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EXPERT'S CORNER: A PERSONAL APPROACH

Hematopoietic stem cell transplants for persons with multiple sclerosis: Is this the best therapeutic option?

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In the field of autoimmune diseases the possibility to obtain curative therapy is exceptional, and the use of drugs has several limitations, besides, it is important to note that the apparition of undesirable effects are not rare; therefore the use of new ways to treat or cure this kind of diseases is always attractive for patients and the medical scientific world. In this setting, multiple sclerosis (MS) is an autoimmune, chronic, inflammatory, debilitating disease that causes destruction of central nervous system (CNS) myelin, with varying degrees of axonal damage. It mainly affects young adults and is twice as common in women than in men.[1] Studies published from the 1990s brought animal models and theoretical considerations of hematopoietic stem cell transplantation (HSCT) being useful in the prevention and treatment of autoimmune diseases, with clinical responses in some patients, suggesting that high-dose chemotherapy followed by HSCT rescue could ''reset'' the immunological changes through the control of autoreactive clones, followed by immunological tolerance after immune reconstitution. In the autologous HSCT, stem cells are collected after the administration to the MS patient of cyclophosphamide and filgrastim, this combination is using for mobilization of stem cells from bone marrow to the peripheral blood, and the effects of the chemotherapy reduces the amount of lymphocytes in the final stem cell collection, afterwards more chemotherapy is administered and then the stem cells are infused to the patient.[2] As mentioned before, many studies have led to the conclusion that HSCT may be a viable therapeutic option for MS.[1–10] Autologous HSCT have been given to patients with MS since 1996 and more than 1000 HSCTs have been performed around the world.[1–10] Most patients have been treated in small trials or in multicenter studies. In retrospective analysis, a progression-free survival of more than five years after transplant has been observed, the neurological outcomes being considerably more favorable in patients with the relapsing-remitting type and/or those who showed an inflammatory pattern in magnetic resonance imaging (MRI) during the pre-transplant screening. Reports of good results, particularly in the aggressive forms of MS, reinforce the effectiveness HSCT in MS patients with prominent inflammatory activity. The risk of transplant related mortality in HSCT for MS was conventionally considered very high but has declined since 2001 to less than 1.3%,[1–10] this probably being the result of the changes in the conditioning regimens, thus reducing toxicity and in turn, complications. Recent data, with more than

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Table 1 No evidence of disease activity in multiple sclerosis according to the therapeutic option.

Study	NEDA at 2 years
HALTS-MS	83%
Swedish aHSCT	78%
Drugs[a]	15–50%
Placebo	5%

NEDA = No evidence of disease activity in active forms of multiple sclerosis (MS). HALT-MS = Hematopoietic cell transplantation for relapsing-remitting multiple sclerosis. aHSCT = autologous hematopoietic stem cell transplantation.
[a] Drugs include daclizumab, ocrelizumab, interferon B 1a, alemtuzumab and glatiramer acetate.
Adapted from Ref. 11.

1000 autologous transplants for MS in all the world, show an overall survival of above 90% in five years and a progression-free survival of around 50%, the main cause of mortality and morbidity being the recurrence of the autoimmune disease.[2–10] The forms of the disease that might benefit from transplantation are: relapsing remitting, primary or secondary progressive, and the ''malignant'' form[2–10]; there are however, studies showing response in all types of MS.[10]

Despite the current availability of disease modifying therapies for the treatment of MS such as daclizumab, ocrelizumab, interferon B 1a, alemtuzumab and glatiramer acetate, there are still patients who suffer from severe neurological dysfunction in the relapsing-remitting or early progressive forms of the disease. For these patients, autologous HSCT offers an important therapeutic solution to prevent progression to irreversible disability. Table 1 shows the results of the use of HSCT or other novel drugs in the treatment of patients with active forms of MS, based on the paper by Sormani et al.[11] There is not enough information about the costs of these therapeutic approaches for individuals with MS, but similar to what has been proven in other hematologic diseases,[12] HSCT may be, on the long term, the best therapeutic option endowed with an adequate cost-benefit ratio, probably better than that of the novel drugs in MS. Detailed information on this topic is urgently needed.

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Conflicts of interest

Authors declare no conflicts of interest

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