ELSEVIER

Intravenous Immunoglobulin Treatment in Autoimmune Neurological Disorders—Effects on Quality of Life

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ABSTRACT: Autoimmune neurological disorders are very common. Health-related quality-of-life measures, obtained through a patient-oriented tool (a self-administered questionnaire), are now considered essential in the evaluation of therapies, especially for pathologies that may affect patients' general status. We reviewed the most common autoimmune neurological disorders and their treatment, and we report on our experience on intravenous immunoglobulin (IVIG) administration and the relationship between IVIG and health-related quality of life. Generally, IVIG administration is effective in the most common autoimmune neurological diseases. Concerning the relationship between IVIG treatment and health-related quality of life, our results reveal an improvement of physical aspects of patients' health-related quality of life after IVIG administration. Conversely, the comparison of mental scores between the evaluation at baseline and the evaluation at follow-up exhibited no difference. Although the use of IVIG is effective for autoimmune neurological disorders, there are no commonly accepted protocols for the use of IVIG treatment. Further controlled studies on IVIG, including quality-of-life assessments, are necessary to develop needed evidence on the use of IVIG in clinical practice. *Human Immunology 66, 417–421 (2005).*

KEYWORDS: autoimmune neurological disorders; immunoglobulin treatment; quality of life; therapy

ABBREVIATIONS

Abs	antibodies
CIDP	chronic inflammatory demyelinating polyneuropathy
DASH	Disability of Arm Shoulder and Hand questionnaire
GBS	Guillain-Barré syndrome
IVIG	intravenous immunoglobulin
MG	myasthenia gravis
MMN	multifocal mononeuropathy
MS	multiple sclerosis
P-E	plasma exchange
SF-36	Short Form 36 questionnaire
SNMG	seronegative MG
SPS	stiff-person syndrome

INTRODUCTION

Autoimmune diseases are very common; they are estimated to affect more than 8.5 million Americans [1], and many of these diseases are neurological disorders. The most common autoimmune neurological disorders are Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal mononeuropathy (MMN), myasthenia gravis (MG), and multiple sclerosis (MS). Here, we briefly describe each one of these pathologies, report the most commonly accepted treatments, and provide our opinion on intravenous immunoglobulin (IVIG) treatment for these disorders in clinical practice. Treatments for these autoimmune neurological disorders include corticosteroids, plasma exchange (P-E), IVIG treatments, and chemotherapeutic agents.

Among the new immunotherapies, IVIG plays a very important role; IVIG has multiple actions on the immunoregulatory network. For each autoimmune neuromuscular disease, however, there is a predominant mechanism of action that relates to the underlying immunopathogenetic cause of the respective disorder. The best understood actions of IVIG include the follow-

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Received November 30, 2004; accepted January 19, 2005.

0198-8859/05/$–see front matter
doi:10.1016/j.humimm.2005.01.023

ing: (a) modulation of pathogenic autoantibodies, an effect relevant in MG, Lambert-Eaton myasthenic syndrome, GBS, CIDP, and stiff-person syndrome (SPS); (b) inhibition of complement activation and interception of membranolytic attack complex formation, an action relevant to the complement-mediated mechanisms involved in GBS, CIDP, MG, and dermatomyositis; (c) modulation of the inhibitory or activation Fc receptors on macrophages invading targeted tissues in nerve and muscle, as seen in CIDP, GBS, and inflammatory myopathies; (d) downregulation of pathogenic cytokines and adhesion molecules; (e) suppression of T-cell functions; and (f) interference with antigen recognition.

IVIG has a remarkably good safety record for long-term use. However, the following side effects have been observed: mild, infusion-rate-related reactions, such as headaches, myalgia, or fever; moderate but inconsequential events, such as aseptic meningitis and skin rash; and severe, but rare, complications, such as thromboembolic events and renal tubular necrosis [2].

Health-related quality-of-life measures, obtained through a patient-oriented tool (self-administered questionnaire), are now considered essential in the evaluation of therapies, especially in those pathologies that may affect the patients' general status [3]. By incorporating patient outcomes, such as health-related quality of life, into practice, researchers, administrators, and clinicians can determine optimal strategies for the care of patients because quality-of-life measures provide additional data for making clinical and health care policy decisions. The most used generic health tool is Short Form 36 questionnaire (SF-36), which consists of 36 questions covering the general health status of patients.

This questionnaire provides eight specific categories (eight subscores) of physical and emotional scores resumed on two main scores: Physical Composite Score and Mental Composite Score. Very low scores for the Physical Composite Score indicate severe physical dysfunction, distressful bodily pain, frequent tiredness, and unfavorable evaluation of the health status. Very low scores for Mental Composite Score indicate frequent psychological distress, and severe social and role disability due to emotional problems [4].

GUILLAIN-BARRÉ SYNDROME

GBS is clinically defined as an acute peripheral neuropathy causing weakness that progresses over days or, at most, up to 4 weeks. GBS occurs all over the world, with a median annual incidence of 1.3 cases per 100,000 population, with men being more frequently affected than women. GBS is an autoimmune disease, and data suggest that sometimes it is triggered by a preceding bacterial or viral infection. *Campylobacter jejuni,*cytomegalovirus, Epstein-Barr virus, and *Mycoplasma pneumoniae* are commonly identified antecedent pathogens. In the acute motor axonal neuropathy (AMAN) form of GBS, the infecting organisms probably share homologous epitopes to a component of the peripheral nerves (molecular mimicry), and therefore the immune responses cross-react with the nerves, causing axonal degeneration. The target molecules in AMAN are likely to be gangliosides expressed on the motor axolemma (GM1, GM1b, GD1a, and GalNAc-GD1a). In the acute inflammatory demyelinating polyneuropathy (AIDP) form, immune system reactions against target epitopes in Schwann cells or myelin result in demyelination; however, the exact target molecules in the case of AIDP have not been identified yet. AIDP is by far the most common form of GBS in Europe and North America, whereas AMAN occurs more frequently in East Asia (China and Japan). The prognosis of GBS is generally favorable, but it is a serious disease, with 10% mortality, and approximately 20% of patients are left with severe disability [5].

In the treatment of GBS, there is no significant difference between IVIG, P-E, or P-E followed by IVIG. However, for convenience and safety, IVIG is used as standard treatment in most centers. So far, there is insufficient evidence for the use of corticosteroid therapy for treatment of GBS [6].

In our experience, and according to the literature, we know that IVIG works well as plasmapheresis, but because of the monophasic course of the illness and the absence of clinical elements, there are no precise suggestions for treatment. Recently in our departments, IVIG treatment has been frequently used because it does not require special equipment and specialized personnel, it is less traumatic for children, and it can be used more quickly than plasmapheresis. This last is one of the most important aspects because the prognosis of GBS most depends on the speed of the treatment.

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

CIDP is an immune-mediated disorder characterized by progressive or relapsing-remitting course. Research criteria for the diagnosis of CIDP include clinical, electrophysiological, cerebrospinal fluid, and histopathological features. The clinical aspect of CIDP is the presence of proximal and distal, usually symmetric, weakness associated with sensory involvement. Current knowledge about the pathogenic mechanisms involved in chronic inflammatory demyelinating polyradiculoneuropathy supports an autoimmune etiology. The effector role of circulating Abs has recently been revisited. In addition histopathologic studies support the heterogeneity of dis-