Comparative Study of the Effectiveness of Oral Fluconazole and Intravaginal Clotrimazole in the Treatment of Vaginal Candidiasis

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ABSTRACT

Objective: A study was carried out to compare 3 treatment regimens for vaginal candidiasis.

Methods: A total of 150 women with clinical and mycological evidence of vaginal candidiasis were randomized to receive 50 mg of oral fluconazole daily for 6 days (50 women), a single oral 150 mg dose of fluconazole (50 women), or 100 mg of intravaginal clotrimazole daily for 6 days (50 women). They were assessed at 5-15 days (short-term assessment) and again at 30-60 days (long-term assessment) after the completion of treatment.

Results: Candida species were completely eradicated from the vagina in 88% or 80% in the 6-day oral fluconazole group, 76% or 70% in the single oral fluconazole group, and 72% or 60% in the intravaginal clotrimazole group at short-term or long-term assessment, respectively. The rates of clinical effectiveness were 92% or 88% in the 6-day oral fluconazole group, 80% or 76% in the single oral fluconazole group, and 72% or 58% in the intravaginal clotrimazole group at the short-term or long-term assessment, respectively. Treatment-related side effects were not found in any group.

Conclusions: This study suggests that the treatment of vaginal candidiasis with oral fluconazole is effective and that a single oral fluconazole dose might be one choice in the treatment of vaginal candidiasis.
MATERIALS AND METHODS

Study Design
An open, comparative study was conducted in the Department of Obstetrics and Gynecology, School of Medicine, Gifu University, Japan. Patients with vaginal candidiasis who agreed to participate in this study were enrolled.

Patients
A total of 150 women with clinical and mycological evidence of vaginal candidiasis were randomly allocated to receive treatment with 50 mg of oral fluconazole daily for 6 days (50 women), a single oral 150 mg dose of fluconazole (50 women), or 100 mg of intravaginal clotrimazole daily for 6 days (50 women). The clinical diagnosis was initially based on the presence of pseudohyphae (pseudo-mycelia) seen in the vaginal discharge with the light microscope and subsequently confirmed by culture on Sabouraud chloramphenicol medium (Nissui Pharmaceutical Co., Ltd., Japan). All patients were symptomatic with at least vaginal pruritus or burning. Patients with any clinically relevant associated disease were excluded, as were patients who were pregnant or lactating or known to have impaired hepatic or renal function. Women with venereal disease, chlamydial infection, trichomoniasis, or vaginitis other than candidiasis were also excluded.

Efficacy Assessment
The mycological examination of the vaginal discharge was performed with 2 vaginal swabs: one was inoculated in a transport medium for Trichomonas or bacteria, and the second was transported for fungal culture on Sabouraud chloramphenicol agar (Nissui Pharmaceutical Co., Ltd., Japan). All patients were symptomatic with at least vaginal pruritus or burning. Patients with any clinically relevant associated disease were excluded, as were patients who were pregnant or lactating or known to have impaired hepatic or renal function. Women with venereal disease, chlamydial infection, trichomoniasis, or vaginitis other than candidiasis were also excluded.

Safety Assessment
The side effects were recorded during treatment. Routine laboratory tests were carried out at the baseline and short-term assessments.
TABLE 1. Comparison of mycological effectiveness of oral fluconazole and intravaginal clotrimazole in the treatment of vaginal candidiasis

| Regimen                              | No. | 5th–15th day assessment | 30th–60th day assessment |
|--------------------------------------|-----|-------------------------|--------------------------|
| 50 mg of oral fluconazole daily for 6 days | 50  | 88                      | 80                       |
| Single oral 150 mg dose of fluconazole | 50  | 76                      | 70                       |
| 100 mg of intravaginal clotrimazole daily for 6 days | 50  | 72                      | 60                       |

RESULTS

Patients

The mean age of all patients was 32.5 years (range 18–54 years) and the mean body weight was 56.5 kg (range 41.0–77.5 kg). In the 6-day oral fluconazole group, the mean age of the patients was 30.4 years (range 20–48 years) and the mean body weight was 56.5 kg (range 41.0–71.0 kg). In the oral 150 mg fluconazole group, the mean age of the patients was 35.0 years (range 18–50 years) and the mean body weight was 56.4 kg (range 43.2–77.5 kg). In the group receiving 100 mg of intravaginal clotrimazole for 6 days, the mean age of the patients was 32.1 years (range 21–54 years) and the mean body weight was 56.6 kg (range 41.5–69.5 kg).

Efficacy

A comparison of the mycological effectiveness of oral fluconazole and intravaginal clotrimazole in the treatment of vaginal candidiasis is shown in Table 1. Candida species were completely eradicated from the vagina in 88% or 80% in the 6-day oral fluconazole group, 76% or 70% in the single oral fluconazole group, and 72% or 60% in the intravaginal clotrimazole group at the short-term or long-term assessment, respectively.

A comparison of the clinical effectiveness of oral fluconazole and intravaginal clotrimazole in the treatment of vaginal candidiasis is shown in Table 2. The rate of clinical effectiveness was obtained in 92% or 88% in the 6-day oral fluconazole group, 80% or 76% in the single oral fluconazole group, and 72% or 58% in the intravaginal clotrimazole group at the short-term or long-term assessment, respectively. A significant difference was not noted in the different therapies.

Safety

Neither adverse side effects to the drug nor abnormal laboratory values were noted during the treatment or observation periods.

DISCUSSION

The symptoms of vaginal candidiasis vary from irritation and discharge in a mild infection to perineal discomfort and dyspareunia in a severe infection. The long-term cure of vaginal candidiasis is clinically significant in view of its high recurrence rate and frequent relapses after conventional topical therapy. Topical treatment, although effective, is associated with poor compliance and premature discontinuation of the treatment.11 The relapses associated with vaginal fungal infections are also related to the difficulty of completely eradicating fungi from the vagina in certain physiological conditions. Moreover, a single negative culture of the vaginal lumen does not guarantee that the organisms have been totally eliminated. Since Candida species invade the tissues, systemic treatment with fluconazole could eliminate Candida from the vaginal tissues.

The rectum, an important reservoir of Candida species, may also be responsible for relapses. In a previous study on vaginal candidiasis, we detected C. albicans in 35% of women with first-episode candidiasis and 46% of women with recurrent candidiasis. Since intravaginally administered antifungal agents are minimally absorbed in the body and are unlikely to influence the rectal flora, the long-term effectiveness noted with oral fluconazole might reflect a concomitant reduction of rectal fungal flora.

In comparing the effectiveness of these 3 regimens of treatment, we found each regimen to be...
Table 2. Comparison of clinical effectiveness of oral fluconazole and intravaginal clotrimazole in the treatment of vaginal candidiasis

| Regimen                                      | No. | 5th–15th day assessment (%) | Statistical analysis | 30th–60th day assessment (%) | Statistical analysis |
|----------------------------------------------|-----|-----------------------------|----------------------|-----------------------------|----------------------|
| 50 mg of oral fluconazole daily for 6 days   | 50  | 92                          | N.S.*                | 88                          | N.S.                 |
| Single oral 150 mg dose of fluconazole       | 50  | 80                          | N.S.                 | 76                          | N.S.                 |
| 100 mg of intravaginal clotrimazole daily for 6 days | 50  | 72                          | N.S.                 | 58                          | N.S.                 |

*N.S. = not significant.

very effective in the treatment of vaginal candidiasis. A significant difference was not noted in the different therapies, which may be attributable to the small number of patients or poor statistical power of this study. However, oral fluconazole might be more effective in short-term and long-term assessments, as suggested in previous studies. At the same time, fluconazole, even as a single oral dose, is effective and reliable in the treatment of vaginal candidiasis. In addition, the symptoms of candidiasis are rapidly relieved by oral treatment.

In the United States, a comparison of drug treatment costs for vaginal candidiasis revealed that the single dose treatment with fluconazole (150 mg) is less expensive than intravaginal treatment with clotrimazole, miconazole, or terconazole. On the contrary, in Japan, the national health insurance (NHI) price of 150 mg of fluconazole is 2,882 yen, while a 6-day course of intravaginal clotrimazole, 100 mg daily, costs 477.6 yen. Nevertheless, cost reductions resulting from decreases in physician office visits and associated laboratory tests may result if recurrences and relapses can be reduced with fluconazole treatment.

The results of our study suggest that the treatment of vaginal candidiasis with oral fluconazole is effective and that a single oral fluconazole dose might be one choice in the treatment of vaginal candidiasis.

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