Treatment with Levasimole of Recurrent Herpes Genitalis

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A double-blind study was carried out to investigate the possibility of therapeutic effect of levasimole on recurrent genital herpes. One hundred and nine patients, including 53 females, entered the study, but only 75 completed. Levasimole, 50 mg three times daily for 3 days, was started at the first sign of recurrence. The study period consisted of 6 visits or 12 months, whichever came first. No statistical differences were observed between levasimole and placebo groups when comparing the duration of the lesion and the degree of pain, although less pain was observed among those on levasimole. The interval between attacks was increasingly prolonged in the levasimole-treated group, and reached a significant level at the sixth visit. However, analysis on the basis of mean cumulative number of days between attacks showed no significant differences throughout the study period. Because of occasional neutropenia and generalized urticaria, and because of the absence of clear-cut clinical improvement of statistical significance, levasimole was considered of limited benefit to patients with recurrent genital herpes infection.

Levasimole hydrochloride is a phenyl-thiazo-lidone with anthelmintic and antianergic properties. It may restore the function of phagocytes and T-lymphocytes in compromised hosts, but is without effect on cells from normal hosts. It does not seem to affect B-cells directly (1, 5, 9).

Recurrent herpes simplex infection involving the genital tract has become a common problem during recent years, especially among young adults. Since there is no cure for this condition, and since there is some evidence to indicate an association between the recurrence of herpes simplex and decreased cell-mediated immunity towards the herpes viral antigens (3, 6, 7), attempts have been made to study the effects of levasimole on recurrent herpes infection. Earlier reports indicated that levasimole administration was beneficial to herpes labialis. The frequency, duration, and intensity of attacks decreased in a majority of patients. Genital herpes responded less well to levasimole than herpes labialis (2, 4, 8). A double-blind study in patients with severe and intractable herpes genitalis failed to show an advantage of levasimole over placebo (S. M. Bierman, personal communication). In an open study, however, there was a good correlation between virus-specific immune responses and clinical improvement (4). The present communication describes the effect of levasimole on recurrent genital herpes in humans.

MATERIALS AND METHODS

A total of 109 patients, 53 female and 56 male, entered the study. The criteria for entering the study were more than six recurrences per year and positive virus culture. At the first sign of recurrence, patients received either levasimole, 50 mg three times daily for 3 days, or the same number of placebo tablets. The study period consisted of either 6 visits or 12 months, whichever came first. Each visit was dated within 3 days of a new recurrence, or at 2-month intervals when there was no recurrence.

Virus isolation was performed by inoculation of infected material directly into primary human amnion cell culture. The isolates were identified by the presence of specific cytopathic effects and positive direct immunofluorescent staining, using commercially available reagents. Complete blood counts were obtained before treatment and at every other visit thereafter. A diary was given to each patient at each visit for the recording of symptoms and signs on a daily basis.

RESULTS

Seventy-five patients completed the study; 35 received levasimole and 41, placebo. Most were under 25 years of age, with about an equal number of each sex in both groups. The mean total days of study period were 157.4 days in the placebo group, and 186.8 days in the drug-treated group.

Figure 1 shows the effect of levasimole on the duration of lesions. Starting from the pretreat-
ment visit and through six visits or recurrences, the data did not reveal any statistical differences between levamisole and placebo groups.

The effect of levamisole on pain is shown in Fig. 2. The numbers 1, 2, 3, and 4 represent the degree of pain: severe, moderate, slight, and none, respectively. There was a general tendency for pain to diminish following each attack, but the decrease ran parallel to both placebo and levamisole groups. Although less pain was seen with levamisole, the difference was not statistically significant.

The effect of levamisole on the frequency of recurrence is shown in Fig. 3. None of the differences between levamisole and placebo groups had reached a significant level with the exception of that observed during the last period ($P = 0.05$). However, further analysis based on the cumulative number of days between attacks failed to substantiate the significance (Fig. 4).

Side effects included dysgeusia, or change of taste, and hyperosmia, or abnormal sense of smell, which were observed in about a third of patients on levamisole. Occasional nausea was reported. Two patients had transient neutropenia of mild degree. Two others developed generalized urticarial lesions with edema of both hands, which required prednisone treatment.

**Fig. 1.** Effect of levamisole on duration of lesions.

**Fig. 2.** Effect of levamisole on pain. The numbers 1 through 4 represent decreasing pain from severe to none. Pl, Placebo; L, levamisole.
The rash appeared within 24 h after the first dose of levamisole during the third and fourth course of treatment.

**DISCUSSION**

In a double-blind study, the effects of interrupted administration of levamisole on recurrent herpes genitalis were evaluated in 75 patients, using the duration of the lesion, the degree of pain, and the length of interval between attacks as criteria for evaluation of clinical response. No statistical differences were observed between levamisole and placebo groups when the duration of lesion and the degree of pain were compared, although less pain was observed among those on levamisole. The interval between attacks was increasingly prolonged in the levamisole-treated groups, and reached a significant level at the sixth visit, as compared to that in the placebo group. However, analysis on the basis of mean cumulative number of days revealed no significant difference between the
groups throughout the study period. It is possible that this discrepancy was related to the variability of the disease and that the analysis based on the cumulative number of days was less reliable. More study may be needed to clarify this point.

Because of the absence of clear-cut statistically significant clinical improvement and the occurrence of occasional neutropenia and generalized urticaria, levamisole is considered of limited value in the treatment of recurrent genital herpes infection.

Because of frequent occurrence of changes in taste and smell, it is possible that some psychological effects might have been induced among the drug recipients.

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LITERATURE CITED


