

Single-dose fluconazole versus standard 2-week therapy for oropharyngeal candidiasis in HIV-infected patients: A randomized, double-blind, double-dummy trial

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Introduction



- Oropharyngeal candidiasis is the most common opportunistic infection in subjects infected with HIV
- In Tanzania, fluconazole, at a dose of 150 mg o.d for 2 weeks, is included in the guidelines for the treatment of OPC in HIV-infected patients
- Because of convenience, cost and reluctance to complicate antiretroviral treatment regimens, single-dose fluconazole may be a more favourable regimen for treatment of HIV-associated OPC than the recommended dose of 150 mg of fluconazole for 2 weeks



Aim

- The aim of our study was to determine whether a single dose of 750 mg of fluconazole was as effective as the standard 14-day course of fluconazole for the treatment of OPC in HIV-infected patients



Patients and Methods 1

- **Participants were recruited at the HIV clinic of the MNH from Nov 2006 through Dec 2007**
- **Eligibility criteria: ≥ 18 years of age, with documented HIV infection (positive ELISA); clinical symptoms of OPC; characteristic visual lesions; and microbiological confirmation**



Patients and Methods 2

- **Exclusion criteria:** previous antifungal therapy within 3 days; allergy to azoles; evidence of significant hepatic or renal disease; inability to tolerate oral drug administration; current pregnancy or breast feeding; current participation in another clinical trial; current treatment with drugs that are known to interact with fluconazole; documented systemic fungal infections; and symptoms suggestive of esophageal candidiasis



Study Design and Procedures

- A prospective randomized double-blind, double dummy trial was performed.

110 pts

Single dose FCZ (750 mg)

+

Placebo

110 pts

14 days of FCZ (150 mg)

+

Placebo

Endpoints: Efficacy (clinical and microbiological)
Safety



Study Design and Procedures 2

- **Visits: day 0 (baseline), day 3 or 4, day 6 or 7, day 14 (end of therapy), and day 42 or earlier (follow-up)**
- **Questionnaires were used, general and oral examinations were performed**
- **On days 3 or 4, 6 or 7 and 14, patients were examined and assessed for signs and symptoms, adverse drug effects, and compliance with the regimen**



Study Design and Procedures 3

- Blood samples were obtained on days 0 and 14 for hematology and biochemical tests
- Also on days 1, 4 or 5, 7, and 14, for determination of fluconazole plasma concentrations



Efficacy evaluations

Clinical responses were defined as:

- **Cured (complete resolution of lesions, signs, and symptoms of OPC)**
- **Improved (a reduction in the number of lesions and symptoms but persisting typical oropharyngeal lesion)**
- **Failed (no resolution of signs and symptoms; i.e., either no change or OPC that has progressed)**



Efficacy evaluations 2

Evaluation of results of mycological cultures on day 14:

- Mycological cured (no growth of *Candida* species)
- mycological failure (any growth of *Candida* species)



Safety evaluations

- Safety and tolerability were assessed by the observation of adverse events
- Baseline and post treatment blood investigations included biochemical tests and full blood count and were compared between the 2 regimens



Statistical Analysis

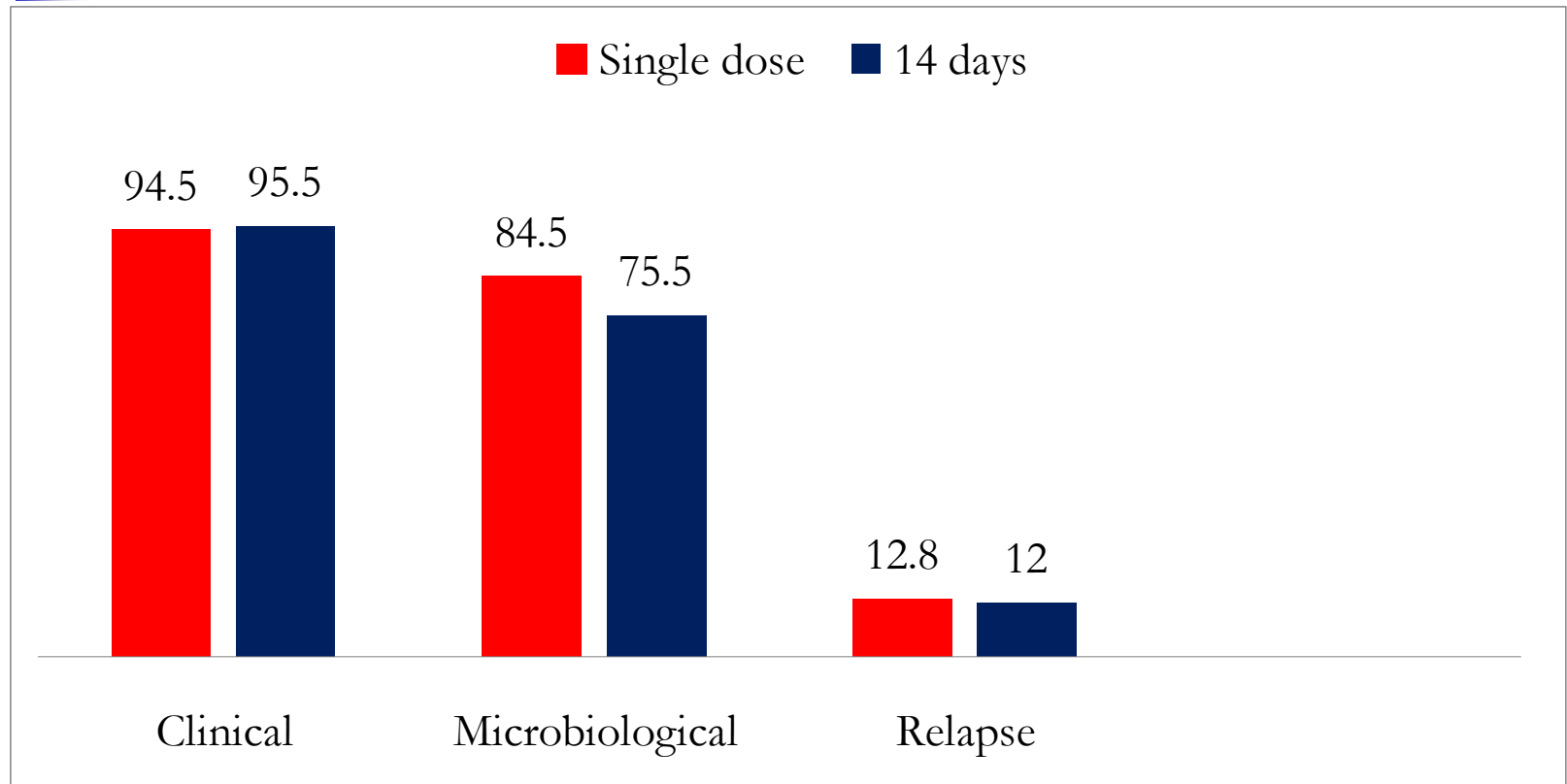
- This trial was designed to have 80% power to demonstrate equivalence (within 20%) in clinical response between the 2 regimens, and the 95% CI of the difference in response rates were used in determination of equivalence
- Comparisons between the 2 groups were performed either using Student's *t*-test, the Mann-Whitney *U* test or Fisher's exact test
- The results of posttreatment liver function test and full blood count were compared by analysis of covariance, with the pretreatment test result as a co-variate



Results

- The baseline clinical and demographic characteristics were similar in both treatment groups
- In the single-dose group, 104 patients (94.5%) were clinically cured, 2 (1.8%) had improved, and 4 (3.6%) experienced treatment failure
- In the 14-day group, 105 patients (95.5%) were clinically cured, 4 (3.6%) had improved clinically, and 1 (0.9%) experienced treatment failure

Results



The difference in clinical, mycological success between the 2 groups were not significant $p=0.99$ and $p=0.129$ respectively

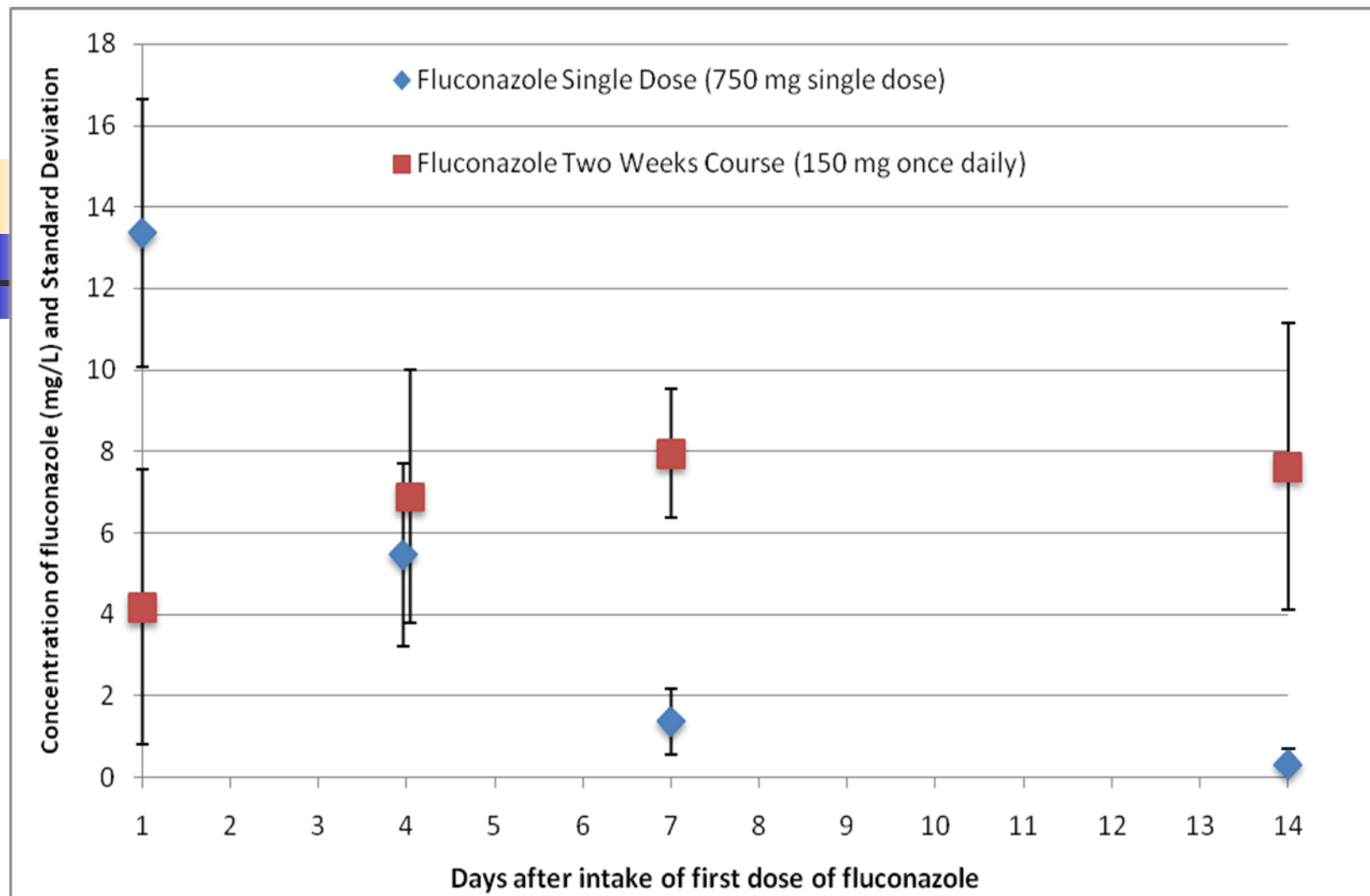


Figure 1: Plasma concentrations were significantly different on days 1, 7 and 14 ($P < 0.01$), but not on day 4 ($P = 0.23$). Fluconazole exposure was greater for patients who received the single dose of fluconazole, at least until day 4 or 5, compared with those who received the 14-day course.



Safety analysis

- Overall, adverse events were mild mostly being gastrointestinal, and no differences in frequency of adverse events were noted between patients in the 2 treatment regimens
- No clinically significant changes in FBC and liver function parameters were observed after treatment in either of the 2 groups



Discussion and conclusion

- The results of the present study demonstrate that a single-dose regimen of 750 mg was as effective as a standard 14-day fluconazole regimen in achieving clinical and mycological cure in the treatment of OPC in patients with HIV infection and AIDS
- The use of a single high dose of fluconazole presents the advantages of simplicity and convenience, thus improving compliance and reducing the cost of therapy



Discussion and conclusion 2

- Due to low cost single dose (750mg) fluconazole therapy could be used, especially in resource-limited settings like in sub-Saharan Africa
- Single dose therapy can be observed directly by medical personnel, thereby assuring patient compliance



Thank You
