DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20221567

Letter to the Editor

Comparative real-world effectiveness and safety of super-bioavailable itraconazole 50 mg bd and 65 mg bd in the management of dermatophytosis

Sir,

In recent times, India has witnessed a steep surge in prescription of itraconazole in the management of dermatophytosis.[1] But due to its pharmacokinetics, it has shown multiple variations in the results. To overcome these challenges, a newer itraconazole formulation i.e. super-bioavailable itraconazole (SBITZ) has been launched recently in India. Currently, there are 4 different strengths of SBITZ which are approved by DCGI.[2,3] But there is no any clinical data regarding comparison of different strength of SBITZ. This retrospective analysis aimed to compare two different strengths of SBITZ; 50 mg and 65 mg in the management of dermatophytosis.

A multicentre, retrospective data analysis was carried out at 184 dermatology outpatient clinics during July 2021 to February 2022 after ethics committee approval. The data blueprint was created by generating a list of all adult patients prescribed either SBITZ 50 mg or 65 mg as twice a day regimen in dermatophytosis. Effectiveness was assessed by total symptom score (TSS), (range, 0-9) consisting of the sum of the scores for erythema, pruritus and scaling, all scored on a 4-point (range, 0-3) scale. In addition, mycological clearance was assessed wherever available. Primary endpoint was comparative assessment of percentage of patients achieving complete cure (KOH negative and clearance of symptoms), clinical cure (clearance of symptoms) and mycological cure (KOH negative) in both groups at different intervals. Additionally, clinical improvement (improvement by >50% in TSS) and failure (improvement by <50% in TSS) was also assessed. Safety was assessed by no. of adverse events (AE) reported by patients. Results were presented as mean scores, and groups were compared using unpaired t test and fisher exact test with level of significance as $p<0.05$. Data was analyzed using the IBM statistical package for social sciences (SPSS) statistics version 20. Study design and baseline demographics are depicted in Figure 1 and Table 1 respectively.

Both the groups were found to be statistically significant in achieving cure rates at the end of week 6 and 8. At week 6, clinical cure was achieved by 151/238 patients and 364/658 patients in group I (SB 65) and II (SB 50) respectively whereas clinical improvement was attained by 203/238 patients and 495/658 patients in group I and II respectively. In both the conditions, group I was statistically significant than group II as shown in Table 2. Mycological cure rate could not be assessed.

KOH report was available in only 139/238 patients (58.4%) and 271/658 patients (41.18%) in group I and II respectively. At week 8, mycological cure was achieved by 111/139 (80%) patients and 191/271 (70%) patients respectively in group I and II and clinical cure was seen in 214 (90%) and 573 (87%) patients respectively in group I and II. As a result, complete cure was noticed in 104/139 (75%) patients in group I and in 172/271 (63%) patients in group II respectively.

There was statistical difference in terms of mycological cure ($p=0.04$) and complete cure ($p=0.02$) but no statistical difference was noted between groups in clinical cure, improvement and clinical failure (Table 2). The percentage of patients achieving cure rates is shown in Figure 2.

Both the treatments were found to be safe and well tolerated by patients with no discontinuation in any of groups. A total of 43 patients (18.07%) in group I and 136 patients (20.67%) in group II reported to have AE. There was no statistical difference between both the groups ($p=0.44$). Table 2 depicts the distribution of all AE in both groups.

Table 1: Baseline demographics.

Demographics	SB 65 mg (group I)	SB 50 mg (group II)	P value
N	238	658	
Male	94	279	
Female	144	379	
Mean age, years (SD)	40.46±12.82	39.58±12.40	0.35
Concomitant medications; N (%)			
Luliconazole	113 (47.48)	298 (45.29)	
Sertaconazole	39 (16.39)	114 (17.33)	
Eberconazole	14 (5.88)	33 (5.02)	
Older azoles	17 (7.14)	36 (5.47)	

Continued.

Demographics	SB 65 mg (group I)	SB 50 mg (group II)	P value
Amorolfine	25 (10.50)	64 (9.73)	
Ciclopirox	11 (4.62)	46 (6.99)	
Terbinafine	5 (2.10)	15 (2.28)	
Combination of two antifungals	45 (18.91)	131 (19.91)	
Oral anti histamine	10 (4.20)	78 (11.85)	
No information available	0 (0)	29 (4.41)	
Mean TSS (SD)	7.31±3.11	7.37±3.43	0.8
KOH positive; N (%)	139 (58.40)	271 (41.19)	

Table 2: Effectiveness assessment with multiple cure rates at week 6 and 8 and safety assessment.

Variables	SB 65 mg (N)	SB 50 mg (N)	P value
Effectiveness assessment			
Week 6			
Clinical cure	151/238	364/658	0.03*
Clinical improvement	203/238	495/658	0.001*
Week 8			
Mycological cure	111/139	191/271	0.04*
Clinical cure	214/238	573/658	0.29
Complete cure	104/139	172/271	0.02*
Clinical improvement	223/238	634/658	0.09
Clinical failure	15/238	24/658	
Safety assessment			
N (%)	43 (18.07)	136 (20.67)	0.44
Gastrointestinal disorders; N (%)			
Abdominal pain	12 (5.04)	40 (6.08)	
Nausea	8 (3.36)	22 (3.34)	
Diarrhea	12 (5.04)	35 (5.32)	
Nervous system disorders; N (%)			
Headache	8 (3.36)	25 (3.8)	
Renal and cardiovascular disorders; N (%)			
Pedal edema	3 (1.26)	14 (2.13)	

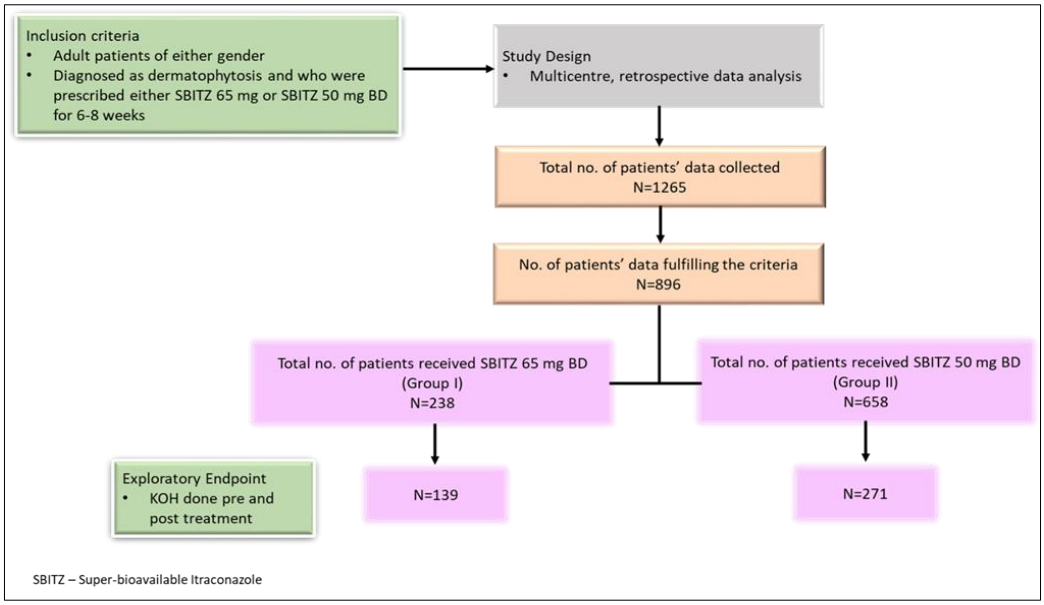

Figure 1: Study design.

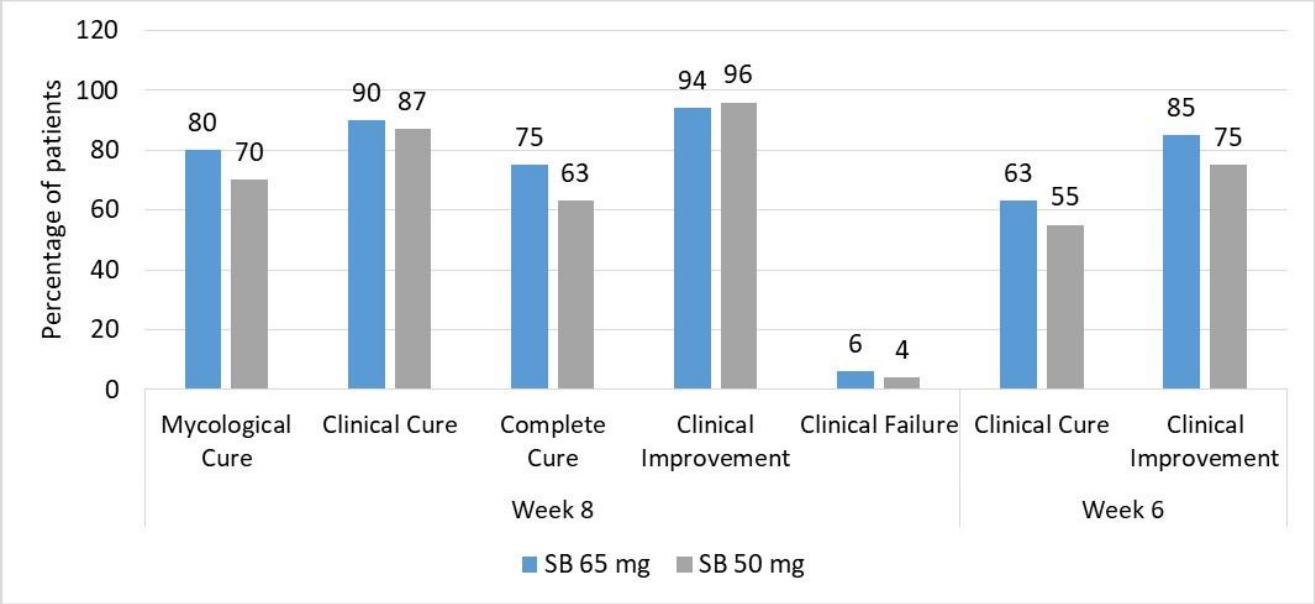

Figure 2: Cure rates at week 6 and 8.

Super-bioavailable itraconazole 50 mg and 65 mg are approved by Drugs Controller General of India (DCGI) in invasive mycosis but are commonly prescribed in dermatophytosis as off label indication.[2,3] Both the strengths have proven bio-equivalence to conventional itraconazole 100 mg. But due to availability of two strengths, there was dilemma at the dermatologists' level. Hence, we conducted this retrospective study to compare the clinical utility of both the strengths.

In our study, SBITZ 65 has shown statistically significant results over 50 mg in terms of clinical effectiveness. This could be due to better serum concentration achieved by SBITZ 65 mg. It was found that SB 50 mg delivers around 46-47 mg of actual itraconazole while SB 65 delivers about 58 mg.[4-7] Hence, the percentage of patients achieving therapeutic concentration of itraconazole was 81% in SB 65 against 69% of SB 50 mg.[8,9]

In current scenario, itraconazole is prescribed for longer duration in dermatophytosis and sebum concentration plays important role which can be achieved by higher serum concentration only.[10] Thus, the high concentration achieved in sebum may be responsible for the better improvement in SB 65 mg group.

Due to its retrospective design, there were certain limitations in the present study impacting the results of the study like use of concomitant medications and lack of data on relapse rates. But from result, it was concluded that both the strengths of SBITZ i.e. 50 mg and 65 mg were found to achieve clinical improvement in dermatophytosis; however, SBITZ 65 mg was found to be better therapeutic option than 50 mg but long term clinical trials are warranted to validate the results of the present study.

Namrata Mahadkar, Dhiraj S. Dhoot*, Hanmant Barkate

Global Medical Affairs, Glenmark Pharmaceuticals Ltd. Mumbai, Maharashtra, India

***Correspondence to**
Dr. Dhiraj S. Dhoot,
E-mail: dhiraj.dhoot@glenmarkpharma.com

REFERENCES

1. Das S, De A, Saha R, Sharma N, Khemka M, Singh S, et al. The Current Indian Epidemic of Dermatophytosis: A Study on Causative Agents and Sensitivity Patterns. Indian J Dermatol. 2020;65(2):118-22.
2. Recommendations of the SEC (Dermatology & Allergy) made in its 46th meeting held on 19.06.2020 at CDSCO HQ New Delhi. Available at: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadCommitteeFiles/46thSECDermatology%20%20AllergyRecommendation19.06.2020.pdf. Accessed on 24 April 2022.
3. Recommendations of the SEC (Antimicrobial & Antiviral) made in its 102 and meeting held on 27.07.2021 at CDSCO HQ, New Delhi. Available at: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadCommitteeFiles/Recommendations%20Antimicrobial%20&%20Antiviral%2027.07.2021.pdf. Accessed on 24 April 2022.
4. Lozanoc 50 mg Capsules. Available at: https://www.nps.org.au/medicine-finder/lozanoc-capsules. Accessed on 27 March 2022.
5. Highlights of Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208901s000lbl.pdf. Accessed on 27 March 2022.

6. Battles Against Fungal Infections Can Leave You Wishing You Had Superpowers. Available at: https://tolsura.com/. Accessed on 24 April 2022.
7. Abuhelwa AY, Foster DJ, Mudge S, Hayes D, Upton RN. Population pharmacokinetic modeling of itraconazole and hydroxyitraconazole for oral SUBA-itraconazole and sporanox capsule formulations in healthy subjects in fed and fasted states. Antimicrob Agents Chemother. 2015;59(9):5681-96.
8. Thompson GR, Lewis P, Mudge S, Patterson TF, Burnett BP. Open-Label Crossover Oral Bioequivalence Pharmacokinetics Comparison for a 3-Day Loading Dose Regimen and 15-Day Steady-State Administration of SUBA-Itraconazole and Conventional Itraconazole Capsules in Healthy Adults. Antimicrob Agents Chemother. 2020;64(8):e00400-20.
9. Lindsay J, Sandaradura I, Wong K, Arthur C, Stevenson W, Kerridge I, et al. Serum levels, safety and tolerability of new formulation SUBA-itraconazole prophylaxis in patients with haematological malignancy or undergoing allogeneic stem cell transplantation. J Antimicrob Chemother. 2017;72(12):3414-9.
10. Shenoy M, Dhoot D, Mahajan H, Barkate H. An Open-Label, Randomized, Double-Arm Clinical Trial to Compare the Effectiveness and Safety of Super Bioavailable Itraconazole Capsules and Itraconazole Capsules in the Management of Dermatophytosis in India. Clin Cosmet Investig Dermatol. 2021;14:1367-76.

Cite this article as: Mahadkar N, Dhoot DS, Barkate H. Comparative real-world effectiveness and safety of super-bioavailable itraconazole 50 mg bd and 65 mg bd in the management of dermatophytosis. Int J Res Dermatol 2022;8:433-6.