Short-Course Human Leukocyte Interferon in Treatment of Herpes Zoster in Patients with Cancer

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Because of encouraging results when human leukocyte interferon was given for 5 to 7 days to treat early localized herpes zoster in patients with cancer, a small placebo-controlled, randomized, double-blind trial was set up involving only 48 h of therapy. In this trial, there was no effect on acute pain or disease progression in the primary dermatome. However, a modest but significant effect was noted in that distal cutaneous spread was diminished in the treated patients compared with the controls and the treated patients had diminished severity and duration of postherpetic neuralgia. No evidence of impairment in varicella-zoster–specific lymphocyte transformation was observed in interferon-treated patients.

Herpes zoster infection is a common complication of the treatment of malignancy. As shown in our previous placebo-controlled, randomized, double-blind study, human leukocyte interferon effectively limited the progression of herpes zoster within the primary dermatome and prevented cutaneous and visceral dissemination when given to cancer patients early in the course of the infection (5). Interferon was given to these patients daily for 5 to 7 days. Because interferon is presently in short supply, the present study was designed to determine whether treatment with interferon for 2 days during the early phase of infection was adequate to control local disease and dissemination.

Patients with malignancy who could be enrolled in the study within 72 h after the appearance of localized disease were eligible. The diagnosis was made by a direct fluorescent-antibody stain of a lesion scraping. The majority of patients had lymphoma, and the pretreatment disease characteristics were equivalent in the placebo and the interferon recipients. Fifteen patients were randomly assigned to the placebo group, and 17 were assigned to the interferon group. Patient monitoring for disease progression was done as described previously (5).

Human leukocyte interferon for this study had a specific activity of $10^6$ U/mg and was prepared by Kari Cantell (2). The interferon recipients were given $2.55 \times 10^5$ U/kg intramuscularly every 12 h for a total of four doses. The placebo consisted of 0.05% human serum albumin in normal saline.

The in vitro lymphocyte transformation responses to inactivated varicella-zoster virus antigen in 7 patients who had received interferon for 5 to 7 days and 4 patients treated for 2 days were compared with the responses of 10 placebo recipients (Table 3). Patients were tested at less than 1 week after the onset and during convalescence 2 to 4 weeks later by the transformation assay as previously described (1). Serum interferon levels were measured by an assay of reduction in vesicular stomatitis virus plaque formation (5). Placebo recipients had no detectable serum interferon.

The interferon and placebo groups were comparable in having an average of 2 days of disease before treatment was initiated (Table 1). Interferon recipients did not have diminished progression in the primary dermatome. In addition, there was a tendency for progression to continue for more days in the interferon recipients compared with the placebo group. However, significantly fewer interferon recipients had distal cutaneous spread (5.8%) (Table 2). The incidence of cutaneous dissemination in the placebo group in this study was 33%, which is comparable to its occurrence in our previous experience (5).

The mean peak daily serum interferon level in the interferon group was 452 ± 62 U/ml,

| Table 1. Primary dermatome progression in herpes zoster treated with interferon or placebo |
|-----------------------------------------------|---|---|---|
| Group | Mean days before treatment (±SE)* | % of primary dermatome involved | Day of continued progression in primary dermatome |
| Placebo | 1.9 ± 0.3 | 24 | 43 | 2.9 |
| Interferon | 2.1 ± 0.3 | 19 | 37 | (NS)* |

* SE, Standard error.

NS, Not significant.
which is also in keeping with our previous results (5).

No significant visceral complications were reported in either the treated or placebo groups. Pain evaluated during the immediate treatment period while disease was active in the primary dermatome was not diminished in the interferon recipients compared with placebo recipients. The number of days of pain per total days of patient observation was 74 of 96 days for the interferon group and 77 of 105 days for the placebo group. However, during the 6-month follow-up period, the interferon-treated patients had significant lessening of postherpetic neuralgia. Based on our follow-up of 13 interferon recipients and 12 placebo recipients, 5 interferon recipients and 8 placebo recipients experienced postherpetic neuralgia. The total patient-months with pain per total months of follow-up was 11 of 68 months for the interferon group and 27 of 68 months for the placebo group ($P < 0.005$, $\chi^2$ test).

Table 3 presents data on the development of varicella-zoster-specific lymphocyte transformation in interferon and placebo recipients. No significant differences between the two groups were detectable at less than 1 week and at 2 to 4 weeks after the onset of infection either by assessing mean transformation indices or by the percentage of patients with a greater than threefold response to the antigen.

In this randomized, double-blind, placebo-controlled trial, human leukocyte interferon given for 2 days produced only partial improvement in localized herpes zoster compared with our previous study in which patients received $5.1 \times 10^5$ U/kg for 5 to 7 days (5). Specifically, the shorter treatment course decreased distal cutaneous spread and postherpetic neuralgia. The effect on distal cutaneous spread seems most likely to be mediated through an effect on viremia. Viremia has been documented (3) in cancer patients during the first 3 days after onset of disease in the primary dermatome, the period in which interferon therapy was being given in this study. However, considering the large amount of virus present in the primary dermatome area, it is perhaps not surprising that local lesion formation continued with short-term interferon treatment. It is interesting that in the only treated patient who had dissemination, distal cutaneous spread occurred 7 days after disease started in the primary dermatome and 5 days after therapy was stopped. This course could result from the waning of a transient interferon effect due to the short-term nature of the therapy.

Our previous studies indicated no suppression in production of varicella-zoster complement-fixing antibody titers with high doses of interferon (5). The studies of cellular immunity were done to determine whether interferon diminished the specific lymphocyte transformation response which we have observed (1, 4, 6) with recovery from herpes zoster in compromised patients. Lymphocyte transformation developed as expected for immunosuppressed patients among the interferon recipients.

The results of the present study indicate that in addition to a high dosage, a significant duration of treatment with human leukocyte interferon is required to modify herpes zoster infections in patients with cancer.
We are indebted to Janet Kahl, Barbara Graves, and Pat Chen for technical assistance and to the staffs of the Division of Oncology (Department of Medicine), and the Division of Radiotherapy (Department of Radiology), Stanford University School of Medicine.

This work was supported by Public Health Service contract AI-42527 from the National Institute of Allergy and Infections Diseases.

LITERATURE CITED


