Original Article

Effectiveness and safety of oral acyclovir 1 g twice a day for 3 days in the management of genital herpes

Kaushal K. Verma, Mahendra Sonune, Lalit Dar[1], Neetu Bhari, Banwari Lal Jangid
Departments of Dermatology and Venereology and [1]Microbiology, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence:
Prof. Kaushal K. Verma, Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, India.
E-mail: prokverma@hotmail.com

Abstract

Context: Acyclovir is the most commonly used drug in genital herpes; however, with existing acyclovir regimens, the drug needs to be taken five times a day which is inconvenient for patients. **Aims:** The aim of the study was to evaluate the efficacy and safety of oral acyclovir 1 g twice a day for 3 days in genital herpes. **Methods:** The patients of genital herpes were treated with oral acyclovir 1 g twice a day for 3 days and followed up after day 3, 5, 7, and 10 to determine the response to therapy. The response was assessed by physicians' assessment of percentage healing of the ulcer and mean healing time as well as patients' assessment of improvement in the Visual Analog Scale (VAS). **Results:** Twenty-three patients of genital herpes were recruited of which 21 (91.3%) had recurrent episodes, whereas 2 (8.7%) patients had first episode. One patient was lost to follow-up and 22 were analyzed. Complete healing of ulcer was seen in 9 (40.9%), 17 (77.27%) and 20 (90.90%) patients after day 3, 5 and 7 following the treatment respectively, with a mean healing time of 4.91 ± 2.16 days. The mean healing time of recurrent disease was 4.67 ± 1.87 days. Complete improvement in VAS was seen in 9 (40.9%), 21 (95.45%) and 22 (100%) patients after day 3, 5 and 7 following the treatment respectively, with a mean time for complete improvement being 4.27 ± 1.16 days. There were no significant side effects of therapy. **Conclusion:** Acyclovir 1 g twice a day for 3 days is an effective treatment for genital herpes with advantages of comparable healing time and convenient dosage schedule.

Key words: Acyclovir, dose, genital herpes, healing time

INTRODUCTION

Genital herpes is a common sexually transmitted infection caused by herpes simplex virus (HSV), predominantly HSV-2.[1-3] The rates of genital herpes among Sexually Transmitted Disease (STD) clinic attendees range from 4% to 27.9% in India.[4] It is a disease of public health importance due to its morbidity, frequency of recurrences, associated psychosocial distress, and rarely neonatal transmission.

Acyclovir, valacyclovir, and famciclovir are the common antiviral agents used in the treatment of genital herpes and have been found to be equally effective and superior compared to placebo.[5] The important factors in choosing a drug over others are the cost of therapy, convenience of administration, and dosing schedule. Acyclovir is the most commonly used drug in genital herpes; however, with existing acyclovir regimens, the drug needs to be given 3–5 times in a day for 7–10 days in the first episode and for 5 days in recurrent herpes infection.

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Five times a day intake of a drug may be particularly inconvenient for patients, and some of the doses may be missed. A convenient alternative regimen may be a higher dose which should help in the reduction of frequency of administration and a short course of therapy, based on the fact that viral replication is maximal within the first 24 h.[6]

We studied the efficacy and safety of oral acyclovir 1 g twice a day for 3 days in genital herpes as a cheaper and convenient regimen.

METHODS

This was an open-label pilot study. The patients above 16 years of age and either sex with clinically active genital herpes attending our outpatient department between May 2010 and May 2012 were recruited in the study. The study was approved by the institutional ethics board.

Patients with severe renal, hepatic or heart disease; pregnant and lactating women; known hypersensitivity to acyclovir; use of antiviral therapy within previous 14 days; immunosuppressed patients including transplant recipients; patients on immunosuppressive drugs; human immunodeficiency virus (HIV)-positive patients; and patients unwilling to consent were excluded from the study.

All patients were treated with oral acyclovir 1 g twice a day orally for 3 days. The patients were evaluated after day 3, 5, 7, and 10 by physician clinically and pre- and posttreatment photographs. The Visual Analog Scale (VAS) was also used to assess the response to treatment. VAS was measured by asking the patient, "how better you feel about your condition as compared to pretreatment status," which was composite of symptomatic improvement and patients' understanding of improvement in ulcer. The VAS was then correlated with physician assessment of healing of lesions.

Laboratory procedures

A complete clinical and laboratory evaluation including routine hematological, biochemistry, urine and stool routine/microscopy, Tzanck smear, Gram's smear, dark-ground illumination, VDRL test, enzyme-linked immune-assay for HIV, and HSV culture was done in each patient before starting the treatment. Serologic testing for HSV using complement fixation test and EUROIMMUN ELISA were done in 21 and 11 patients respectively. The routine investigations were repeated on completion of the treatment to determine any changes in these parameters. Data analysis was carried out using Stata 12.0 (College Station, Texas, USA). Data were presented as number (%) or mean ± standard deviation/median (min–max) as appropriate and $P < 0.05$ was considered statistically significant.

RESULTS

In this study, 44 patients of genital herpes were screened of which 21 patients were excluded as four patients were receiving antiviral therapy, the lesions were epithelizing in three while the diagnosis was doubtful in three and lesions were not active in six patients. Three patients had positive retrovirus status, whereas two patients were not willing for sampling. Thus, 23 patients were recruited in the study of which 21 (91.3%) patients had recurrent episodes and 2 (8.70%) had first episode. Twenty-two patients completed the study and one patient was lost to follow-up. The mean age was 28.95 ± 8.21 years (range: 18–55), with a male and female ratio of 10.5:1. The mean duration of the disease was 33.80 ± 50.56 months (range: 0.1–204). Mean number of sexual partners was 2.47±1.73 (range:1-6). Fifteen (65.2%) patients were married. The disease presented as multiple small erosions in 14 (60.9%) patients, vesicles in 7 (30.4%) and both vesicles and erosions in 2 (8.7%) patients. The most common symptoms were itching and burning sensation in 14 (60.9%) patients, followed by pain in 11 (47.8%) and dysuria in 4 (17.4%) patients. Regional lymphadenopathy was noted in 7 (30.4%) patients.

Routine laboratory investigations were within the normal limits in all the patients, whereas serology for HIV and syphilis were negative. Tzanck smear showed the presence of multinucleated giant cells in 10 (43.5%) patients, Gram's smear did not reveal any organism, and dark-ground illumination was negative in all the cases. The HSV culture was positive in

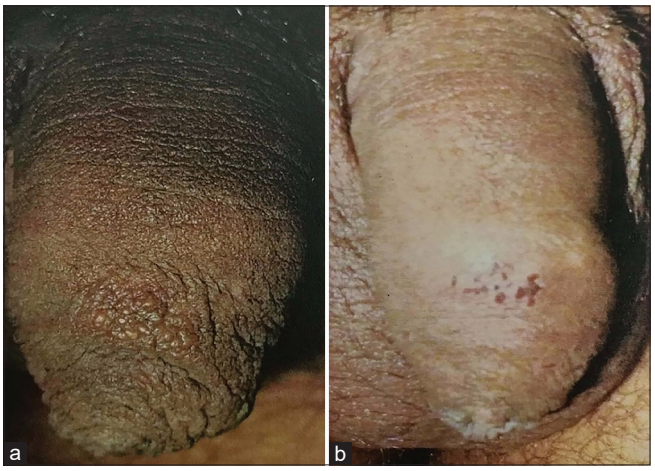

Figure 1: Grouped vesicles over the shaft of the penis before treatment (a) and near-complete resolution after treatment (b)

7 (30.4%) patients. HSV-1 was isolated from 1 (4.5%) patient, whereas HSV-2 was isolated from 6 (27.3%) patients. Complement fixation test was done in 21 patients and was positive in 15 (71.4%) patients. HSV-1 and HSV-2 IgM and IgG ELISA were done in 11 patients. HSV-1 IgM was not positive in any of the patients, whereas HSV-1 IgG was positive in 8 (71.7%) patients. HSV-2 IgM was positive in 2 (72.7%), whereas HSV-2 IgG was positive in 4 (36.4%) patients.

Complete healing of ulcer was seen in 9 (40.9%) patients after 3 days of treatment, with a mean percentage healing of 77.95 ± 26.03% [Figure 1]. However, at day 5 and day 7, complete healing was seen in 17 (77.27%) and 20 (90.90%) patients with a mean percentage healing of 90± 16.20% and 95±7.07%, respectively. Complete healing was seen in all 22 (100%) patients at day 10 with a mean percentage healing of 100±0.00%. The mean healing time of ulcers was 4.91 ± 2.16 days. The mean healing time of recurrent disease was 4.67 ± 1.87 days. Complete improvement in VAS was seen in 9 (40.9%) patients after 3 days of treatment, with a mean percentage improvement of 80.45% ± 25.30%. On day 5 and day 7, 21 (95.45%) and 22 (100%) patients showed a complete improvement in VAS, respectively. The mean time for complete improvement in VAS was 4.27 ± 1.16 days.

The therapy was tolerated well in all patients except some minor adverse effects like nausea, headache, altered taste sensation, diarrhea, and drowsiness in one patient each. There were no significant changes in laboratory parameters in any of the patients after the treatment.

DISCUSSION

Antiviral chemotherapy with acyclovir, famciclovir, and valacyclovir offers clinical benefit to majority of symptomatic patients and is the mainstay of management in genital herpes.[7-10] The drugs can be used for episodic as well as suppressive therapy.[8-10]

Of these, oral acyclovir is the most commonly used drug with an excellent safety profile and tolerance. In several placebo-controlled studies, oral acyclovir significantly shortened the median complete healing time of lesions[11,12] and median duration of viral shedding compared to placebo in patients with primary and/or nonprimary episodes[13-16] In several large double-blind multicenter studies, patient-initiated oral treatment with acyclovir 200 mg five times daily for 5 days has proven to be the most effective, with a statistically significant reduction in the duration of viral shedding and formation of new lesions during the treatment;[17] however, five times a day dose administration is inconvenient and cumbersome to patients which may result in missing of some of the doses. Although valacyclovir and famciclovir can be given at less frequent intervals, the cost of therapy with these agents is much higher compared to acyclovir and so are the adverse effects.

Therefore, we evaluated high dose and less frequently administered dose regimen of oral acyclovir 1 g twice a day for 3 days to determine its effectiveness and safety in genital herpes.

The earlier studies have compared different doses of acyclovir with placebo or with conventional acyclovir regimen. Goldberg *et al*, used oral acyclovir 800 mg twice a day for 5 days and found it as effective and safe as acyclovir 200 mg five times a day for 5 days in 157 recurrent genital herpes patients.[18] In another randomized, double-blind, placebo-controlled study, Wald *et al*, used 800 mg three times daily oral acyclovir for 2 days in 84 patients of recurrent genital herpes and found it to shorten the duration of episodes and viral shedding compared to placebo.[7]

In our study, the complete healing of ulcer was seen in 40.9% (9), 77.27% (17) and 90.90% (20) patients after 3,5 and 7 days following treatment, respectively. The mean healing time of ulcers was 4.91 ± 2.16 days, with a mean time for complete improvement of ulcers on VAS being 4.27 ± 1.16 days. In a placebo-controlled study by Goldberg *et al*, the mean healing time was 5.2 days in patients receiving acyclovir 800 mg twice daily for 5 days and 6.2 days in patients receiving acyclovir 200 mg five times daily for 5 days.[18] Wald *et al*, reported a median healing time of 4 days in patients receiving acyclovir 800 mg thrice daily for 2 days.[7] Similarly, Nilsen *et al*, had a mean healing time of 5 days in patients receiving acyclovir 200 mg five times daily for 5 days in recurrent genital herpes.[19] The mean healing time in our study is comparable to studies by Wald *et al*, Goldberg *et al* and Nilsen *et al*.[7,18,19]

CONCLUSION

Thus, our study has shown that this regimen of acyclovir is effective in genital herpes. There were no significant changes in laboratory parameters in any patient following treatment. Therefore, we

concluded that acyclovir in a dose of 1 g twice a day for 3 days is an effective, cheap, and safe treatment for genital herpes. Moreover, this 3-day regimen has the advantages of convenient dosage schedule and rapid healing of lesions which may reduce morbidity, psychological stress and risk of transmission of infection to a sexual partner. The small sample size is a limitation of our study, therefore, further randomized-controlled studies comparing its efficacy with standard dosage are needed to confirm our results.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Tran T, Druce JD, Catton MC, Kelly H, Birch CJ. Changing epidemiology of genital herpes simplex virus infection in Melbourne, Australia, between 1980 and 2003. Sex Transm Infect 2004;80:277-9.
2. Coyle PV, O'Neill HJ, Wyatt DE, McCaughey C, Quah S, McBride MO. Emergence of herpes simplex type 1 as the main cause of recurrent genital ulcerative disease in women in Northern Ireland. J Clin Virol 2003;27:22-9.
3. Samra Z, Scherf E, Dan M. Herpes simplex virus type 1 is the prevailing cause of genital herpes in the Tel Aviv area, Israel. Sex Transm Dis 2003;30:794-6.
4. Sharma VK, Khandpur S. Changing patterns of sexually transmitted infections in India. Natl Med J India 2004;17:310-9.
5. Fife KH. Are the antiherpes nucleosides really all the same? Sex Transm Dis 2006;33:534-5.
6. Wald A, Benedetti J, Davis G, Remington M, Winter C, Corey L. A randomized, double-blind, comparative trial comparing high- and standard-dose oral acyclovir for first-episode genital herpes infections. Antimicrob Agents Chemother 1994;38:174-6.
7. Wald A, Carrell D, Remington M, Kexel E, Zeh J, Corey L. Two-day regimen of acyclovir for treatment of recurrent genital herpes simplex virus type 2 infection. Clin Infect Dis 2002;34:944-8.
8. Sundharam JA. Herpes genitalis. In: Sharma VK, editor. Sexually Transmitted Diseases and AIDS. 1st ed. New Delhi: Viva Books Pvt. Ltd.; 2003. p. 259-72.
9. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. MMWR 2006:55:194.
10. Gupta R, Wald A. Genital herpes: Antiviral therapy for symptom relief and prevention of transmission. Expert Opin Pharmacother 2006;7:665-75.
11. Corey L, Fife KH, Benedetti JK, Winter CA, Fahnlander A, Connor JD, *et al*. Intravenous acyclovir for the treatment of primary genital herpes. Ann Intern Med 1983;98:914-21.
12. Mertz GJ, Critchlow CW, Benedetti J, Reichman RC, Dolin R, Connor J, *et al*. Double-blind placebo-controlled trial of oral acyclovir in first-episode genital herpes simplex virus infection. JAMA 1984;252:1147-51.
13. Corey L, Benedetti J, Critchlow C, Mertz G, Douglas J, Fife K, *et al*. Treatment of primary first-episode genital herpes simplex virus infections with acyclovir: Results of topical, intravenous and oral therapy. J Antimicrob Chemother 1983;12 Suppl B: 79-88.
14. Fiddian AP, Kinghorn CR. Topical acyclovir in the treatment of genital herpes: A comparision with systemic therapy. J Antimicrob Chemother 1983;12:67-77.
15. Kinghorn GR, Turner EB. Efficacy of topical acyclovir cream in first and recurrent episode of genital herpes. Antiviral Res 1983;3:291-301.
16. Bryson YJ, Dillon M, Lovett M, Acuna G, Taylor S, Cherry JD, *et al*. Treatment of first episodes of genital herpes simplex virus infection with oral acyclovir. A randomized double-blind controlled trial in normal subjects. N Engl J Med 1983;308:916-21.
17. O'Brien JJ, Campoli-Richards DM. Acyclovir. An updated review of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. Drugs 1989;37:233-309.
18. Goldberg LH, Kaufman R, Conant MA, Sperber J, Allen ML, Illeman M, *et al*. Oral acyclovir for episodic treatment of recurrent genital herpes. Efficacy and safety. J Am Acad Dermatol 1986;15:256-64.
19. Nilsen AE, Aasen T, Halsos AM, Kinge BR, Tjøtta EA, Wikström K, *et al*. Efficacy of oral acyclovir in the treatment of initial and recurrent genital herpes. Lancet 1982;2:571-3.