Interferon β-1a prevented the development of clinically definite multiple sclerosis after a first demyelinating event


**QUESTION:** In patients with a first confirmed demyelinating event, does interferon β-1a reduce the incidence of clinically definite multiple sclerosis (MS)?

**Design**
Randomised (allocation concealed†)[‡] blinded (patients, clinicians, and outcome assessors),[‡] placebo controlled trial with 3 years of follow up (Controlled High Risk Subject Afoxon Multiple Sclerosis Prevention Study [CHAMPS]). An interim analysis was planned.

**Setting**
50 clinical centres in North America.

**Patients**
383 patients (mean age 33 y, 75% women, 86% white) who had a first acute clinical demyelinating event confirmed by magnetic resonance imaging (MRI). Inclusion criteria were age 18–50 years; involvement of optic nerve, spinal cord, brain stem, or cerebellum; ≥2 clinically silent brain lesions ≥3 mm in diameter; and symptom onset < 14 days from corticosteroid treatment and < 27 days from randomisation. Exclusion criterion was previous demyelinating event lasting > 48 hours. Loss to follow up was 4%, and 15% stopped early.

**Intervention**
All patients were given intravenous methylprednisolone, 1 g/day for 3 days, and then prednisone, 1 mg/kg of body weight per day orally for 11 days, followed up by tapering for 4 days. 193 patients were allocated to interferon β-1a, 30 µg/week by intramuscular injection, and 190 were allocated to placebo.

**Main outcome measures**
Development of clinically definite MS, changes in MRI findings, and adverse effects.

**Main results**
By 3 years, fewer patients in the interferon group than in the placebo group had developed clinically definite MS (adjusted p < 0.001) (table). Interferon group patients also had lower increases in lesion volume on MRI at 6, 12, and 18 months and fewer new or enlarging lesions measured with T₂ weighted scans (mean 2.1 v 5.0 lesions/patient at 18 mo) and gadolinium enhancing lesions at 6, 12, and 18 months (mean 0.4 v 1.4 lesions/patient at 18 mo) (p < 0.05 for all comparisons). Interferon group patients had a higher rate of the influenza-like syndrome during the first 6 months of treatment (5% v 26%, p < 0.001) and a higher rate of depression (20% v 13%, p = 0.05).

**Conclusion**
Patients with a first demyelinating event and lesions on MRI had a lower incidence of clinically definite multiple sclerosis by 3 years.

†See glossary.
‡Information provided by author.

**COMMENTARY**

Jacobs et al have published an important paper. They show that interferon β-1a treatment of patients with a single symptom suggestive of MS and ≥2 lesions on MRI that are strongly suggestive of MS delays the appearance of the second symptom, thus delaying the diagnosis of MS (ie, to satisfy the criterion for dissemination of white matter lesions in time and space).

Previous studies with interferons and glatiramer acetate have shown that in relapsing MS the time to next attack was prolonged by treatment. The results of this study were expected therefore to be in favour of interferon treatment. Serious side effects of this treatment are flu-like symptoms, liver function test abnormalities, and leukopenia. Liver necrosis occurs rarely in these patients during treatment.

If accepted as an indication for the earliest possible treatment for MS, this study could result in a more effective overall treatment strategy. If accepted as an indication for the earliest possible treatment for MS, this study could result in a more effective overall treatment strategy. As the authors state in their discussion, other studies have shown that frequent relapses and the number and extent of lesions on MRI have an influence on the long term outcome of the disease. Therefore, significantly and persistently reducing the relapse rate, prolonging the interval between relapses, and reducing the number of new lesions on MRI could have a major effect on the clinical outcome of the disease. However, as the authors state, such a conclusion needs to be supported by long term studies.

Donald Paty, MD
University of British Columbia
Vancouver, British Columbia, Canada

