GUILLAIN BARRÉ SYNDROME: RE-TREAT WITH A SECOND IVIG INFUSION

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The term Guillain Barré Syndrome (GBS) encompasses a number of acute paralytic disorders of the peripheral nerves, which are grouped together because they may overlap and because they share a similar clinical course and presumed pathogenesis. These include: Acute inflammatory demyelinating polyradiculoneuropathy (AIDP), Acute motor axonal neuropathy (AMAN), Acute motor and sensory axonal polyneuropathy (AMSAN) and the Fisher syndrome as well as some other cranial nerve involving variants. GBS is in most cases a single mono-phasic disorder with eventual recovery. Still many patients are severely debilitated during the stage of peak weakness, close to one third of the patients require respiratory support and a significant proportion of patients die or remain with severe residual disability, emphasizing the need for effective therapeutic interventions which need to be administered immediately following the diagnosis.

Ample evidence supports the hypothesis that GBS is an immune mediated disorder. Key elements include the post-infectious occurrence in close to 2/3 of cases and the presence of anti-Ganglioside antibodies in sera of most patients during the acute paralytic phase, presumably, induced thorough molecular mimicry, at least in those cases ante-ceded by Campylobacter jejuni enteritis. Somewhat surprisingly, corticosteroids appear to be ineffective in treating GBS and the currently accepted, “evidence based” therapies include plasma exchange (6 changes delivered during 2 weeks) or high dose intravenous immunoglobulins (IVIg), 2g/kg delivered over a 2-5 day period. The two treatments appear to be comparably effective in shortening the severe paralytic period and hastening recovery. For the past 13 years, current guidelines recommend treating patients with moderate to severe weakness (unable to walk independently) with either modality. In practice a tendency to prefer IVIg appears to prevail in most centers caring for GBS patients.

Among the many unanswered questions regarding GBS therapy, 2 converge on the issue of the correct dose and rate of delivery of IVIg. The standard 2g/kg given to all patients was arbitrarily chosen based on experience with immunodeficiency patients, and as this was the dose used in the pivotal clinical trials, it became canonized as the only possible and correct dose. Recently, a retrospective analysis of GBS participants of 2 clinical trials showed a marked variation in the rise of serum globulin levels at 14 days post infusion, and a positive correlation between low globulin level increment and poor clinical outcome. This study suggests that some patients may require higher IVIg doses to achieve a discernible benefit, and that serum globulin level may serve as a surrogate marker to determine the correct dosage.

The second unanswered dilemma revolves around the correct approach to patients who fail to improve within the 2-3 weeks after the initial IVIg infusion. Following our report (Farcas et. al. Lancet 1997;350:1747), on 4 initially “nonresponsive” patients who appeared to improve rapidly after delivery of a second IVIg course delivered after 14 days, this approach was adopted by many clinicians. A controlled clinical trial to corroborate or refute our conclusion, however, has not been carried out and is still sorely awaited.

At this point, we could all agree that there is no evidence in favour of retreating GBS patients with a second IVIg infusion. Lack of evidence, however, should never be equated to evidence for lack of efficacy. The recent work by Kuitwaard et.al (Ann Neurol 2009;66:597) suggests that patients who are severely affected and slow to improve need higher IVIg doses, and the correlation of serum globulin level increment at 2 weeks post-infusion with clinical outcome suggests that this time point may be a reasonable point to consider retreating patients who show signs of inadequate recovery or a low increase in serum globulin levels. As long as more effective therapeutic modalities or high quality evidence in regard to this issue are lacking, reinfusion with IVIg is a definitely reasonable approach.