Suppression of frequently recurring genital herpes: acyclovir v inosine pranobex

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SUMMARY The suppressive action of acyclovir and inosine pranobex was compared in a randomised double blind controlled trial in patients with frequently recurring genital herpes. Fourteen patients received acyclovir and 17 inosine pranobex. Treatment continued for 12 weeks. The time to the first recurrence was significantly longer and the frequency of recurrences significantly less in the recipients of acyclovir. No important side effects were noted. It is concluded that acyclovir is the treatment of choice to suppress often recurring genital herpes.

Frequently recurring genital herpes may cause profound emotional and sexual disturbances,1 2 and until recently little could be done to help. Suppressive treatment with two drugs, acyclovir and inosine pranobex, has, however, been reported to reduce the frequency of recurrences.3 10 Acyclovir is a specific antiviral compound with pronounced antitherpetic activity,11 12 and inosine pranobex is reported to have both antiviral and immune potentiating properties.13 14

The aim of this study was to compare the suppressive action of the two preparations in a randomised double blind trial in patients with frequently recurring genital herpes.

Patients and methods

We recruited men and women patients who had at least eight recurrences of genital herpes a year. Exclusion criteria were identical to those used in previous studies.3 4 In addition, patients who had not had a culture positive recurrence in the two months before the onset of treatment were excluded, as were those with a history of gout, hyperuricaemia, or severe atopic eczema. Informed consent was obtained from all the participants.

The treatment was randomised, double blind, and double dummy. Patients received either active acyclovir and dummy inosine pranobex or active inosine pranobex and dummy acyclovir. The dosage of acyclovir was 200 mg and of inosine pranobex 1 g, each four times a day. Treatment was for 12 weeks. Compliance was assessed by counting the number of tablets missed.

Patients attended every two weeks during the treatment period and once a month for six months after stopping treatment. Additional visits were made during any recurrence. We undertook liver function tests and full and differential blood counts and measured serum concentrations of uric acid, creatinine, urea, and electrolytes at entry and every four weeks during treatment. All information was recorded on a standardised recording schedule.

Statistical tests used included the $\chi^2$, Mann Whitney U, and a log rank test.

Results

PATIENT CHARACTERISTICS

The trial was initially designed to include 100 patients, but after only 32 had been treated some were obviously deriving no benefit from treatment whereas the condition of others had improved considerably. After careful assessment of our previous experience of using suppressive acyclovir,6 we considered it unethical to continue, and halted the trial prematurely.

One of the 32 patients was lost to follow up after two weeks, and was excluded from the analysis. Table 1
shows the demographic characteristics of the remaining 31 patients. No significant differences in age, sex, or the frequency, severity, or duration of previous recurrences were seen between patients receiving each treatment.

**RECURRENCES DURING TREATMENT**

All 17 recipients of inosine pranobex experienced recurrences during treatment, compared with five of the 14 (36%) recipients of acyclovir (p < 0.001), each of whom experienced their first recurrences within the first five days. The time to first recurrence was significantly shorter in the recipients of inosine pranobex (see figure; p < 0.0001).

Table 2 shows that the mean (SD) number of recurrences in 28 days of treatment was 0.16 (0.28) in patients receiving acyclovir compared with 1.22 (0.8) in those receiving inosine pranobex (p = 0.0001).

**RECURRENCES AFTER TREATMENT**

After stopping treatment the mean (SD) frequency of recurrences was similar in the two treatment groups: 1.03 (0.53)/28 days in those receiving acyclovir compared with 1.0 (0.9)/28 days in those receiving inosine pranobex (table 2).

**SAFETY AND COMPLIANCE**

No side effects were noted, and the mean number of missed tablets was similar in the two treatment groups.

**Discussion**

This trial showed that acyclovir is the drug of choice for suppressive treatment of patients with frequently recurring genital herpes. Patients treated with acyclovir showed a significant reduction in the frequency of recurrences, whereas those treated with inosine pranobex continued to have attacks without any apparent reduction. The results of this trial were similar to those of previous trials that compared suppressive acyclovir with placebo. In those studies patients treated with acyclovir showed a pronounced reduction in the frequency of recurrences, whereas those who received placebo did not.

The only recurrences in patients receiving acyclovir occurred within the first five days of treatment, which suggests that viral reactivation of the virus before the onset of treatment was responsible for these outbreaks. Early attacks can be prevented by giving a therapeutic course of acyclovir (200 mg five times a day for five days) before starting suppression.

A previous study showed that inosine pranobex was inferior to acyclovir for treating first attacks of genital herpes, and the study published here raises the question of whether inosine pranobex has any remaining role in treating genital herpes.

Acyclovir is therefore the drug of choice both for treating the first attack and for suppressing recurrences of genital herpes. Any new antivirals will have to be compared with it.

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References
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*Genitourin Med* 1989 65: 103-105
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