# Autologous haematopoietic stem cell transplantation promise for myasthenia gravis

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Study findings in seven patients with severe myasthenia gravis (MG) support the use of autologous haematopoietic stem cell transplantation (HSCT) for achieving long-term remission.

The findings, published in *JAMA Neurology*, show that all seven patients achieved prolonged and complete symptom- and treatment-free remission following the treatment.

"This treatment aims to wholly replace an autoreactive immune system with one that is protective and self-tolerant", Harold Atkins (University of Ottawa, Ontario, Canada) and co-researchers explain.

It involved an immunoablative conditioning regimen consisting of high-dose chemotherapy with or without total-body irradiation and administration of antilymphocytic antibodies to destroy the existing autoreactive immune system.

Autologous haematopoietic stem cell grafts, previously harvested, depleted of residual mature immune cells and mobilised with cyclophosphamide and granulocyte colony-stimulating factors, were then infused to reconstitute the bone marrow and immune system.

The seven patients receiving the treatment, one of whom had follicular lymphoma with coincident active MG, had moderate (grade III) to life-threatening (grade V) disease, according to the Myasthenia Gravis Foundation of America (MGFA). This was despite having received a variety of intensive immunosuppressive therapies.

Five also had concurrent autoimmune or lymphoproliferative illness relating to their immune dysregulation.

The patients were aged 37 years on average at the time of diagnosis and 44 years when they received autologous HSCT.

At last follow-up, 29-149 months after treatment, all patients were classified as being in complete stable remission according to MGFA classification, with no MG symptoms and no need of MG-directed therapy.

All the patients had discontinued immunosuppressive therapies within 8 months of treatment and six (86%) patients had discontinued MG therapy altogether.

One patient required further hospital admission during the first 18 months after treatment for airway sequelae from previous repeated intubations, but 11 years since had not been re-hospitalised.

The researchers note that the profound immunosuppression caused by the treatment can lead to short-term complications, but only two of the patients had grade 3 mucositis while three had grade 3 febrile neutropenia, and in all cases the conditions were transient.

Similarly, late complications, including transient viral reactivations in three patients and a secondary autoimmune disease likely to be transplant related in one patient, all resolved or stabilised with treatment. And there were no treatment- or MG-related deaths.

"Autologous hematopoietic stem cell transplantation can be considered for select patients at experienced institutions with severe myasthenia gravis for whom the risks of this procedure are outweighed by its potential benefits", the team concludes.

The need to reserve its use to experienced institutions with the infrastructure and staff needed to care for immunocompromised patients was a point echoed by Daniel Drachman (Johns Hopkins School of Medicine, Baltimore, Maryland, USA) in a related editorial.

"It is important to recognize that autologous HSCT is an invasive procedure. It is a major undertaking, involving skilled and experienced management, hospitalization, and important risks", he stresses.