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Low-Dose Naltrexone for Treatment of Multiple Sclerosis: Clinical Trials Are Needed

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TO THE EDITOR: Multiple sclerosis (MS) is generally thought to be an autoimmune disease. Current estimates suggest that there are up to 400 000 patients diagnosed with MS in the US.¹ In all forms of MS, both inflammatory and neurodegenerative processes affect the disease. After receiving several questions regarding the use of low-dose naltrexone for MS, I performed a search of MEDLINE (1966-May 2007) and *International Pharmaceutical Abstracts* (1971-May 2007). One relevant article and one letter to the editor were found. The article offers a hypothesis on the potential mechanism of action of naltrexone in the treatment of MS: astrocytes and microglial cells produce peroxynitrites that inhibit glutamate transporters in neuronal cells and oligodendrocytes, resulting in excitatory glutamate neurotoxicity. Naltrexone may inhibit nitric oxide synthase activity, which may decrease the formulation of peroxynitrites, thus decreasing glutamate neurotoxicity.^{2,3} In this manner, naltrexone would affect the neurodegenerative processes of MS, unlike most of the currently approved treatments, which affect the inflammatory processes of the disease.¹ In the letter to the editor, the author postulates that the same mechanism is the reason that naltrexone has been found to help autistic patients.⁴ Naltrexone is an opiate antagonist approved by the Food and Drug Administration (FDA) for the treatment of alcohol dependence and for the reversal of effects of an opioid.

There are no published scientific studies or case reports that have documented the use of naltrexone for MS. However, much anecdotal information can be found on the Internet: a search for naltrexone and multiple sclerosis yielded over 60 000 results. Numerous Web sites are dedicated to spreading the word on this potential therapy. Several Web sites of compounding pharmacies advertise their experience in compounding formulations of low-dose naltrexone. However, as healthcare professionals know, Internet-based anecdotal evidence is not a replacement for sound scientific data.

In the past, the National Multiple Sclerosis Society (NMSS) has recommended that patients with MS avoid naltrexone.⁵ Many Web sites state that naltrexone works in MS by boosting the immune system.⁶ Because MS is thought to be an autoimmune disease, anything that may boost the immune system has the potential of worsening the disease. Current FDA-approved treatments, including interferon- β and glatiramer, mitoxantrone, and natalizumab, modulate the immune response rather than boost it.¹ However, the NMSS is now encouraging clinical trials on the subject.⁷

Clinical trials involving the use of naltrexone in MS patients are currently underway.^{7,8} The results of these studies, especially those involving patients with MS,⁸ will be important.

Due to the limitations of the conventional therapies for MS, including the potential for serious adverse events, inconvenient administration, and high costs, many patients with MS are eager to try low-dose naltrexone. Given the large worldwide interest in this subject, data from clinical trials will be of great interest.

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