Single-Dose Tioconazole Compared with 3-Day Clotrimazole Treatment in Vulvovaginal Candidiasis

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A total of 80 patients were equally randomized to receive a single dose of 6.5% tioconazole ointment or a 3-day course of 100-mg clotrimazole vaginal tablets for the treatment of vulvovaginal candidiasis. Of the 32 evaluable patients treated with tioconazole, 27 (84%) remained asymptomatic 4 weeks posttreatment, compared with 28 of 33 patients (85%) treated with clotrimazole. A total of 34 patients in each group could be evaluated for mycological response based on culture results 1 and 4 weeks after treatment. Twenty patients (59%) who received tioconazole and twenty-one patients (62%) who received clotrimazole remained culture negative 4 weeks after therapy. Of 40 patients who received tioconazole, 12 (30%) experienced local irritation or itching, compared with 2 of 40 patients (5%) treated with clotrimazole (P < 0.01). Single-dose tioconazole ointment was as effective as a 3-day course of clotrimazole tablets, but significantly more patients in the tioconazole-treated group experienced local side effects.

The duration of treatment for Candida vaginitis has changed dramatically over the past several years. New high-dose imidazole derivatives have produced excellent short-term cure rates with treatment durations as short as 1 to 3 days (1, 3, 4, 13, 16, 21). In addition, 4-week follow-up cultures of patients undergoing short-term treatment have not shown a higher incidence of recolonization by Candida organisms compared with cultures from patients undergoing longer periods of treatment (3, 13, 16, 20, 21). Shorter courses of therapy also encourage compliance and decrease expense and inconvenience (1, 3, 12, 16).

Tioconazole is a new imidazole antifungal agent similar to miconazole and clotrimazole. It has a broad spectrum of activity and is more active than other imidazoles against Candida albicans in vitro (10, 11, 18). In a randomized study of 109 women with vaginal candidiasis, a 3-day course of treatment with 2% tioconazole vaginal cream produced higher cure rates 7 to 10 days (P = 0.01) and 4 weeks (P < 0.05) after therapy than did clotrimazole vaginal tablets (6).

Houang and Lawrence reported a mean vaginal concentration of 21.4 μg/ml 24 h after insertion of a single 300-mg ovule of tioconazole in 10 patients with vaginal candidiasis (8). This concentration is significantly higher than the MIC (1.6 to 12.5 μg/ml) of tioconazole for C. albicans (10). These studies suggest that a single application of the agent could be clinically effective in the treatment of Candida vaginitis.

The study reported here was designed to compare the efficacy and acceptability of a single intravaginal application of 6.5% tioconazole ointment (325 mg) with a 3-day regimen of clotrimazole vaginal tablets in women with vulvovaginal candidiasis.

(The study was presented in part at the 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Las Vegas, Nev., 24 to 26 October 1984.)

MATERIALS AND METHODS

Nonpregnant women, aged 18 to 65, with clinical signs and symptoms of vulvovaginal candidiasis (pruritis, burning, discharge) and pseudohyphae present on microscopic examination of a KOH smear were considered for the study. Women who were menstruating, known to have diabetes, receiving corticosteroids, sensitive to imidazole drugs, or who had a concurrent bacterial, viral, or trichomonal vaginal infection were excluded.

Before admission to the study, written informed consent was obtained from each patient. A medical history was taken, and a physical and gynecological examination, including a Papanicolaou smear cytology, were performed at the initial visit. Two high vaginal swabs were obtained and cultured on sheep blood, chocolate, MacConkey, Thayer-Martin, and Candida-Mycobacterium bovis BCG agar. Plates were incubated at 37°C and read at 18 to 24 and at 48 h. A diagnosis of vulvovaginal candidiasis was confirmed by the presence of Candida sp. on blood and Candida-BCG agar. The germ tube test was used for presumptive identification of C. albicans. Blood chemistry studies, a complete blood count, and urinalysis were also performed on all patients.

Patients were equally randomized by a predetermined numerical code to receive either a single 5-g. application of 6.5% tioconazole ointment (325 mg) (Pfizer Inc., New York, N.Y.) at bedtime or two 100-mg intravaginal tablets of clotrimazole for three consecutive nights. Each patient was instructed not to use any other type of vaginal medication, including vaginal contraceptives and douches, during the entire study period. Patients were supplied condoms and were advised to have their partners use them during sexual intercourse.

Patients were re-examined at 1 and 4 weeks after completion of treatment. Clinical signs and symptoms were assessed and diagnostic smears and cultures were taken for yeast. In addition, at the 1-week follow-up visit, patients were asked about drug-related side effects, and blood and urine laboratory tests were repeated. The results of the two treatment groups were statistically compared by using Fisher’s exact test.

RESULTS

The 80 patients were randomly divided into the two treatment groups. Because of a negative initial culture or lack of follow-up, four patients treated with tioconazole and
TABLE 1. Profile of patients in two treatment groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tioconazole</th>
<th>Clotrimazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients enrolled</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>No. initially culture positive for Candida sp.</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>Mean age in yr (range)</td>
<td>23 (18–39)</td>
<td>23 (18–46)</td>
</tr>
<tr>
<td>Mean duration (days) of symptoms (range)</td>
<td>12.5 (1–60)</td>
<td>13.5 (1–90)</td>
</tr>
<tr>
<td>No. with previous yeast infection during past 12 mo</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>No. taking oral contraceptives</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>No. receiving antibiotics during previous mo</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Mean duration (days) of follow-up for all cures (range)</td>
<td>24.9 (7–33)</td>
<td>29.4 (9–46)</td>
</tr>
</tbody>
</table>

Table 2. Efficacy evaluation of two treatment groups

<table>
<thead>
<tr>
<th>Point of follow-up</th>
<th>Ratio (%) of asymptomatic response</th>
<th>Ratio (%) of negative mycological response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tioconazole</td>
<td>Clotrimazole</td>
</tr>
<tr>
<td>1 wk</td>
<td>34/36 (94)</td>
<td>37/38 (97)</td>
</tr>
<tr>
<td>4 wk</td>
<td>27/30 (90)</td>
<td>28/32 (88)</td>
</tr>
<tr>
<td>Overall</td>
<td>27/32 (84)</td>
<td>28/33 (85)</td>
</tr>
</tbody>
</table>

* Ratios represent number of patients showing no symptoms (or negative cultures) out of patients tested.

* Ratios based on follow-up examinations 1 and 4 weeks posttreatment.
has proved no more effective than local treatment in preventing recurrent infection (15). Single-dose treatment is an effective and safe method of treating acute symptomatic cases of vulvovaginal candidiasis (3, 16). Treatment that can be performed during the patient’s initial visit obviates the problem of compliance and helps reduce the cost of care. For patients with repeated recurrence of symptomatic Candida vaginitis, longer courses of therapy may be of benefit, either with miconazole (23), clotrimazole (12), or ketoconazole (22).

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LITERATURE CITED