Cleveland Clinic

Mellen Center Approaches: IVIG

Q: Can IVIG be used for treatment of acute relapses of MS?

A: There are no blinded randomized controlled trials evaluating the use of IVIG versus placebo or steroids for treatment of acute MS relapses. In an open label study comparing IVIG to intravenous methylprednisolone (IVMP) for treatment of acute relapses, both agents reduced EDSS after relapse and upon 1-year follow up without a statistically significant difference between both treatments. A few studies looked at the additional benefit of adding IVIG to IVMP for acute relapses but the combination was not superior to IVMP alone.

In general we consider IVIG as a third line for treatment of acute MS relapses after IVMP and plasma exchange (PLEX). We will consider IVIG treatment in the setting of acute relapse only if the patient was intolerant or fails to respond to both IVMP and PLEX.

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This information is not intended to replace the medical advice of your health care provider. Please consult your health care provider for advice about a specific medical condition.

Q: Can IVIG be used for prevention of MS relapses?

A: According to the AAN guidelines published in 2002 and the European Federation of Neurological Societies guidelines, IVIG can be used as an alternative to other disease modifying therapies (DMTs) only if all other therapies are not tolerated or contraindicated by the patient. Reduction of relapse rate and MRI progression in patients treated with IVIG is based on low class evidence (class C). A Cochrane Review published in 2010 found evidence to support use of IV immunoglobulins as a preventive therapy for relapses in relapsing remitting MS. In the relapsing remitting group there was a reduction in relapse rate (WMD -0.72 95% CI -0.78 to -0.66), increased time to first relapse and higher proportion of cases remaining relapse free (OR 0.63 [95% CI 0.42-0.94]) during treatment with intravenous immunoglobulins. There is no robust data on disease progression in this group. In the secondary progressive group treatment had no impact on sustained EDSS progression (OR 0.96 95%CIs 0.68-1.37). Fewer primary progressive patients treated with immunoglobulin progressed that those in the placebo group (p=0.016). There is conflicting evidence of reduction in number of new lesions on T2 weighted MRI and gadolinium enhancing lesions on T1 weighted MRI and total MRI lesion burden in relapsing remitting MS but no evidence in secondary progressive disease. IVIG may have special advantage in pregnant or nursing women in whom other DMTs are contraindicated.

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Q: What are the usual dosing and method of administration of IVIG?

A: the usual IVIG dose for treatment of acute relapses is 0.4 g/kg/day for five days given as continuous IV infusion. This can be given in the hospital or at the outpatient infusion center.

The usual dose for prevention of relapses (maintenance therapy) as used by most studies is 0.2 to 0.4 g/kg every four weeks. This can be administered in the outpatient infusion center or at home utilizing home health services.

Q: What are the side effects, risks, and contraindications of IVIG treatment?

A: Generally, IVIG infusion can cause migraine-like headaches, nausea, and dizziness. Infusion reactions including severe allergic reactions have been reported especially in patients with IgA deficiency. It may also promote thrombosis and may result in thromboembolic venous or arterial events. Other adverse effects include acute renal failure, aseptic meningitis, hemolysis, transfusion-related acute lung injury, and transmission of blood-borne infections. IN some cases, IVIG can cause aseptic meningitis which will manifest with severe headache associated with neck stiffness, photophobia, no fever or low grade fever, and accentuation of pain with head movement. Patients who develop aseptic meningitis with IVIG may have increased cell count and protein in their CSF but their culture is typically negative for infectious microorganisms. IVIG is contraindicated in patients with known hypersensitivity to IVIG.

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Q: Does treatment with IVIG require any pretesting and/or premedication?

A: Yes, before treatment with IVIG, IgA level is checked to ensure patient is not IgA deficient. Prior to treatment, patients are usually pre-medicated with acetaminophen 650 to 1000 mg, diphenhydramine 50 mg

Q: Are there any other indications for IVIG in MS patients?

A: There are some anecdotal reports of acute NMO relapses successfully treated with IVIG, following failure of intravenous corticosteroid administration. Patients in whom corticosteroids or plasma exchange are contraindicated or are impractical can also be candidates for IVIG.

For NMO relapse prevention, a few small case series suggest favorable experiences with IVIG for relapse prevention in NMO. In a study of 8 NMO patients treated with IVIG the mean relapse rate decreased from 1.0 in the year pre-IVIG to 0.006 during followup. We generally would consider IVIG for relapse prevention only if other first line agents were not tolerated or were unavailable. As in MS, IVIG can be an option for pregnant or nursing females.

There have been a few reports of IVIG use for PML patients who develop immune reconstitution syndrome (IRIS) after stopping natalizumab. We generally use steroids as a first line for treatment of IRIS but would consider IVIG if there is a contraindication to steroid use.

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