

Low dose interferon- α to treat Behçet's disease

Sirs,

Treatment of Behçet's disease (BD) severe acute symptoms, in particular uveitis, consists of corticosteroid (CS) therapy with immunomodulatory treatments (IS) (1-3). Recent reviews of the literature (4-6) confirmed the efficacy of interferon (IFN) α for BD, mainly prescribed at 6 to 9 million units international (MUI) 3 times a week, with some side effects. In this study, we evaluated the effect of low-dose IFN- α 2b (3 MUI 3 times a week) in 4 patients with severe BD diagnosed according to the International Study Group for Behçet's Disease (ISGBD) (7). Remission was defined by the disappearance of all the signs and symptoms that were present at diagnosis, and the absence of any new BD sign during follow-up.

Demographic data of the patients (3 males and 1 female) were mean age 32.2, and mean disease duration 9 years. One patient had been receiving azathioprine therapy for prior recurrence. At the beginning of IFN treatment, all patients had oral aphthosis, 3 genital aphthosis, 4 uveitis, 1 arthritis and 2 cutaneous signs (pseudofolliculitis, acne). All patients were treated with IFN- α 2b (INTRONA®; Schering-Plough, Bloomfield, USA), 3 MUI 3 times a week in addition to prior CS treatment for 2 patients and with concomitantly prescribed CS for the other 2. A dosage decrease of IFN was planned after 18 months of effective treatment. CS was tapered according to clinical improvement.

The treatment was efficacious in all patients (Table I), with a mean delay to clinical efficacy of 5 weeks. The dosage of IFN- α 2b was never increased. The mean duration of IFN- α 2b treatment was 21.1 months, and IFN- α 2b treatment was stopped in 3 patients. The follow-up duration was 31.4 months, during which only 1 patient experienced a mild relapse of uveitis 11 months after IFN- α 2b discontinuation and was effectively treated with local steroids only. CS treatment was gradually reduced in all patients (mean dose at initiation of CS 47 mg/day [range 15-80 mg/day]; mean dose at end of follow-up 8.5 mg/day [range 0-30 mg/day]) and stopped in 2. Treatment tolerance was good for all patients. Only 1 severe psychiatric adverse event (depression) was noted for 1 patient and subsequently controlled by medical treatment without the need to stop or decrease IFN- α 2b treatment.

Table I. Response to treatment with IFN- α of patients with Behçet's disease.

Patient	Treatment indication	Efficacy	Delay to clinical efficacy (weeks)	Treatment duration	Follow-up	Cause of treatment cessation	Relapse
1	Bilateral panuveitis	1	3	35 months	46 months	remission	Yes*
2	Left panuveitis	1	7	22.5 months	22.5 months	remission	No
3	Bilateral panuveitis	1	8	9 months (on-going)	9 months	0	No
4	Bilateral panuveitis	1	2	18 months	48 months	pregnancy	No

*ocular relapse after 11 months of treatment cessation, controlled by local CS therapy

Thirty studies evaluated the efficacy of treatment for articular and cutaneo-mucous manifestations and 6 ocular signs (reviewed in 4-6). BD symptoms (cutaneo-mucous, articular signs, uveitis) responded in part or completely to IFN after the second week of treatment, with complete remission 4 to 6 weeks after treatment initiation. One open-labelled prospective study (8) evaluated IFN- α 2a in 50 patients with sight threatening posterior uveitis or retinal vasculitis and showed 92% response rate and remission achievement by week 24, demonstrating efficacy of this treatment in severe ocular disease. Only 1 placebo-controlled study (9) showed beneficial effects for cutaneo-mucous signs.

The treatment strategy proposed in several open studies (8, 10) was as follow: treatment initiated at 6 to 9 MUI 3 times a week and decreased to 4.5 MUI after 4 weeks to 3 months and then to 3 MUI until 8 weeks after complete remission. The efficacy on ocular inflammation was convincing. Relapse at treatment discontinuation was reported in up to 38% of cases but with good response to re-treatment in most.

Only one other open study (11) evaluated the effect of low-dose IFN (3 MUI 3 times a week) in 8 patients with BD-associated uveitis resistant to "conventional" therapy and showed good efficacy and tolerance, as in our study.

Thus, within the limitations of this short open study, we suggest that treatment of severe BD with low-dose IFN- α (3 MUI 3 times a week) can be as effective to control ocular inflammation as high doses of IFN or "conventional" IS. Such results are of main interest considering that tolerance to treatment is one of the major concerns in prescribing IFN and that adverse events are seemingly dose-dependent. However, further randomised controlled studies comparing the efficacy of low-dose IFN- α and IS are necessary to confirm these results in BD.

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