THERAPEUTICS

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

Jacobs LD, Beck RW, Simon JH, et al., and the CHAMPS Study Group. **Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis.** N Engl J Med. 2000 Sep 28;343:898-904.

QUESTION

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

DESIGN

Randomized {allocation concealed*}†, blinded (patients, clinicians, and outcome assessors),* placebo-controlled trial with 3-year follow-up (Controlled High Risk Subject Avonex Multiple Sclerosis Prevention Study [CHAMPS]). An interim analysis was planned.

SETTING

50 clinical centers 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 to 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 therapy and < 27 days from randomization. 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/d for 3 days, and then prednisone, 1 mg/kg of body weight per d orally for 11 days, followed by tapering for 4 days. 193 patients were allocated to interferon β-1a, 30 μg/wk 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 T_2-weighted scans (mean 2.1 vs 5.0 lesions/patient at 18 mo) and gadolinium-enhancing lesions at 6, 12, and 18 months (mean 0.4 vs 1.4 lesions/patient at 18 mo) ($P \leq 0.03$ for all comparisons). Interferon-group patients had a higher rate of the influenza-like syndrome during the first 6 months of treatment (54% vs 26%, $P < 0.001$) and a higher rate of depression (20% vs 13%, $P = 0.05$).

CONCLUSION

Patients with a first demyelinating event and lesions on magnetic resonance imaging who received interferon β-1a had a lower incidence of clinically definite MS by 3 years.

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*See Glossary.

†Information supplied by author.

Interferon β-1a vs placebo to prevent multiple sclerosis (MS) after a first demyelinating event‡

Outcome at 3 y	Interferon	Placebo	Adjusted RRR (95% CI) §	NNT (CI)
Definite MS	35%	50%	51% (27 to 67)	4 (2 to 8)

‡Abbreviations defined in Glossary; NNT and its CI calculated from data in article.
§Adjusted for age, type of initial event, and volume of lesions on MRI scans.

COMMENTARY

Jacobs and colleagues 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 (i.e., 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 (1–3). Therefore, the results of this study were expected to be in favor 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 use of disease-modifying drugs in MS. 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.

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References

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