

PROLONG CONTINUOUS VERSUS WEEKLY ORAL ACYCLOVIR IN RECURRENT HERPES GENITALIS

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Patients with frequent recurrences of genital herpes were treated with oral acyclovir tablet, 800 mg once daily or once a week for 2 years. Confirmed recurrences for all patients were treated with acyclovir, 200 mg orally 5 times per day, for five days. Of 58 patients enrolled, 12 of 26 daily acyclovir recipients and 22 of 32 weekly acyclovir recipients completed two years of study. Patients receiving daily acyclovir experienced a mean of 0.0991 recurrences / month compared with mean of 0.113 recurrences / month for patients receiving weekly acyclovir. A total of 33% of daily acyclovir recipients and 27% weekly acyclovir recipients were free of recurrences for two years.

Key Words : Acyclovir, Herpes genitalis

Introduction

Genital herpes is usually due to type 2 virus though HSV 1 can be isolated from genital lesions.¹ Genital herpes infection remains as a major public health problem, causing significant morbidity, particularly in sexually active young and adolescents.² In addition, genital herpes infection during pregnancy often results in serious infant morbidity and mortality.³ Clinical experiences over last several years have demonstrated that the acyclic guanosine derivative, acyclovir is effective in shortening the course of both first episode and recurrent genital herpes.⁴ In addition, recent studies have shown that continuous oral administration of acyclovir can suppress the occurrence of symptomatic recurrent disease.^{2,5-7}

Acyclovir is still costly drug and patients rarely afford daily regimen for long term suppression in our

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setting. This study was designed to evaluate the efficacy of both once-daily and once a week administration of a tablet of acyclovir, 800 mg for suppression of frequently recurring genital herpes infections.

Materials and Methods

Adult men and women with a history of six or more episodes of herpes genitalis within the preceding 12 months were eligible for enrollment. If herpetic lesions were present, patients were excluded or enrollment was deferred until the lesions had completely resolved. Informed consent was obtained from all patients and negative pregnancy test results were required for all female participants.

Eligible patients were randomly distributed into 2 treatment groups. They received either one tablet of acyclovir, 800 mg daily or once a week for two years. In the event of an outbreak of genital herpes, patients in either study group were treated with acyclovir, 200 mg five time a day for five days then resumed their originally designed

study medication. Patients were evaluated monthly throughout the study. A physical examination was performed and pertinent medical history was taken at each visit. The use of any concurrent medication was noted. Routine hematology tests (complete blood cell count with differential and platelet count) and clinical chemistry tests (for levels of blood urea, serum creatinine, alkaline phosphatase and total bilirubin), alanine aminotransferase assay and urinalysis were performed at entry and every three months thereafter. When a recurrence of herpes was suspected, patients were advised to return to the clinic for confirmation. The episode was recorded as either a prodrome, if no lesions were seen, or a physician observed recurrence. Monthly and quarterly (three months) recurrence rates were analysed.

Results

Out of a total of 58 patients enrolled in the study, 26 received acyclovir, 800 mg per day and 32 received acyclovir, 800 mg per week. The age, sex, mean number of episodes in 12 months preceding enrollment in each group is given in table-I. There were twenty-four drop outs from the study during the first two years. In the first year, 6 daily recipients and 7 weekly recipients were lost to follow up.

Table I. Demographics and disease characteristics

	Daily acyclovir	Weekly acyclovir
No. of patients	26	32
Men	18	25
Women	8	7
Age (Mcan)	27.5	26.2
Mean no. of episodes/one year	11.5	12.1
Mean no. of episodes/6 months	6.1	6.5
Mean no. of episodes/Month	1.0	1.1

The number of patients who were free of recurrences are shown in table - II. During the first quarter, 14 of 26 patients (53.8%) receiving acyclovir daily reported no recurrences. For the remainder of the study, the mean number of patients without recurrences increased

to 79.7% (range 76 to 83%). While 15 of 32 (43.1%) weekly acyclovir recipients had no recurrences in the first quarter and a mean of 68.4% (range 62 to 73 %) reported

Table II. Number of recurrence free patients

Quarter	Daily acyclovir	Weekly acyclovir
1	14/26 (53.8%)	15/32 (46.8%)
2	18/23 (78.2%)	18/29 (62.0%)
3	16/21 (76.1%)	20/28 (71.4%)
4	16/20 (80.1%)	16/25 (64.0%)
5	14/17 (82.3%)	17/25 (68.0%)
6	13/16 (81.2%)	15/22 (68.1%)
7	10/13 (77.0%)	16/22 (72.7%)
8	10/12 (83.3%)	16/22 (72.7%)
Year		
1	9/20 (45.0%)	10/25 (40.0%)
2	5/12 (41.6%)	8/22 (36.3%)
Cumulative	4/12 (33.3%)	6/22 (27.2%)

no recurrences in each of the remaining quarters.

Among recipients with daily acyclovir, 85% had fewer than six observed recurrences during the first year, whereas 75% of weekly acyclovir recipients had less than

Table III. Number of patients with recurrences

	Number of recurrences							Total	Rate
	0	1-2	3-4	5-6	7-8	9-10			
Entire first year									
Daily (n=20)	9	5	3	2	1	0	29	0.119	
Weekly (n=22)	10	5	1	4	3	2	73	0.24	
Entire second year									
Daily (n=12)	5	3	1	2	1	0	24	0.164	
Weekly (n=22)	8	6	4	2	1	1	41	0.152	
Completed both years									
Daily (n=12)	4	3	2	2	1	0	29	0.099	
Weekly (n=22)	6	6	4	3	2	1	61	0.113	

six recurrences. (Table III). The cumulative results show that 75% of daily acyclovir recipients had fewer than five recurrences in two years though 72 % weekly acyclovir recipients had less than 5 recurrences. Recurrence rates per 30 day period per patient were calculated. For two years, the mean number of physician observed recurrences per month was 0.0991 for daily acyclovir recipients and

0.113 for weekly acyclovir recipients.

Discussion

This study demonstrates that a weekly single tablet of acyclovir, 800 mg is as effective as daily single tablet of acyclovir, 800 mg in suppression of recurrent genital herpes, though daily acyclovir was marginally superior to weekly acyclovir as patients receiving acyclovir daily experienced recurrence rate (0.099/month) less than patients receiving weekly acyclovir (0.113/month). As reported in other trials,⁷ 17 of 20 (85 %) patients in first year and 19 of 22 (86.3 %) patients in second year with weekly acyclovir reported less than 6 recurrences. Nine of twenty (45 %) patients in first year and 5 of 12 (41.6%) patients in second year remained free from recurrences with daily acyclovir as compared to 10 of 25 (40 %) patients in first year and 8 of 22 (36.3%) patients in second year remained free of recurrences with weekly acyclovir.

The proportion of recurrences in quarter remains consistent from second through to the eighth quarters as observed in earlier studies⁷ indicating that the effects of acyclovir persist during prolonged treatment. The higher rate of break through episodes in the first quarter has been observed in other trials⁵ and suggests that there is a definite interval before the maximum effects are observed. Another investigation examined weekend multiple dose administration (400 mg three times per day on Saturday and Sunday) of oral acyclovir revealed numbers of recurrences in the weekend group were greater than in the daily treatment group⁸. This is in contrast to our experience, as we observed decrease in frequency of recurrences in both groups almost similar.

Acyclovir was well-tolerated throughout the two year period. No serious or unexpected adverse reactions were observed. No clinically significant changes in hematology or in hepatic or renal function occurred in

both groups.

The results of this study are similar to those of a multicentre trial where acyclovir, 800 mg was administered in divided doses in 1,175 patients with frequently recurring genital herpes⁵ and another study where acyclovir, 800 mg was administered in single dose in 46 patients.⁷

In conclusion, a single weekly dose of an acyclovir tablet 800 mg is as effective as once daily dose and it significantly reduced the number of recurrences of genital herpes. Each year, 35 to 45 % of patients remained free of recurrences. A single weekly dose is most cost effective and enhances compliance of patients with recurrent herpes genitalis.

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