Objectives

Genital herpes is one of the most common sexually transmitted diseases, affecting millions of people worldwide [1]. It results from infection with the herpes simplex virus HSV-1 or HSV-2 [2]. HSV-2 antibody prevalence in the general population of developed countries is 15–25% [3]. 20-50% of patients with HSV-2 have recurrent flares [4]. Recurrent genital herpes (GH) is associated with major medical and psychosocial morbidities [5,6].

Previous research has shown that the antiviral, famciclovir, is effective in reducing the severity and duration of episodic outbreaks of RGH [8]. Early studies of antiviral therapy for herpes simplex suggested that treatment should begin as soon as possible after the patient was aware of an outbreak, to maximise efficacy [9]. This has influenced information given to patients. However, little research has been conducted into the relation between promptness of antiviral therapy after first noticing symptoms and subsequent outbreak severity and healing time.

Methods

Analyses were conducted on data derived from a double-blind, randomised, active-controlled study of patient-initiated therapy comparing a 2-day regimen of famciclovir with a 5-day regimen (total dose 1,250 mg in both arms) in adults with recurrent genital herpes [10].

Patients were provided with the study medication and instructed to take the first dose as soon as possible after the next appearance of a genital herpes lesion or onset of typical prodromal symptoms heralding the likely development of an outbreak.

Patients were asked to complete a diary to document the time at which they first noticed a lesion or prodromal symptoms and the time at which they took their medication.

Patients completed the HSC on each of the five day study period. The HSC is a 13-item measure of herpes symptoms (tingling, burning, pain, itching, tiredness, etc) and is used to rate the presence and severity of symptoms on the day of completion. Total scores range from 0 to 39 with high scores indicating greater symptomatic impact.

Tests were conducted to assess whether there were differences in HSC scores for patients who took their medication within 12 hours or after 12 hours of first perceiving their symptoms (Mann-Whitney U-tests).

The proportion of patients healed (without lesions as assessed by a clinician) at day 5 was determined. Healing at day 5 was assessed in relation to the time of taking the medication (within 12 hours or after 12 hours of noticing symptoms (Chi² test)). The odds ratio was calculated to determine the effect size (proportion of patients healed) if medication consumed within 12 hours of noticing symptoms divided by the proportion of patients healed if medication was consumed after 12 hours.

Results

Of the 501 available patients 6 were removed due to incomplete data. Patient demographic information is shown in Table 1 and their disease information in Table 2.

Table 1: Demographic information

<table>
<thead>
<tr>
<th>Year</th>
<th>Mean (SD)</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age</td>
<td>39.2 (11.6)</td>
<td>18 – 79</td>
</tr>
</tbody>
</table>

Table 2: Disease information

<table>
<thead>
<tr>
<th>Duration (Years)</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>7.8 (8.3)</td>
<td>0 – 39.5</td>
</tr>
</tbody>
</table>

Figure 1 shows HSC scores for patients over the five day study period categorised by whether patients administered their medication within 12 hours or after 12 hours of noticing symptoms of a genital herpes outbreak. For the combined 2 and 5-day famciclovir treatment groups, patients who administered their medication within 12 hours had lower HSC scores on day 1 (within 12 hours, median HSC=6; after 12 hours, median HSC=8; Mann-Whitney U=12,733.5, p<0.05).

Patients who administered their medication within 12 hours also had lower HSV area under the curve for the five day study period (AUC, within 12 hours, median HSC=3.8; after 12 hours, median HSC=5.1, Mann-Whitney U=12,751.0, p<0.05).

Significant differences were not apparent for the treatment groups separately.

Conclusions

Administration of famciclovir within 12 hours of first becoming aware of the symptoms of a genital herpes outbreak is associated with reduced outbreak severity and quicker healing.

The 2-day treatment regimen, when administered within 12 hours, is associated with a significantly higher rate of healing by day 5 than the 5-day course of treatment.

Clinical Implications

Patients receiving famciclovir for the treatment of RGH should take their medication as soon as possible after first noticing symptoms to maximise efficacy [9]. This has influenced information given to patients. However, little research has been conducted into the relation between promptness of antiviral therapy after first noticing symptoms and subsequent outbreak severity and healing time.

Figure 2 shows the proportion of patients (for the combined 2 and 5 day famciclovir treatment group) who were healed at day 5 dependent on whether patients took their medication within 12 hours or after 12 hours of noticing genital herpes symptoms. Figure 3 shows the same data for the 2-day treatment group only.

There was a statistically significant association between the time at which patients took their medication and healing at day 5 for the combined 2 and 5-day regimen group (Chi-square=4.95, p<0.05). Participants were 1.7 times more likely to be healed if they administered their medication within 12 hours.

This finding was also observed for the 2-day treatment group (Chi-square=6.3, p<0.05) but not for the 5-day regimen group (Chi-square=0.49, p=0.48). For the 2-day treatment group participants were 2.5 times more likely to be healed if they administered their medication within 12 hours.

References

1. Moss EJ. Epidemiology of genital herpes simplex virus infection in developed countries. Herpes 2004;11(suppl):1S-9S. 2. Meld A, Zeh J, Selke S, et al. Virologic characteristics of subclinical and symptomatic genital herpes infections. N Engl J Med 2005;352:275-85. 3. Whitley RJ, Roizman B. Herpes simplex virus infections. Lancet 2001; 357:1513–1518. 4. Recurrent genital herpes (RGH) is associated with major medical and psychosocial morbidities [5,6]. 5. Early studies of antiviral therapy for herpes simplex suggested that treatment should begin as soon as possible after the patient was aware of an outbreak, to maximise efficacy [9]. 6. The proportion of patients healed (without lesions as assessed by a clinician) at day 5 was determined. Healing at day 5 was assessed in relation to the time of taking the medication (within 12 hours or after 12 hours of noticing symptoms (Chi² test)). 7. The 2-day treatment regimen, when administered within 12 hours, is associated with a significantly higher rate of healing by day 5 than the 5-day course of treatment.

Clinical Implications

Patients receiving famciclovir for the treatment of RGH should take their medication as soon as possible after first noticing symptoms to maximise efficacy [9]. This has influenced information given to patients. However, little research has been conducted into the relation between promptness of antiviral therapy after first noticing symptoms and subsequent outbreak severity and improved healing.