Cleveland Clinic

Mellen Center Approaches: Initial Treatment of Relapsing Forms of MS

Should MS treatment start early?

We start disease modifying therapy in patients upon the diagnosis of relapsing MS with active disease, defined either through recent relapses or new or active lesions on MRI. We also start therapy in patients with a clinically isolated syndrome and typical MS lesions on MRI.

Pathologic studies have shown that MS inflammation leads to significant brain and spinal cord injury, even during the early stages of disease. Many believe that this injury is what leads to the progressive disability commonly seen in the later years of MS. Despite excellent clinical recovery in early MS, clinical relapses and new lesions on imaging represent active, destructive injury. Once disability has developed, it is very difficult to reverse. Therefore, a Consensus Statement of the National Multiple Sclerosis Society recommends that MS disease modifying therapy be started in "as soon as possible following a definite diagnosis of MS with active, relapsing disease." In addition, the same Consensus Statement indicates that therapy may be considered for patients with a first episode of demyelination who are at high risk of developing MS.

REFERENCE:

Disease Management Consensus Statement, National Clinical Advisory Board of the National Multiple Sclerosis Society, 2007.

Are there some patients that do not need to start MS therapy?

There are some patients with a new diagnosis (CIS or MS) who are followed without disease modifying drug therapy. Sometimes, a patient is given a diagnosis of MS, and the history indicates an initial episode may years prior to the diagnosis. In that situation, if the disease appears benign by clinical and imaging criteria, most MC neurologists monitor the patient without disease modifying therapy. Also, patients with clinically isolated syndromes (i.e. isolated optic neuritis or transverse myelitis) with normal or equivocal brain MRI scans can often be followed without disease modifying therapy. In these circumstances, we fully inform patients of the rationale for observation, and the need for monitoring. Follow-up typically involves monitoring clinically and with MRI.

What are the initial treatment options for relapsing forms of MS?

Four therapies are considered standard, first-line treatment options for relapsing forms of MS:

- Interferon ß-1a intramuscular once weekly (Avonex)
- Interferon ß-1a subcutaneous thrice weekly (Rebif)
- Interferon ß-1b subcutaneous every other day (Betaseron)
- Glatiramer acetate subcutaneous daily (Copaxone)

All four therapies have been shown to decrease the rate of clinical relapses and development of new brain lesions. Where clinical trials were properly powered, therapies have also been shown to slow the progression of disability. In patients with a single demyelinating attack (clinically isolated syndrome) and an MRI suggestive of MS, all four therapies have been shown to decrease the risk of developing clinically definite MS. All of these treatments are only partially effective when assessed in large groups of patients, although individual patients may have their disease completely controlled by any of these therapies.

REFERENCE:

Disease Management Consensus Statement, National Clinical Advisory Board of the National Multiple Sclerosis Society, 2007.

continued on next page

13-NEU-538

Mellen Center Approaches: Initial Treatment of Relapsing Forms of MS, continued

When are more aggressive therapies used as initial treatment of relapsing MS?

Natalizumab is considered as a first-line therapy in patients with very aggressive disease, as defined by amount of active inflammation on MRI, poor recovery from relapses, and frequent of relapses. Additional initial treatment options for very aggressive MS include cyclophosphamide and mitoxantrone. For severe demyelinating events in which corticosteroid therapy is ineffective, we will consider using plasmapheresis.

REFERENCE:

Kappos et al, Lancet Neurology, 2007; 6(5):431-41

Weinshenker et al, Ann Neurol, 1999 ;46:878

What is the best initial treatment for relapsing MS?

When starting therapy, we first choose between either interferon or glatiramer acetate therapy based upon side-effect profile and patient preference for frequency/route of administration. No injectable therapy has documented long-term superiority over any other. Among interferon therapies, we generally use weekly intramuscular interferon because of good patient tolerability, low frequency of administration, low immunogenicity (neutralizing antibodies), and low frequency of laboratory abnormalities (i.e. transaminitis, cytopenia). Some patients prefer subcutaneous rather than intramuscular interferon because of the needle size. Problematic headache disorder, spasticity, or depression, and pre-existing liver disease or seizure disorder are relative contraindications for use of interferon.

REFERENCE:

Cavadid et al, Neurology, in press

Mikol et al, Lancet Neurology, 2008;7:903–14

O'Connor et al, Neurology 2008;70(11):LBS.004.

What factors relate to treatment effectiveness?

All MS therapies are only partially effective, and so require clinical and radiologic surveillance. Patient adherence is perhaps the most important modifiable aspect of treatment effectiveness. Adherence can be increased through initial and ongoing education, with attention to expected benefits and side effects, and regular follow-up. Patient expectations and the need for strict adherence are very important in maintaining long term treatment. Patients need to recognize that these therapies are primarily preventative, not curative of pre-existing symptoms.

Can injectable therapies be used as initial treatment of progressive MS?

Injectable therapies can be used in progressive MS if active inflammation is present. Several studies have shown that interferon therapies reduce the frequency of relapses, development of new brain lesions, and progressive disability in patients with secondary progressive MS. Patients most likely to benefit are those who are younger, have shorter disease duration, had a recent clinical relapse, and have gadolinium-enhancing lesions on MRI. Patients without these characteristics are unlikely to benefit from injectable therapies.

REFERENCE:

European Study Group, Lancet 1998; 352:1491-7

Cohen et al, Neurology 2002; 59:679-87

Is neuromyelitis optica (Devic disease) treated differently than standard relapsing remitting MS? (See also Mellen Center Approach – Neuromyelitis Optica)

Neuromyelitis optica (NMO, Devic disease) is treated differently than conventional MS. Although well-controlled trials are lacking, we generally use azathioprine and corticosteroids. As second-line therapy, we consider rituximab, plasma exchange, intravenous immunoglobulin, and mycophenolate mofetil. We avoid interferon therapies; in our experience interferon has not been helpful for NMO.

REFERENCE:

Jacob et al, Arch Neurol 2008; 65:1443-1448

Can interferon and glatiramer acetate medications be used in pediatric patients?

Interferon and glatiramer acetate medications can be used in pediatric patients. Although there is limited data available on the use of injectable MS therapies in pediatric patients, initial reports suggest safety and tolerability of these therapies is similar in pediatric patients as that seen in adults. In our experience, pediatric patients generally prefer a less frequently dosed injectable.

REFERENCE:

Banwell et al, Neurology 2006; 66:472-6.

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