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Autologous Hematopoietic Stem Cell Transplantation for Stiff-Person Spectrum Disorder

A Clinical Trial

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Study Question

Is nonmyeloablative hematopoietic stem cell transplantation (HSCT) a safe and effective treatment for stiff person spectrum disorder (SPSD)?

What Is Known and What This Paper Adds

The existing therapies for SPSD include benzodiazepines, muscle relaxants, and various immunotherapy options. This trial's results indicate that nonmyeloablative HSCT improves outcomes in a subset of patients with SPSD.

Methods

For this open-label trial, the investigators recruited 23 adults with SPSD (91% female; mean age, 48 years; age range, 28–60 years) who had antibodies against glutamic acid decarboxylase in their peripheral blood, CSF, or both. Trial procedures occurred through Northwestern University in Chicago between May 2015 and August 2018. For stem cell mobilization, the participants received IV cyclophosphamide (2 g/m^2) 10 days before peripheral blood stem cell collection and daily subcutaneous filgrastim doses (5–10 μg/kg/d) starting 5 days after cyclophosphamide treatment. For immunoablation in preparation for HSCT (day 0), the participants received daily 50-mg/kg IV cyclophosphamide doses on days −5 to −2, rabbit anti-thymocyte globulin infusions at increasing daily doses of 0.5–1.5 mg/kg on days −5 to −1; and 500-mg rituximab doses on days −6 and +1. The primary outcomes were adverse events, particularly grade 3 and 4 toxicities as rated with criteria from the National Cancer Institute. The investigators defined responders as participants who experienced continuous immunotherapy-free remission and a ≥50% decrease in antispasmodic medication doses.

Results and Study Limitations

No participants died during or due to treatment, although 1 participant died a year after HSCT. The observed grade 4 toxicities were anorexia/vomiting (n = 2) and hyperglycemia (n = 1). Grade 3 toxicities were much more common. Seventeen participants (74%) responded; 48% fully and 26% partially to treatment. The 11 full responders entered an IVIG and immune drug free remissions and came off or had a 90% reduction in benzodiazepines. Two of these patients were wheelchair confined before HSCT, 1 improved to a walker and 1 became free of ambulatory assistance; 3 patients were using a walker and 2 were using a cane and after HSCT required no ambulatory assistance, while one who was bedridden was able to walk with one arm assistance after HSCT. The beneficial effect of HSCT was variable and predominately confined to participants with episodic spasms, normal tendon reflexes, without simultaneous co-contraction of limb agonist antagonist muscles, and who were not taking SSRI or SNRI antidepressants. These findings are Class IV evidence that nonmyeloablative HSCT improves outcomes for some patients with SPSD. This trial's limitations include retrospective data mining to identify responders, and the trial's single-center nature may limit generalizability.

Table The Most Common Grade 3 Toxicities

Grade 3 toxicity	No. of cases observed
Hypophosphatemia	13
Febrile neutropenia	13
Hyperglycemia	5
Hypokalemia	4
Dyspnea	4

Registration, Study Funding, and Competing Interests

This study received no funding. The trial was registered at ClinicalTrials.gov (NCT02282514). Dr. Balabanov reports receiving lecture honoraria and advisory board appointments from Biogen Idec, Sanofi-Genzyme, Genentech, and Alexion. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.