IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 12 Ser.4 (December. 2022), PP 53-57
www.iosrjournals.org

Efficacy and Safety of Recommended High Dose Oral Fluconazole in the Treatment of Tinea Corporis

Ayesha Siddiqua[1], Mohammad Rahmat Ullah Siddique[2]
[1]*Delta Medical College and Hospital, Bangladesh.*
[2]*Department of Dermatology, Banghabandhu Sheikh Mujib Medical University, Bangladesh.*
Corresponding Author: *Dr. Ayesha Siddiqua, Delta Medical College and Hospital, Bangladesh*

Abstract
Background: *In Southeast Asian countries like Bangladesh, management of tinea is difficult where uses of several systemic antifungal agents are very common. Fluconazole is a well-known hydrophilic triazole which is available, cost effective and frequently used in treating several tinea infections in Bangladesh. For this reason, information regarding the efficacy and safety of recommended high dose oral fluconazole in treating tinea corporis is very important. We have not enough research-based data regarding this issue.*
Aim of the study: *The aim of this study was to evaluate the efficacy and safety of recommended high dose oral fluconazole in treating tinea corporis.*
Methods: *This prospective observational study was conducted at Delta Medical College and Hospital, Bangladesh during the period from January 2022 to June2022. In total 87 patients with tinea corporis were enrolled in this study as study subjects. Proper written consents were taken from all the participants before data collection. In the treatment procedure, all the patients were given oral fluconazole 300 mg once daily at night regardless of meal for 6 weeks. Along with treatment data, all demographic and clinical information of the participants were recorded. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23 program as per necessity.*
Results: *In this current study, at follow up stage, the Mean ± SD clinical score was found 1.14 ± 0.15 which was 2.06 ± 0.27 at baseline and this change was significant where the P value was <0.0001. Besides these, in final outcome assessment we observed that, among majority of the participants (62%), the signs and symptoms were totally absent at the end of the treatment tenure of 6 weeks and their grade was 'A'. Moreover, 23% patients got the grade 'B' who got >50% clinical improvement. In this study, as the remarkable side effects, nausea and headache were found which were in only 11% and 9% patients respectively. After 2 weeks of treatment, fluconazole SGPT was found mildly elevated in only 2% cases and after 4 weeks of treatments, it was found elevate but not more than 2-fold in only 4% cases.*
Conclusion: *As per the findings of this study, we can conclude that, as a recommended high dosage treatment schedule, oral fluconazole 300 mg once daily at night regardless of meal for 6 weeks is an effective and safe treatment option for the treatment of tinea corporis. Most of the patients of tinea corporis are comfortable with the convenient dosage schedule of this treatment regime.*
Keywords: *Dermatology, Efficacy, High dose, Oral fluconazole, Tinea corporis, Antifungal.*

Date of Submission: 02-12-2022 Date of Acceptance: 14-12-2022

I. Introduction

In Southeast Asian countries like Bangladesh, management of tinea is difficult where uses of several systemic antifungal agents are very common. Fluconazole which is a hydrophilic triazole, counts among the recently developed antifungal agents. Fluconazole is characterized by excellent bioavailability, favorable pharmacokinetic properties, low affinity for plasma proteins, long serum half-life and a large volume of distribution corresponding to the total body fluid [1]. In a study [2] it was reported that, fluconazole is eliminated from the stratum corneum 2 to 3 times more slowly than from plasma or serum. Besides the efficacy of fluconazole in treating tinea corporis, a number of studies have established the effectiveness and good toleration of fluconazole in treating oropharyngeal and mucosal mycosis [3, 4]. Specific measurements have exposed that, fluconazole levels attained in the stratum corneum of the skin are 45 times those remain in the serum. [5] That study also investigated whether 2 to 4 weeks of treatment at fluconazole 150 mg/week would also render good efficacy results in this indication [5]. In recent years, there has been a prompt increase in occurrences of dermatophytosis and unusual presentation [6]. Even, the suggested management of regularly prescribed antifungal treatment does not appear to be applicable in this current circumstance, resulting in treatment failures as well as relapses when administered in normal doses and for standard time [7].As a result, to overcome these problems, dermatophytosis

care is becoming increasingly subjective [8, 9].Moreover, various criteria such as hair follicles, concurrent involvement of a large body area, history of treatment failures, relapses and recurrences influence the choice of therapy. [10]

II. Methodology

This prospective observational study was conducted at Delta Medical College and Hospital, Bangladesh during the period from January 2022 to June 2022. In total 87 patients with tinea corporis were enrolled in this study as study subjects. Proper written consents were taken from all the participants before data collection. The whole intervention was conducted in accordance with the principles of human research specified in the Helsinki Declaration [11] and executed in compliance with currently applicable regulations and the provisions of the General Data Protection Regulation (GDPR) [12]. As per the inclusion criteria of this study, only culture positive tinea corporis patients of both genders and from several age groups, who were not responding to conventional antifungal therapy were included. On the other hand, according to the exclusion criteria of this study, cases with evidence of hepatic or renal disease, nursing mother, pregnant females and patients with hypersensitivity or intolerance to treatment were excluded. In the treatment procedure, all the patients were given oral fluconazole 300 mg once daily at night regardless of meal for 6 weeks. The signs and symptoms were rated as clinical score 0 to 3: 0 referred absent, 1 referred mild; 2 referred moderate and 3 referred severe symptoms of tinea corporis. At the global clinical evaluations, we rated the clinical findings as A: Healed (absence of signs and symptoms), B: Markedly improved (>50% clinical improvement), C: Considerable residual lesions (< 50% clinical improvement), D: No change and E: Worse. Along with treatment data, all demographic and clinical information of the participants were recorded. A predesigned questioner was used in data collection. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23 program as per necessity.

III. Result

In this study, among total 87 participants, 32% were male whereas the rest63% were female. So, female participants were dominating in number and the male-female ratio was 1:1.7. The mean ±SD age of participants was 43.52±14.72. Majority of the participant were married. In this study among total participants, 41% and 24% participants were housewife and student respectively which was noticeable. In this current study, in analyzing the changes in clinical scores of participants between baseline and follow up stages we observed that, at follow up stage, the mean (± SD) clinical score was found 1.14 ± 0.15 which was 2.06 ± 0.27 at baseline and this change was significant where the P value was <0.0001. Besides these, in final outcome assessment we observed that, among majority of the participants (62%), the signs and symptoms were totally absent at the end of the treatment tenure of 6 weeks and their grade was 'A'. Moreover, 23% patients got the grade 'B' who got >50% clinical improvement. Then 8%, 5% and 2% patient got 'C', 'D' and 'E' grades at the follow up stage. In this study, as the remarkable side effects, nausea and headache were found which were in only 11% and 9% patients respectively. After 2 weeks of treatment with fluconazole SGPT was found mildly elevate in only 2% cases and after 4 week's treatment it was found elevate but not more than 2-fold in only 4% cases.

Table 1: Demographic status of participants (N=87)

Variables	**n**	**%**
Gender distribution of participants		
Male	32	37%
Female	55	63%
Mean ±SD age of participants		
Age in year	43.52±14.72	
Marital status of participants		
Married	58	67%
Unmarried	29	33%
Occupational status of participants		
Housewife	36	41%
Student	21	24%
Service holder	13	15%
Businessmen	10	11%
Farmer	7	8%

Table 2: Changes in clinical scores between baseline and follow up stages (N=87)

Stages	Score (Mean ± SD)	P value
Baseline	2.06 ± 0.27	<0.0001
Follow up	1.14 ± 0.15	

Table 3: Final outcomes at follow up state of treatment (N=87)

Global status	n	%
A: Healed (absence of signs and symptoms)	54	62%
B: Markedly improved (>50% clinical improvement)	20	23%
C: Considerable residual lesions (< 50% clinical improvement)	7	8%
D: No change	4	5%
E: Worse	2	2%

Table 4: Distribution of side effects among participants (N=87)

Side effects	n	%
Nausea	10	11%
Headache	8	9%

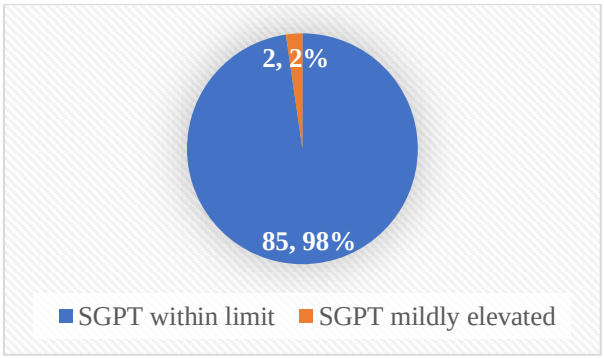

Figure 1: Fluconazole SGPT level distribution among participants after 2 weeks (N=87)

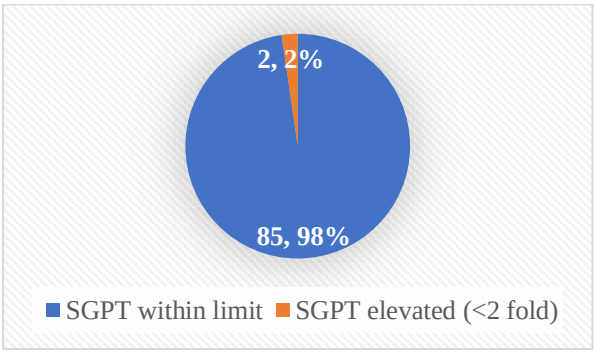

Figure 2: Fluconazole SGPT level distribution among participants after 4 weeks (N=87)

IV. Discussion

The aim of this study was to evaluate the efficacy and safety of recommended high dose oral fluconazole in treating tinea corporis. Tinea corporis occurs worldwide and it is relatively frequent, but its incidence is higher in tropics and subtropics. [13] Although in our study female patients were dominating in number in many studies male patients were found more than female. In a study [14], the male to female ratio was 1.86, i.e., 65.00% were males and 35.00% were females. The mean ±SD age of our participants was 43.52±14.72.In another study Decroix et al. [15], the mean age of tinea corporis patients was 39.7 years.In this current study, in analyzing the changes in clinical scores of participants between baseline and follow up stages we observed that, at follow up stage, the mean (± SD) clinical score was found 1.14 ± 0.15 which was 2.06 ± 0.27 at baseline and this change was significant where the P value was <0.0001.In such high dose treatment, safety is a vital issue. In our study, as the remarkable side effects, nausea and headache were found which were in only 11% and 9% patients respectively. After 2 weeks of treatment with fluconazole SGPT was found mildly elevate in only 2% cases and after 4 week's treatment, it

was found elevate but not more than 2-fold in only 4% cases.In many other studies [16, 17] we found the uses of such higher dosage schedule. In a study it was reported that, the serum levels of oral fluconazole measured and were comparable to some other

Studies using daily doses of 200 to 400 mg [18] or of 800 mg [19]. In another study, it was reported that, among patients with cryptococcosis managed with daily doses of 800as well as1000mg/day the mean levels of serum fluconazole were found as 37.0 µg/mLand42.5 µg/mL, [20] respectively. Fluconazole is widely used in several dermatomycosis. [21] An in vitro study to determine the activity of ten antifungals against dermatophytes has shown that, T. rubrum, was more susceptible to fluconazole than other species. [22] Besides oral administration, topical fluconazole has shown to be effective and safe in superficial dermatomycosis. [23] The effectiveness as well as tolerability of fluconazole in the treatment of dermatomycoses with localized lesions was found in Italian patients also. [24] So, the treatment regime of oral fluconazole 300 mg once daily at night regardless of meal for 6 weeks may be considered as an effective treatment option for the treatment of tinea corporis.

Limitation of the study:

This was a single centered study with small sized samples. Moreover, the study was conducted at a very short period of time. So, the findings of this study may not reflect the exact scenario of the whole country.

V. Conclusion & Recommendation

As per the findings of this study, we can conclude that, as a recommended high dosage treatment schedule, oral fluconazole 300 mg once daily at night regardless of meal for 6 weeks is an effective and safe treatment option for the treatment of tinea corporis. Most of the patients of tinea corporis are comfortable with the convenient dosage schedule of this treatment regime. As fluconazole is a water-soluble molecule, it may be well tolerated for several aged patients. We would like to recommend for wide range of use of fluconazole in treating such tinea infection.

Funding: No funding sources.
Conflict of interest: None declared.

References

[1]. macokinetics and tissue penetration of fluconazole in humans. Rev Infect Dis 1990;12(suppl 3):318–326.
[2]. Wildfeuer A, Laufen H, Pfaff G, Zimmermann T, Lach P: Bioverfügbarkeit von Fluconazol in der Haut nachoralerMedikation. Mycoses 1992;35(suppl):65–68.
[3]. Tschechne B, Brunkhorst U, Ruhnke M, Traut- mann M, Dempe S, Deicher H: Fluconazol in der Therapie der Candidose des Mund-Rachen-RaumesbeiPatientenmit HIV-Infek- tion. Med Klin1991;86:508–511.
[4]. Stoehr A, Plettenberg A, Begemann F, Heise W, Höffken G: Therapie der SoorösophagitismitFluconazolbei AIDS-Patienten. Chemo-ther J 1992;1: 116–119.
[5]. Stary, A., and E. Sarnow. "Fluconazole in the treatment of tinea corporis and tinea cruris." Dermatology 196.2 (1998): 237-241.
[6]. Verma, S., & Madhu, R. (2017). The great Indian epidemic of superficial dermatophytosis: An appraisal. Indian journal of dermatology, 62(3), 227.
[7]. Bishnoi, A., Vinay, K., Dogra, S. (2018). Emergence of recalcitrant dermatophytosis in Bangladesh. Lancet Infect Dis, 18(3); 250–51.
[8]. Layton, A. M., Eady, E. A., Whitehouse, H., Del Rosso, J. Q., Fedorowicz, Z., & van Zuuren, E. J. (2017). Oral spironolactone for acne vulgaris in adult females: a hybrid systematic review. American journal of clinical dermatology, 18(2), 169-191.
[9]. Panda, S., Verma, S. (2017). The menace of dermatophytosis in Bangladesh: The evidence that we need. Bangladeshn J Dermatol, Venereol, Leprol, 83(3); 281–4.
[10]. Hossain, Mohammed Mosharraf, et al. "Comparison of the Efficacy of Terbinafine versus and Co-Administration of Terbinafine and Fluconazole in Patients of Tinea Corporis." Sch Acad J Biosci 5 (2022): 110-115.
[11]. World Medical Association. (2001). World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bulletin of the World Health Organization, 79 (4), 373 - 374. World Health Organization. https://apps.who.int/iris/handle/10665/268312.
[12]. Voigt, Paul, and Axel von dem Bussche. "Enforcement and fines under the GDPR." The EU General Data Protection Regulation (GDPR). Springer, Cham, 2017. 201-217.
[13]. Amit, Kumar, et al. "A comparative study of efficacy of terbinafine and fluconazole in patients of tinea corporis." International Journal of Biomedical Research 4 (2013): 11.
[14]. Acharya K M, Mukhopadhyay A, Thakur R K, Mehta T, Bhuptani N and Patel R (1995), "Itraconazole versus griseofulvin in the treatment of tinea corporis and tinea cruris", Indian J Dermatol VenereolLeprol, Vol. 61, pp. 209-11.
[15]. Decroix J, Fritsch P, Picoto A, Thürlimann W and Degreef H (1997), "Short-term itraconazole versus terbinafine in the treatment of superficial dermatomycosis of the glabrous skin (tinea corporis or cruris)", Eur J Dermatol, Vol. 7, pp. 353-7.
[16]. Sinnollaredy MG, Roberts JA, Lipman J, et al. Pharmacokinetic variability and exposures of fluconazole, anidulafungin, and caspofungin in intensive care unit patients: data from multinational Defining Antibiotic Levels in Intensive care unit (DALI) patients study. Crit Care. 2015;19:33.
[17]. Manosuthi W, Chetchotisakd P, Nolen TL, et al. Monitoring and impact of fluconazole serum and cerebrospinal fluid concentration in HIV associated cryptococcal meningitis infected patients. HIV Med. 2010;11:276–81.

[18]. Buijk SLCE, Gyssens IC, Mouton JW, Verbrugh HA, Touw DJ, Bruining HA. Pharmacokinetics of sequential intravenous and enteral fluconazole in critically ill surgical patients with invasive mycoses and compromised gastro-intestinal function. Intensive Care Med. 2001;27:115–21.
[19]. Sobue S, Tan K, Layton G, Leclerc V, Weil A. Pharmacokinetics of fosfluconazole and fluconazole following multiple intravenous administration of fosfluconazole in healthy male volunteers. Br J Clin Pharmacol. 2004;57:773–84.
[20]. Menichetti F, Fiorio M, Torti A, et al. High-dose fluconazole therapy for cryptococcal meningitis in patients with AIDS. Clin Infect Dis. 1996;22:838–40.
[21]. Gupta AK, Albreski D, Del Rosso JQ, Konnikov N. The use of the new oral antifungal agents, itraconazole, terbinafine, and fluconazole to treat onychomycosis and other dermatomycoses. Curr Problems Dermatol. 2001;13:220-46.
[22]. Fernández-Torres B, Carrillo AJ, Martı´n E et al. In vitro activities of 10 antifungaldrugs against 508 dermatophyte strains. Antimicrob Agents Chemother. 2001;45:2524-8.
[23]. Yim SM, Ko JH, Lee YW et al. To compare the efficacy and safety of fluconazole cream with flutrimazole cream in the treatment of superficial mycosis: a multicentre, randomised, double-blind, phase III trial. Mycoses. 2010;53:522-9.
[24]. Aste N, Baldari U, Bellini M et al. Efficacy and Tolerability of the topical formulation of fluconazole 0.5% (gel containing an emulsion oil/water) for the treatment of dermatomycoses with localized lesions. Italian J Dermatol Venereol. 1999;134:61-5.

Ayesha Siddiqua, et. al. "Efficacy and Safety of Recommended High Dose Oral Fluconazole in the Treatment of Tinea Corporis." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(12), 2022, pp. 53-57.