Interferon beta in the management of multiple sclerosis

In a review on multiple sclerosis (MS) in the April issue of the Journal on page 157, I stated that ‘the expense, inconvenience of administration, frequent occurrence of flu-like symptoms and lack of proven effect on disability are major factors limiting the usefulness of interferon beta (in the management of MS)’. However, since the time of writing, Jacobs et al. have published an article providing convincing evidence that intramuscular interferon beta-1a reduces the progression of disability in relapsing-remitting MS. They administered interferon beta-1a, 6.0 million units (30 μg), by intramuscular injection once weekly in a randomised, double-blinded, placebo-controlled, multicentre trial. The primary outcome variable was time to sustained progression of disability by at least 1.0 point on the Kurtzke Expanded Disability Status Scale. Treatment with interferon beta-1a significantly prolonged this time. The proportion of patients showing progression by the end of two years was 35% in the placebo group and 22% in the interferon-beta-1a-treated group. Patients treated with interferon beta-1a also had significantly fewer exacerbations and a significantly lower number and volume of gadolinium-enhanced brain lesions on magnetic resonance imaging (MRI). Interferon beta-1a was well tolerated, and 93% of patients completed the planned course of treatment. There were no major adverse events related to treatment. Flu-like symptoms were significantly more frequent in the interferon-beta-1a-treated group but these were mild and transient, and had been minimised by the routine administration of paracetamol around the time of each injection. Serum neutralising anti-interferon activity was observed in 14% of the interferon beta-1a recipients after one year and in 22% after two years. It will be important in future studies to determine whether the development of these antibodies continues to increase with increasing duration of therapy and whether their development is associated with a loss of therapeutic efficacy. Further studies will also be needed to determine whether interferon beta-1a inhibits the progression of disability in secondary progressive MS and in primary progressive MS.

Previous studies have shown that the subcutaneous injection of interferon beta-1b (1.6 or 8.0 million units) on alternate days significantly reduces the frequency of relapses and the accumulation of brain lesions on MRI in relapsing-remitting MS. However, this therapy has not been shown to have any significant effect on the progression of disability. These studies on interferon beta-1b were not primarily designed to detect a beneficial effect on disability, and it is possible that future studies will demonstrate such an effect, as has been demonstrated with interferon beta-1a. Nevertheless, it should not be assumed that these two types of interferon beta will be equally efficacious. Interferon beta-1a is a natural-sequence, glycosylated, recombinant Chinese hamster ovary product; interferon beta-1b is a serine-substituted, nonglycosylated recombinant protein produced in Escherichia coli. The route of administration and dosage also need to be taken into account.

The mechanism whereby interferon beta achieves its beneficial effect in MS is unclear. The anti-viral action of interferon beta may be responsible, as viral infections may trigger attacks of MS. Alternatively, the beneficial effect may be due to the downregulation of interferon-gamma-induced expression of class II major histocompatibility complex antigens in the central nervous system. The administration of interferon gamma precipitates attacks of MS.

In conclusion, the publication of the paper by Jacobs et al. is an important milestone in the search for better management of MS. Intra-muscular interferon beta-1a therapy provides a means of reducing the accumulation of physical disability in relapsing-remitting MS.

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References
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