Short review

IS IT POSSIBLE TO PREVENT THE CLINICAL MANIFESTATIONS OF GENITAL HERPES SIMPLEX VIRUS INFECTIONS?

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SUMMARY

The paper reports about genital herpes simplex virus (HSV) infections, especially recurrences of genital herpes and their pharmacological management. Some clinical studies with acyclovir and its important results for the management of genital herpes are reviewed.

KEY WORDS

genital HSV infections, pharmacological management, prevention, suppression

INTRODUCTION

The incidence of genital herpes simplex virus (HSV) infection is increasing (1), particularly in industrial developed countries. It is caused in 70 to 95% by herpes simplex virus type 2 (HSV-2). It can also be caused by herpes simplex virus type 1 (HSV-1). Clinical manifestations of genital HSV infection are divided into initial and recurrent episodes, which can be asymptomatic or symptomatic. The virus stays in the host for the whole life.

PHARMACOLOGICAL MANAGEMENT OF GENITAL HSV INFECTIONS

The acyclic nucleoside analogue acyclovir with high affinity and selectivity for herpesviruses is a first-line therapy in the management of genital herpes (1). But it cannot eradicate the virus.

Recommended treatment for initial genital HSV infection is oral acyclovir 200 mg 5 times daily for 5 days and intravenous therapy for severe cases. A topical formulation is less effective. No preparation prevents the onset of recurrent episodes. Oral acyclovir is also recommended for recurrent genital herpes. Mild and rare episodes are treated episodically (episodic therapy). Patients with frequent (more than 6 attacks per year) and/or more severe recurrences and those who are very troubled by recurrences should be given continuous daily acyclovir (suppressive therapy) for several months to 1 year. After one year's therapy it is evaluated if suppressive therapy should be continued (Fig. 1).

Several studies have demonstrated that acyclovir significantly reduces the number of recurrent episodes of genital herpes compared with placebo (2, 3).

A study of 5 years of suppressive therapy with acyclovir found a progressive decrease in the frequency

Tab. 1. Mean annual recurrence rates (4).

Therapy group	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5
E_1S_4 (n=179)	120	12.5	1.6	1.2	1.0	0.8
S_5 (n=210)	12.9	1.7	1.3	1.0	0.9	0.8
P-value		0.0001	0.02	0.05	0.2	0.3

E_1S_4: episodic therapy year 1, suppressive therapy years 2 through 5.
S_5: suppressive therapy years 1 through 5.

of recurrences over the 5-year period of continuous acyclovir therapy (4). (Tab. 1).

A progressive decrease in the percentage of patients reporting recurrences was also seen with years on therapy. By the 5th year of the study, approximately 70% of patients reported a year free of genital herpes, and 20% of the patients had been recurrence-free for the entire study period (5). (Fig. 2).

Table 2. Effects of oral suppressive and intermittent acyclovir therapy and placebo on genital herpes recurrence (6)

Treatment group	Median time to first recurrence (days)
Placebo	23
Intermittent	28
Suppressive	250
P-value	0.001

A study of 156 patients with 6 or more recurrences of genital herpes a year compared the efficacy and safety of suppressive acyclovir therapy versus episodic treatment of recurrences. It was shown that daily suppressive acyclovir therapy significantly reduced the median recurrence rate, compared with episodic treatment (6). If a recurrence occurred during suppressive therapy, the duration of the attack was shorter than was observed with episodic therapy. Time to first recurrence in days was statistically significant longer (p 0,001) in the suppressive group than in patients on episodic therapy (28 days). (Tab. 2).

It was shown that the safety profile of acyclovir was similar whether treatment was used episodically or continuously. There was no loss of efficacy over time and no emergence of resistant virus.

Pregnancy

Recurrent episodes of genital herpes during pregnancy are not thought to be harmful to the fetus, but a recurrence or primary episode close to term does pose the risk of neonatal infection during delivery. In such a case a caesarian section is necessary. In this moment acyclovir is administered

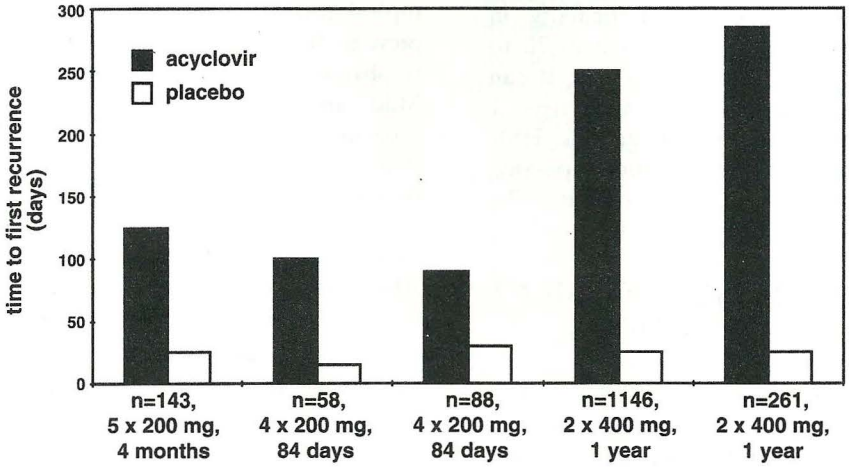
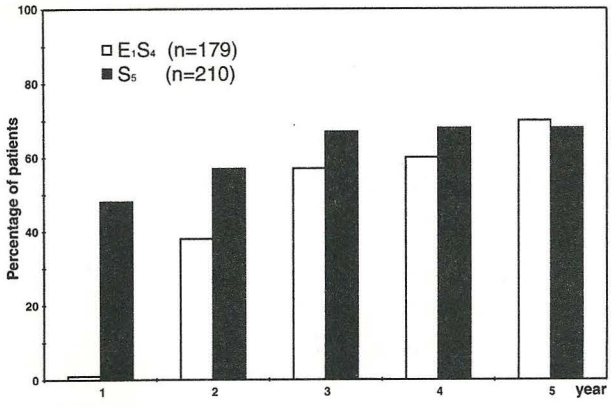


Figure 1. Controlled trials using suppressive acyclovir therapy in patients with frequently recurring genital herpes (2, 3)



E_1S_4: Episodic therapy year 1, suppressive therapy years 2 to 5, n=179.

S_5: Suppressive therapy years 1-5, n=210.

Figure 2. Annual percentage of patients recurrence-free (5)

during pregnancy only in life-threatening herpes diseases (7). It is currently under investigation for potential use in genital HSV infection in last weeks of pregnancy. Prepartal therapy with acyclovir should decrease the rate of caesarian section and prevent neonatal HSV infection during delivery.

Immunocompromised patients

Patients with immunological deficit resulting from human immunodeficiency virus (HIV) infection or immunosuppressive therapy for organ transplant recipients or malignancy are at particular risk of reactivation of HSV infection, also genital. Intravenous or oral acyclovir provides effective prophylaxis against HSV infection in immunocompromised patients (8,9).

CONCLUSIONS

After primary genital HSV infection the virus can not be removed from the organism. Clinical manifestations of genital herpes are treated according to the intensity of clinical manifestations of the disease.

The frequency of genital herpes recurrences can be significantly reduced by a suppressive therapy. Patients are treated with 800 mg acyclovir orally in 2 or 4 doses daily for up to 1 year. After one year's therapy it is evaluated if suppressive therapy should be continued.

Prepartal therapy with acyclovir should prevent neonatal HSV infection during delivery and decrease the rate of caesarian section.

On the whole, prophylaxis with acyclovir in immunocompromised persons is effective and reasonable.

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