Multiple sclerosis treatment: Some safety issues to keep in mind

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Interferon drugs and the treatment of multiple sclerosis

The treatment of multiple sclerosis (MS) has been revolutionized by the discovery of interferons. The interferons are man-made molecules that mimic the action of interferon molecules that are made by the body. The interferons are part of the immune system, which works to clear invaders from the body. The name “interferon” comes from “interference,” because they interfere with the growth of viruses. More information about MS can be found on the next page.

In MS, part of the immune system reacts against myelin. Myelin is a cover that surrounds the nerves in the brain and allows them to carry impulses through the brain more efficiently. We believe treatment with interferons decreases the number of attacks on myelin.

How are interferon drugs made?

The interferon drugs are produced by bacteria (*Escherichia coli*) in the laboratory. All the interferon drugs have been shown to cause liver damage in some people. We detect this damage by measuring liver function tests in the blood. The interferon drugs are not only used for the treatment of MS. These medications have been used also for the treatment of hepatitis, myeloma, leukemia, and other diseases.

How many interferon drugs are there?

There are three interferon drugs available for the treatment of MS: interferon B1a (Avonex), interferon B1b (Betaseron), and interferon B1a (Rebif). All of the interferon drugs must be injected. None are available to take by mouth. The interferon drugs have different doses and routes of injection. Betaseron is injected every other day subcutaneously (under the skin). Rebif is injected three times per week subcutaneously. Avonex is injected once a week intramuscularly (into a muscle).

Interferon drugs can affect the liver

In this issue of *Neurology*, Tremlett and colleagues reviewed the liver function tests of 835 patients with MS who were using one of the three available interferon drugs. The investigators reviewed medical records for patients aged 18 to 60 years who had two or more attacks of MS during the 2 years prior to entering the study. Liver function tests were checked before treatment with interferon drugs and at 3, 6, and 12 months after treatment was started. After the first year of interferon treatment, liver function tests were checked every year. Patients who had been on interferon treatment in the past or who had any other medical problems that could cause liver abnormalities were not included in the study.

Overall, nearly one third (36%) of the patients treated with interferon

drugs developed abnormal liver function tests. All of the three interferon drugs caused some abnormality in liver function tests. Avonex caused slightly less problems than Betaseron and Rebif. Most patients had minimal abnormalities (33 to 38%), 4 to 7% had mild to moderate abnormalities, and only 1 to 2% had severe abnormalities on the liver function tests. The “highest risk” period for developing liver abnormalities seemed to be in the first 12 months of beginning treatment.

Risk factors for liver problems in patients taking interferon drugs

Men seemed to be at higher risk than women for developing liver function abnormalities. Other factors, such as obesity, alcohol use, and other medications (i.e., acetaminophen) used simultaneously, also increased the risk of developing liver function abnormalities. The medical significance of a slight abnormality in liver function tests is unknown.

What have we learned from this study?

In conclusion, MS patients must be aware of the risk of developing liver abnormalities while on interferon therapy. It could be harmful to the liver if patients taking interferon therapy use alcohol, become obese, or take other medications that can also be harmful to the liver. Liver function tests should be checked periodically during interferon therapy, especially during the first year of treatment.

What is MS?

MS is a disabling neurologic disorder of young adults, affecting at least 300,000 Americans. The average age at diagnosis is 30, typically starting between the ages of 15 and 50. Women are affected at least twice as often as men. It is more common in persons of northern European heritage and those living furthest from the equator.

MS involves inflammation within the central nervous system (the brain and spinal cord), followed by the loss of the protective myelin sheath that surround nerve fibers. When the myelin is damaged, nerve impulses are not quickly and efficiently transmitted. Besides damage to the myelin sheaths, it is now recognized that the nerve fibers, called axons, also are damaged in MS to varying extent. Lesions (called plaques) develop in the brain and spinal cord and can cause the symptoms of MS listed below.

What are the symptoms?

There are several types of MS. Most people with MS begin with relapsing-remitting disease. This means that the symptoms come and go, often leaving the person feeling nearly normal until another relapse, or MS attack, occurs. Symptoms associated with relapses usually develop over a period of days. The problems can last for a matter of days or weeks and then go away, sometimes even without any treatment. New attacks occur at irregular intervals, usually one attack every 1 to 2 years. Common symptoms include the following:

- Vision loss
- Numbness or tingling
- Weakness or fatigue
- Unsteadiness in walking
- Double vision
- Heat intolerance
- Partial or complete paralysis
- Electric shock sensations when bending the neck

About 50% of patients with relapsing-remitting MS develop a progressive form of MS, called secondary progressive MS, in which there is continual worsening. In this phase of the disease, patients may continue to have relapses or may stop having them altogether. About 15% of patients have progressive-worsening from the beginning of their MS and do not experience relapses of MS. This form of MS is called primary progressive MS.

How is MS diagnosed?

The diagnosis of MS is based on a history of multiple attacks over time of neurologic lesions that affect different parts of the central nervous system. A neurologist will order tests that will help confirm the diagnosis. Usually a magnetic resonance imaging (MRI) scan of the brain (and possibly the spinal cord) is ordered to find evidence of abnormal areas. Lumbar puncture (spinal tap) is also helpful to detect specific problems with the cerebrospinal fluid.

What causes MS?

The cause of MS is unknown. There is strong evidence that MS is immune mediated. This means that the person's own immune system attacks the central nervous system (an autoimmune disease).

What are the treatments?

Currently, there is no prevention or cure for MS. However, this is a promising time for people with MS, as several new medications that affect the underlying disease process have been approved or are awaiting approval by the US Food and Drug Administration (FDA). You should ask your neurologist about the best treatment options for you. Current treatments are divided into three categories:

1. Medications that treat the symptoms of MS. These include medications

to treat depression, decrease muscle stiffness, reduce fatigue, control bladder symptoms, reduce pain, and address sexual dysfunction.

2. Medications that modify attacks when they occur. These are primarily corticosteroids (a synthesized adrenal hormone) that can shorten an attack.
3. Medications that modify disease activity. These are taken on a regular basis to help reduce the frequency of attacks and the long-term damage to brain caused by MS. FDA-approved disease-modifying therapies for treating MS include recombinant β -interferons (Avonex, Betaseron, and Rebif), glatiramer acetate (Copaxone), and an immunosuppressant/chemotherapy drug, mitoxantrone (Novantrone).

For more information

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