Clinical study

ITRACONAZOLE IN THE THERAPY OF CANDIDOSIS OF URO-GENITAL SYSTEM AND/OR ORAL CAVITY AND THROAT MUCOSA IN A DAILY DOSE OF 100 mg

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ABSTRACT

The results of a clinical study on the effectiveness and tolerability of itraconazole used in oral therapy of candidosis in a single dose of 100 mg daily were presented.

Investigations were performed in 3 groups: 20 persons with candidosis of the uro-genital system, 18 persons with candidosis of the oral cavity and throat mucosa, 10 persons with candidosis of the uro-genital system coexisting with candidosis of oral cavity and throat mucosa. All strains of yeast-like fungi isolated from patients were susceptible to itraconazole. The values of MIC were from 0,01 to 20,0 ug/ml. In three groups of patients results and duration of treatment were:1st group - 90%, from 4 to 8 days; 2nd group- 88,9%, from 4 days to 10 weeks; 3rd group - 90%, from 4 days to 12 weeks. Two weeks after the end of the therapy the recurrence of the disease was observed in 4 persons (8,3%). In 2 patients (4,2%), transient adverse reactions - nausea and stomach ache were observed. No changes in laboratory tests (Aspat, Alat, bilirubin) were noticed. It was concluded that itraconazole applied in a single dose of 100 mg daily is effective and safe.

In the authors' opinion therapy should be continued until negative results of clinical and mycological studies of all morbid yeast foci.

KEY WORDS

candidosis, uro-genital system, oral cavity, throat, mucosa, Itraconazole

INTRODUCTION

Fungi of the genus Candida are frequent causes of infections of the skin and mucous membranes. The most common of these organisms is C. albicans, but other species as C. tropicalis, C. guilliermondii, and C. parapsilosis, may also cause infection (1).

These organisms, especially C. albicans are common in the microflora of the mouth, throat, gastrointestinal tract, urethra and/or vagina, they appear as pathogen only under a variety of circumstances.

Candida infections of the skin and mucous membranes had been exclusively treated topically until a period of ten years ago. Indeed, only the availability of orally active ketoconazole made it possible in the early 1980s to start oral treatment for vaginal and oral candidosis (2). Recently, new oral therapy with itraconazole and fluconazole have

Table I. Candidosis of mucous membranes. Sites of involvement

SITE OF INFECTION	sex	total No.	vagina	urethra	vagina and urethra	penis
urogenital tract	M	3		1		2
	F	17	9	3	5	
			oral cavity	throat		
oral cavity, throat	M	6	6	-		
	F	12	12	-		
			vagina, oral cavity, throat	urethra, oral cavity, throat	vagina, urethra, oral cavity, throat	penis, oral cavity, throat
urogenital tract, oral cavity, throat	M	4				4
	F	6	3	1	2	

become available.

Itraconazole, a new oral triazole derivative, a third-generation, has a broad spectrum of antifungal activity. In vitro and in vivo it is active against yeasts, dermatophytes, Aspergillus species and dimorphic fungi (1,4). Extensive clinical testing has shown that highly lipophylic itraconazole has a favourable tissue/plasma level ratio (5). This affinity for tissue results in therapeutically beneficial effects. This antimycotic has been tested extensively for treatment of vaginal and oral candidosis and other mycoses (6,7,8,9).

MATERIALS AND METHODS

Forty-eight patients (13 males, 35 females) with candidosis of the uro-genital system and/or candidosis of the oral cavity and throat mucosa, divided in 3 groups were treated with a single daily dose of 100 mg; 1st - with candidosis of urogenital system; 2nd - with candidosis of oral cavity and throat mucosa; 3rd - with candidosis of the urogenital system coexisting with candidosis of the oral cavity and throat mucosa. Written consent was obtained from all patients before their enrollment in the study. Patients were included when microscopic examination was positive for mycelial elements, cultures were also made on Sabouraud's agar. When growth was observed, the colonies were reinoculated on Nickerson medium for further identification on the Api 20 C AUX test. Then, the activity of itraconazole against all isolated strains was determined by plate dilution method ranging from 0.02 to 55.0 ug/ml of classic Sabouraud agar medium after initial solution in 96% vol. ethanol. Media controls without solvent and with solvent at various concentrations were used. The inoculum was 10 ce11s per 1 ml saline. The minimal inhibitory concentration (MIC) was established after 72 hours.

Patients with serious concurrent diseases, treated with systemic and/or topical antifungal agents within 1 month, with mixed infections (e.g., Candida + Trichomonasis + Neisseria gonorrhoea + gonorrhoea vaginalis + Bacteria) and those who were pregnant or who were not using adequate birth control were excluded.

Table II. Activity "in vitro" of itraconazole against yeast-like fungi isolated from patients.

Species	Number of strains	*MIC ug/ml of medium
Candida albicans	45	0,01 - 20,0
Candida crusei	2	0,1
Torulopsis glabrata	1	0,1

**MIC - Minimal Inhibitory Concentration*

Table III. Efficacy of itraconazole used in oral therapy of candidosis of uro-genital system and/or oral cavity and throat mucosa in a single daily dose of 100 mg. Clinical and mycological investigation were evaluated.

	Results at the end of treatment		Results at a follow'up visit (2 weeks later)	
Site of infection	No. of patients cured	%	No. of patients cured	%
urogenital system	18/20	90	17/20	85
oral cavity	16/18	88,9	14/18	77,8
urogenital tract, oral cavity	9/10	90	8/10	80

Each patient was instructed to apply one capsule of 100 mg itraconazole once a day immediately after a meal. All patients were evaluated clinically before starting the treatment as well as 2 week after treatment. An additional evaluation was carried out in patients with candidosis of the urogenital system on days 2,4,6 and at weeks 1 to 12 in patients with candidosis of the oral cavity and throat mucosa. Symptoms and/or signs were scored as: absent - 0, mild - 1, moderate - 2, severe - 3. The microscopic examinations and cultures were made at the start of treatment, at each therapy visit and at follow-up visits.

We also noted predisposing and coexisting factors (sexual partners and members of the family) in patients with candidosis.

The biochemical parameters as bilirubin, aspartate aminotransferase and alanine aminotransferase were determined in 2-week periods in patients who were treated longer than 2 weeks. Adverse reactions and acceptability were recorded.

The Candida infection was considered cured clinically and microbiologically if the symptoms had disappeared and if no fungi were found by direct microscopy or culture.

RESULTS

All the 48 patients were included in the analysis of clinical and mycological efficacy and were evaluated for adverse reactions. The sites of involvement are shown in table I, the activity "in vitro" of itraconazole against yeast-like fungi in table II, efficacy of itraconazole therapy in table III, and duration of treatment with a single dose of 100 mg daily in table IV.

In 11 patients predisposing factors (oral contraceptive - 1, diabetes - 2, antibiotic therapy -7, steroid therapy - 1) and in 16 patients coexisting factors (sexual partner - 7, member of family - 9) were noted.

All of the strains isolated before treatment were "in vitro" sensitive to itraconazole.

Two weeks after the end of the therapy the recurrence of the disease was observed in 4 persons (8.3%). In 2 patients (4.2%) with candidosis of the oral cavity and throat mucosa transient adverse reactions - nausea and stomach ache - have been observed. No changes in laboratory tests (Aspat, Alat, bilirubine) were noticed.

DISCUSSION AND CONCLUSIONS

The results of this study demonstrate that itraconazole applied in a single dose of 100 mg daily is an effective and safe drug in short treatment of candidosis of the uro-genital system and also in longer therapy of candidosis of the oral cavity and throat mucosa.

Table IV. Duration of oral itraconazole treatment in candidosis of uro-genital system and/or oral cavity and throat mucosa in a single daily dose of 100 mg.

Site of infection	Time of treatment	Mean (days)
urogenital system	4 - 8 days	5,7
oral cavity	4 days - 10 weeks	23,75
urogenital system and oral cavity	4 days - 12 weeks	19,1

Generally, for non immunocompromized patients, the main treatment is topical (miconazole, clotrimazole, nystatin and amphotericin B). For more persistent candidosis and in patients with immunosuppression, it is necessary to use oral therapy (ketoconazole, fluconazole or itraconazole) because responses to topical agents are often poor. Itraconazole is usually effective in the treatment of acute vaginal candidosis at a total dose of 400 mg to 600 mg, given as 200 mg twice daily for 1 day or 200 mg daily for either 2 or 3 days; 200 mg for 3 days or 100 mg for 5 days reportedly give better results in chronic vaginal candidosis and oral candidosis in dose of 100 mg daily for 1 to 3 weeks.

In our patients with candidosis of the uro-genital system we also found minimal symptoms and/or signs and/or only positive results of mycological examination in oral cavity and throat. And vice versa. In patients with candidosis of the oral cavity and throat mucosa we found fungi in the uro-genital system. The authors suggest that treatment should be continued until the lesions are healed and mycological tests become negative.

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