

The role of IVIg in the treatment of patients with stiff person syndrome and other neurological diseases associated with anti-GAD antibodies.

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Abstract

INTRODUCTION: High-titre anti-GAD antibodies are characteristically seen in patients with stiff person syndrome (SPS). Other CNS disorders, rarely associated with high anti-GAD antibody titres, include: a) SPS-plus, a syndrome characterised by SPS and cerebellar ataxia; b) Batten's disease; and c) rare patients with epilepsy and idiopathic cerebellar ataxia. Currently, high-titre anti-GAD antibodies serve only as markers of an autoimmune process within the CNS because their pathogenic role in the afore-mentioned disorders has not been established. In SPS, there is evidence of autoimmune pathogenesis based on: the association of the disease with other autoimmune disorders or autoantibodies; immunogenetic background; presence of oligoclonal IgG bands in the CSF with increased intrathecal anti-GAD antibody synthesis and response to immunotherapies. SPS is the only GAD-positive CNS disease where a controlled study with immunotherapy has been conducted.

METHODS: Sixteen anti-GAD antibody-positive patients were randomised to receive IVIg or placebo for 3 months. After a washout, they crossed to the alternative therapy for another three months. Efficacy was based on the difference in scores of the distribution of stiffness index and heightened sensitivity (spasms) from baseline to the second and third month of the infusions. Direct treatment and carry-over effect were compared for both groups.

RESULTS: The stiffness scores in the IVIg-randomised patients declined significantly from month 1 through 4, but rebounded when they crossed to placebo. In contrast, the scores in the placebo-randomised group remained constant from month 1-4 but dropped significantly after crossing to IVIg. Eleven patients who received IVIg became able to walk unassisted, stopped falling and assumed household or work duties. The duration of benefit varied from 6-12 weeks or up to a year. The anti-GAD(65) antibody titres declined after IVIg, but not after placebo.

CONCLUSION: Based on a controlled study, IVIg is a safe and effective therapy for SPS in patients unresponsive to other agents. Whether IVIg has a role in the other GAD-positive patients with neurological disease, or in SPS patients without GAD antibodies, remains unknown.