6. HEMATOPOIETIC STEM CELL TRANSPLANTATION

Principles

- Providers, patients, and families should be informed about the role of HSCT in the treatment of sickle cell disease based on current scientific evidence.
- For every patient with sickle cell disease, the benefits and risks of HSCT should be carefully weighed within the context of his or her individual disease severity and age. The criteria for eligibility continue to evolve and should be updated regularly.
- Following HSCT, close follow-up is indicated to monitor for acute and long-term complications of HSCT and sickle cell disease.

Recommendations

- Information regarding HSCT should be part of the counseling process of patients and families with sickle cell disease. Any potentially eligible patients for HSCT should be referred for consultation at a specialist centre where HSCT is available.
- HSCT should be performed in accordance with the specialist centre's guidelines, and should align with evidence-based recommendations from major sickle cell disease transplant centres.
- During the transplant period, and in the long term, a comprehensive sickle cell team must closely follow patients who undergo HSCT in consultation with any other relevant sub-specialties.
- HLA-typing and storage of umbilical cord blood should be considered for siblings of patients with sickle cell disease. HLA typing may be coordinated with pre-natal diagnostic techniques (such as chorionic villus sampling, amniocentesis or pre-implantation genetic diagnosis) to determine if the fetus is affected with sickle cell disease. Ethical concerns regarding the use of pre-implantation genetic diagnosis (PIGD) must be addressed.
- Male patients should be referred for sperm banking prior to HSCT. Consider ovarian cryopreservation for female patients with sickle cell disease who undergo HSCT.[4]
- Develop a protocol for the prevention of neurological complications following HSCT, which may include the use of anticonvulsant prophylaxis during treatment with cyclosporine.
- There must be a close liaison with the blood bank to individualize red cell and platelet transfusion needs.
- After HSCT, patients should be followed in long-term, multidisciplinary follow-up clinics to ensure early detection of complications such as infertility, growth failure, and chronic graft-versus-host disease.
- More research is needed to guide the development of non-myeloablative conditioning regimens that have reduced toxicity but allow sufficient donor engraftment to provide significant clinical benefit.[2,5]

Background

Hematopoietic stem-cell transplantation (HSCT) is currently the only curative therapy for patients with sickle cell disease. Donor stem cells used for HSCT come from donors with either hemoglobin AA (normal) or AS (sickle trait) to promote a successful transplant and a clinically asymptomatic patient. Successful HSCT has been found to improve sickle cell vasculopathy, splenic and pulmonary function, and to stabilize sickle cell-related neurological complications.[1,2] Excellent outcomes have been reported following matched sibling donor transplants with an overall survival of greater than 90% and event-free survival of greater than 80%.[1,3] Some patients with stable mixed donor and recipient chimerism have also been reported to have substantial clinical benefits.

The decision to have a patient with sickle cell disease undergo HSCT is one that should be considered carefully. The risk of toxicity and potential mortality from HSCT must be balanced against the morbidity of sickle cell disease-related complications. Long-term complications following HSCT such as gonadal failure (particularly among females) and chronic graft-versus-host disease must also be considered.[1] The timing in HSCT is very challenging. Ideally, HSCT should be performed once the disease has been identified as having a moderate to severe phenotype, but prior to the occurrence of end-organ damage from sickle cell disease.

One of the major limitations in performing HSCT in patients with sickle cell disease is the lack of suitable human leukocyte antigen (HLA)-matched sibling donors.[4,7] Less than 14% of patients with sickle cell disease have an unaffected matched sibling donor. Unrelated donor HSCT and haploidentical HSCT are considered experimental.

Proposed indications for HSCT in patients with sickle cell disease include patients aged less than 16 years with at least one of the following: stroke or a CNS event lasting longer than 24 hours, impaired neuropsychological function with abnormal cerebral MRI scan, recurrent acute chest syndrome with multiple hospitalizations or previous exchange transfusions, recurrent severe vaso-occlusive pain or priapism, sickle nephropathy, stage I or II sickle lung disease, bilateral proliferative retinopathy and major visual impairment, osteonecrosis of multiple joints, and red cell alloimmunization during long-term transfusion therapy.[7,8]

Patients with sickle cell disease undergoing HSCT also have special considerations. An increased risk of acute neurologic complications (e.g., due to cyclosporine toxicity) such as seizures and intracranial hemorrhage has been reported at a median of about one month following HSCT.[5,6] Patients with sickle cell disease undergoing HSCT are also more likely to have a red blood cell alloimmunization and iron overload compared with the general population of children with sickle cell disease due to numerous red cell transfusions prior to HSCT.[9]

Future directions for HSCT in the treatment of sickle cell disease include the use of alternative sources of stem cells (such as matched unrelated donors, umbilical cord blood, and haploidentical donation) and measures to reduce toxicity of current HSCT conditioning regimens.[10] Non-myeloablative (or reduced intensity conditioning) allogenic-HSCT in children and adult patients with sickle cell disease has enabled stable mixed hematopoietic chimerism with promising results, and reduced HSCT-associated morbidity and mortality.[11] These alternative approaches are currently under investigation.

References

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