressive therapy in patients with acquired severe aplastic anaemia. The focus of the evaluation was on patient-relevant therapy goals.

Methods

All study types with a control group were to be included. Insofar as a change in therapy had taken place, the study was only to be accepted if primary therapy vs. primary therapy or secondary therapy vs. secondary therapy were compared, in order to conduct the evaluation on the basis of comparable baseline situations. In this case, the interval between the start of the primary therapy and the change in therapy was to be at least 6 months.

The endpoints selected were outcomes that enabled an assessment of patient-relevant therapy goals such as survival time, disease-free survival, therapy-related complications, and health-related quality of life.

The literature search was performed in the bibliographic databases MEDLINE, EMBASE, and Cochrane Central in April 2006. An additional search was performed in October 2006. Several other sources were screened to identify further published and unpublished studies. These included online trial registries, institutions that published evidence reports or were involved in stem cell research, corresponding study groups, reference lists of relevant study publications and reviews, as well as relevant congress proceedings.

Results

Despite an extensive systematic literature search, no direct comparative fully-published studies (i.e. studies evaluable with sufficient certainty) were identified for the aim of this report, the comparison between unrelated donor stem cell transplantation versus immunosuppressive therapy in patients with acquired severe aplastic anaemia. Only one prospective comparative study including 60 patients, which has not yet been published, was

identified. This study may be considered in a future evaluation as soon as the study data are published or made publicly accessible.

In order to gain further information, we then searched for studies that reported the use of stem-cell transplantation with unrelated donors in patients who had undergone unsuccessful immunosuppressive therapy (according to the definition in the separate studies). The only restriction was a minimum sample size of 10 patients. Based on the study pool retrieved for the original aim of this report, 9 such studies including data on a total of 749 patients were identified. Mainly children and adolescents were investigated in these studies; the median age of patients lay between 8 and 19 years. For year 2 to about year 7 after transplantation, survival rates between 28% and 89% were reported. Studies on transplantations performed in recent years and those solely including children showed better results.

Data on transplantation-related complications were mainly limited to graft-versus-host disease (GVHD) rates and causes of death. The acute GVHD rates lay between 11% and 75% (between 13% and 37% for grade III/IV disease); the chronic GVHD rates lay between 24% and 57% (15% for extensive disease).

However, these data are only of limited interpretability, as the patient characteristics were insufficiently described in the available publications. In many studies, mixed populations of patients with a lack of response to immunosuppressive therapy and those with a recurrence of disease after initial treatment success were investigated; a clear and consistent definition of these 2 criteria was lacking.

Conclusion

No data are currently available from direct comparative studies that can be interpreted with sufficient certainty regarding the benefit of allogeneic stem cell transplantation with unrelated donors vs. immunosuppressive therapy in patients with acquired severe aplastic anaemia. In affected patients, the widespread use of allogeneic stem cell transplantation with unrelated donors outside the framework of controlled clinical trials does not therefore seem currently justifiable. “Controlled clinical trials” also refer to non-randomised trials, insofar as appropriate procedures to achieve as unbiased a comparison as possible were applied (e.g. by minimising selection bias). In the interest of patients, a substantial improvement of the data situation, including the mandatory publication of study results, is urgently required.

However, it seems justifiable to offer unrelated donor stem cell transplantation to patients in whom immunosuppressive therapy is no longer a treatment option, i.e. where no alternative treatment is available. The data from the studies additionally reviewed (one-arm studies reporting unrelated donor stem cell transplantation in patients with failure of immunosuppressive therapy or disease reoccurence) do not clearly define when such a refractory situation has occurred. Clear criteria are necessary in this regard in order to be able to describe the benefit of therapy for such patients. The prerequisite for the use of unrelated donor stem cell transplantation in patients in such a desperate situation is to inform patients appropriately about the uncertain data situation.

Key words

Systematic review, acquired severe aplastic anaemia, stem cell transplantation, immunosuppressive therapy, unrelated donor