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Alpha Interferon Treatment in Atopic Dermatitis

D. JULLIEN[1], J. F. NICOLAS[1], A. FRAPPAZ[2] and J. THIVOLET[3]

[1]INSERM U.346, [2]PECLIC and [3]Dermatological Clinic, Hôpital E. Herriot, Lyon, France

Eight patients suffering from atopic dermatitis were treated with interferon α2b. They received low or intermediate doses (9–15 × 10^6 U/week) for a short period of time (4–8 weeks), with a moderate improvement of skin lesions in 4 of them and no change or an exacerbation of the disease in the other 4. Among the 4 patients who slightly improved at 4 weeks, 3 did not show any beneficial effect of interferon after 8 weeks. Serum IgE levels, which were increased in all patients before treatment, were not reduced under interferon therapy. This study shows that intermediate doses of interferon α2b are not effective in the short-term treatment of atopic dermatitis.

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D. Jullien, Hôpital E. Herriot, Pav. R, *INSERM* U.346, 69437 Lyon Cx 03, France.

Alpha interferon treatment has been associated with improvement in the clinical condition of patients with chronic inflammatory and autoimmune diseases such as rheumatoid arthritis (1), multiple sclerosis (2) and discoid and subacute cutaneous lupus erythematosus (3, 4). It was recently reported that interferon alpha (IFN-α) was responsible for improvement in the clinical condition of a patient with a hyper-IgE syndrome (5) with a parallel decrease in serum IgE levels, suggesting that this agent could be effective in the treatment of allergic diseases associated with hyper-IgE production, particularly atopic dermatitis. An antagonistic effect of IFN-α on interleukin-induced IgE production was suggested as a mode of action (6). The results are reported of a therapeutic trial using low doses of IFN-α in 8 patients with atopic dermatitis.

MATERIALS AND METHODS

Patients

Eight adults with a chronic severe form of atopic dermatitis (AD) gave informed consent to participate in the study. The clinical data concerning the 8 patients are listed in Table I.

The study was conducted in the winter of 1990. The criteria for inclusion in the study comprised: stable or progressive disease at the initial consultation; measurable lesions; no specific treatment (PUVA, topical steroids) for at least 4 weeks before IFN therapy.

Routine laboratory tests and serum IgE levels (radioimmunoassay, Pharmacia, St Quentin sur Yvelines, France) were determined at the initial consultation and at 4 and 8 weeks.

Interferon α2B (Intron-A®) administration

Recombinant IFN-α2b was provided by Laboratoires Schering-Plough (Paris, France) as lyophilized powder in vials of 3.0 and 5.0 × 10^6 U. Patients were treated for 4 to 8 weeks with doses of IFN-α2b that varied from 9 to 15 × 10^6 U/week (Table I).

Evaluation of response to therapy

At the initial visit and at two intervals of 4 weeks the patients were assessed and indicator lesions were monitored for the following symptoms: erythema, infiltration, crusts, scaling, excoriations and pruritus. Each of the six parameters were given a score, graded as 0 (none), 1 (mild), 2 (moderate) and 3 (severe). The total clinical severity score (TCSS) was defined as the sum of the six individual scores. The extent of skin disease (percent of body involvement – PBI) was estimated using the rule of nines. Patients with a PBI > 20% and a TCSS of at least 9 (Table I) were included.

Clinical response to therapy at 4 and 8 weeks (t) was defined on the total rate of improvement (TRI), as follows:

$$TRI = \frac{\left[1 - \frac{TCSS_t}{TCSS_{t_0}}\right] \times 100 + \left[1 - \frac{PBI_t}{PBI_{t_0}}\right] \times 100}{2}$$

Table I. *Characteristics of patients enrolled in the study*

Patient	Sex/Age	Duration (years)	P.B.I.[a] (%)	T.C.S.S.[b] (%)	Serum IgE[c] (KU/L)	Dosage (× 10^6 U/W)
1	M/35	3	20	15	3245	9
2	F/25	24	20	13	15318	9
3	F/20	20	90	13	–	9
4	F/26	20	90	13	1656	9
5	M/34	3	30	17	3565	9
6	F/44	5	30	9	2300	9
7	M/30	30	90	15	4351	15
8	M/40	36	60	10	16203	15

[a] Percent body involvement at J0
[b] Total clinical severity score at J0
[c] IgE serum level at J0. Normal serum IgE level: 0–175

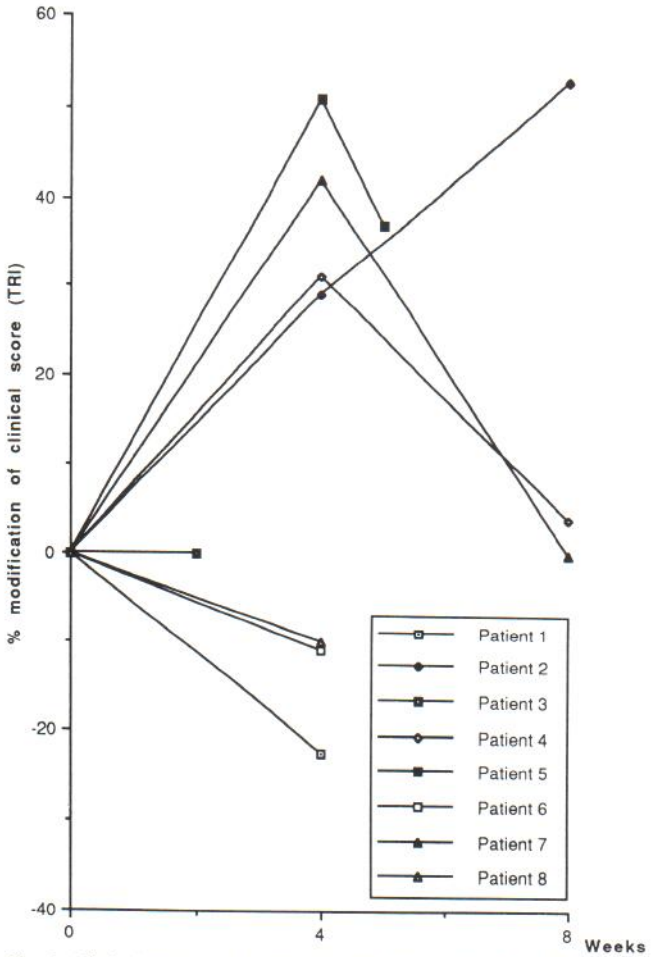

Fig. 1. Clinical results observed under IFN-α2b treatment. Results are expressed as % modification of the clinical status before treatment.

On the basis of the TRI determination, four levels of response were quoted: major (≥ 70%), mild (30–70%), minor (30–10%), no response or exacerbation (≤ 10%).

RESULTS

Among the 8 patients of the study, the clinical condition of 3 worsened rapidly under therapy, leading to the discontinuation of IFN at 4 weeks (Fig. 1). One patient who improved mildly after 4 weeks dropped out of the study at 5 weeks because of a sudden exacerbation of atopic eczema. Another patient (patient 3) did not show any change in his clinical condition during the first 2 weeks of treatment and then dropped from the study because of a fever higher than 40°C.

Only 3 patients out of 8 completed the study; only one of these 3 patients improved at the end of the survey, whereas the clinical score of the 2 others went back to the pre-treatment value.

No changes in serum IgE levels were noted in any patients treated for up to 8 weeks with IFN-α (Fig. 2).

Except for patient 3, no significant adverse reactions were noted during treatment. Although the treatment consisted of low or intermediate doses of IFN, all the patients had a flu-like syndrome associated with the treatment.

Laboratory tests revealed no significant abnormalities during the treatment apart from one patient with a mild and reversible decrease in white blood cells.

DISCUSSION

The rationale of the use of IFN in AD was mainly based on experimental data: 1) indirect evidence suggests that hyper-IgE production to environmental allergens plays a role in the pathogenesis of the disease (7, 8); 2) recent data have shown that IL-4 is the main cytokine involved in IgE production (9, 10), and interestingly T cells from patients with AD produce excessive amounts of IL-4 (11, 12); 3) IFN-α, like IFN-γ and PGE2, inhibits IL4-induced IgE production by normal human lymphocytes (4) and, more importantly, both forms of IFN also inhibit the spontaneous in vitro IgE production of mononuclear cells from atopic patients (13). Thus, experimental data have suggested that the hyper-IgE production in AD could be secondary to a hyperproduction of IL-4 by T cells and that this imbalance could be corrected by IFN. Consequently, the clinical status of the patients with AD should be improved.

From a clinical point of view, the present study demonstrates that recombinant IFN-α is not efficient in AD. Only one out of the 8 patients showed an improvement in the clinical condition after 2 months, whereas 3 patients worsened

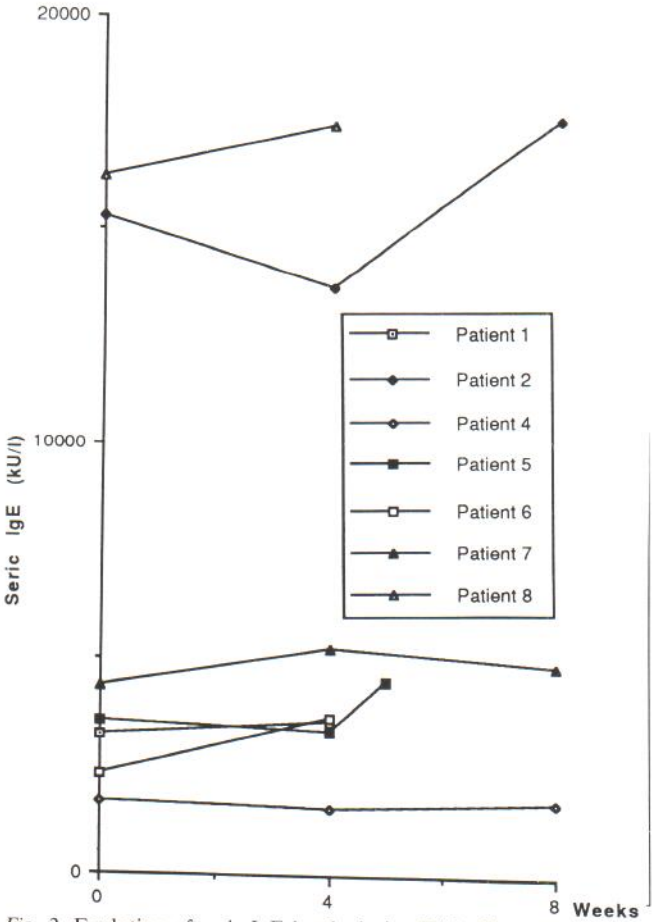

Fig. 2. Evolution of seric IgE levels during IFN-α2b treatment. Results are expressed as kUnits of IgE/l.

and the remaining 4 were not affected by IFN. Our results do not confirm the previous results of Souillet et al. (5), who obtained a reduction in the eczema of a patient with the hyper-IgE syndrome using low doses of IFN-α for 4 weeks. Alternatively, we obtained results similar to MacKie (14) who showed an absence of clinical efficacy of IFN-α given for 3 months in 2 patients with AD.

Since IFN-α was shown to down-regulate IgE production, we monitored in the present trial seric IgE levels during IFN treatment. We did not observe any decrease in IgE levels in the 7 patients under IFN therapy for at least 4 weeks. Our results, together with those of MacKie and Boguniewicz et al. using IFN-α and IFN-γ respectively (14, 15), suggest that down-regulation of IgE production in vivo in AD patients could not be obtained by intermediate doses of IFN, whereas it is possible in vitro.

Taken together, our results and previously published studies show that IFN-α is not useful in the treatment of AD, although it is still possible that higher doses or longer treatment might be beneficial to patients. Further studies will address these questions.

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