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A COMPARATIVE STUDY OF EFFICACY OF ORAL TERBINAFINE VERSUS ORAL ITRACONAZOLE IN TREATMENT OF TINEA CORPORIS AND TINEA CRURIS INFECTION

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ABSTRACT

Background: Recently, it was noted that the spread of superficial fungal infections with widespread resistance to various antifungal drugs used in the traditional dose, with an increase in relapse rates, which caused a real medical problem due to the skin manifestations and clinical symptoms (itching) disturbing to the patient. **Objectives:** This study was designed to evaluate and compare the efficacy of oral terbinafine versus itraconazole in the treatment of Tinea Corporis and Tinea Cruris. **Materials and Methods:** This was a prospective, randomized comparative study. It was conducted at Tishreen University Hospital, Lattakia, during the period between 2022-2023. The study included 90 patients. After confirming the diagnosis, the patients were randomly divided into two groups. The first group: 45 patients treated with terbinafine orally at a dose of 500 mg daily for 4 weeks. The second group: 45 patients who were treated with itraconazole orally at a doseof 200 mg daily for 4 weeks. **Results:** There were statistically significant differences between the two researchgroups regarding the evaluation of recovery between the two research groups, where we find that the cases of complete recovery amounted to 86.7% in the oral itraconazole treatment group compared to 72.7% in the terbinafine group. **Conclusion**: Itraconazole is better than terbinafine in the treatment of TineaCorporis and Tinea Cruris and can be considered as the first line. The safety of both drugs, even after using higher concentrations and a longertreatment period.

KEYWORDS: Dermatophyte, Tinea Corporis, Tinea Cruris, Itraconazole, Terbinafine.

1. INTRODUCTION

Fungi are ubiquitous and capable of colonizing almost any environment. Although they were once belived to be descended from plants, it was recognized over 20 years ago that they represent a distinct kingdom, and that certain features of their biochemistry, such as the pathway of lysine synthesis, are quite different from those found in bacteria and plants.[2] Some dermatophytes are restricted geographically, while others are found worldwide. Trichophyton rubrum, for example, is the most common dermatophyte and has a global distribution, while T. concentricum is endemic to certain parts of the South Pacific and South America.[1-7] Human travel and migration, coupled with advances in antifungal therapy, have brought about significant changes in the geographic distribution of dermatophytes. Although dermatophyte infections do occur worldwide, they are more common in tropical environments. Other important epidemiologic factors include socioeconomic status, occupation, air conditioning, and the use of footwear.[1-10] More than 20 types of fungi that cause tinea were isolated, the most common of which are (Trichophyton rubrum, Epidermophyton floccosum, Trichophyton tonsurans and Microsporum canis).[1] Tinea may be strongly suspected based on clinical examination however a koh test which will show fungal hyphae is recommended in order to confirm the diagnosis due to clinical resemblance to other lesions. The treatment is topical or systemic, and there are several types of antifungals (azole compounds, allylamine compounds (terbinafine), amphotericin B, and griseofulvin). Despite the variety of treatments, an increase in failure and chronicity rates has been observed in the recent period.

2. MATERIALS AND METHODS

Recently, it was observed that superficial fungal infections spread with widespread resistance to various

antifungal drugs used in the traditional dose, with an increase in relapse rates, which caused a real medical problem due to skin manifestations and clinical symptoms (itching) disturbing to the patient. Hence the idea of our study came in order to find the most effective and safest drug among antifungal drugs by evaluating differences in the results of drug treatment and reaching the appropriate dose and schedule for the duration of treatment in order to achieve the best results.

2.1- Main objective: To evaluate and compare the effectiveness of oral terbinafineversus itraconazole in the treatment of Tinea Corporis and Tinea Cruris.

2.2- Secondary objectives

Evaluation of effectiveness according to the following variables.

1- Age (in years)
2- Sex
3- Area
4- Duration of injury (in months)
5- Undergoing or without prior treatment
6- Associated with diabetes or other diseases

2.3- Study population and methods

Study Design: After approval by local research ethics committee, a prospective, randomized, comparative study was conducted in Department of Dermatology and Venereology at Tishreen University Hospital between in Lattakia, Syria between 2022-2023.

2.4- Inclusion Criteria.

Patients with Tinea Corporis and\or Tinea Cruris that have not been treated for weeks and achieve all of the following criteria.

1- Clinically diagnosed tinea
2- Diagnosed by direct microscopic examination with potassium hydroxide (KOH)3- Age is over 18 years.

2.5- Exclusion Criteria

1- Pregnant
2- Lactating
3- Patients who have (kidney disease - liver disease - heart failure
4- Patients with a history of allergy to drugs
5- Patients taking systemic immunosuppressive drugs

The final research sample consisted of 45 patients who underwent treatment withterbinafine and 45 patients who underwent treatment with itraconazole.

The data in this study were collected prospectively, and all research participants were fully aware of the procedure, and their written informed consent or their families' consent to participate in the research was obtained after receiving sufficient information. This study did not face serious ethical challenges. Upon admission, research participants underwent a clinical and laboratoryevaluation and then initiation of treatment

2.6- Clinical evaluation

It involved taking a detailed clinical history and documenting the followinginformation:

1- gender
2- age
3- Duration of injury
4- The injury is located
5- Comorbidities
6- Previous treatment

Clinical, microscopic and laboratory examination

Before starting treatment

We photographed the lesions (all images were taken with the same camera and thesame lighting and magnification conditions were observed)

Direct microscopy was performed

Laboratory analyzes were performed, including

Blood count and formula, liver enzymes ALT, AST, kidney function, creatinine, urea,blood sugar.

After confirming the diagnosis, the patients were randomly divided into two groups.

The first group: were treated with terbinafine orally at a dose of 500 mg daily for 4weeks.

The second group: was treated with itraconazole orally at a dose of 200 mg daily for4 weeks.

Patients were followed up and evaluated at the first visit, after two weeks, and at the end of treatment (the fourth week), the evaluation was in terms of erythema, itching, and scaling.

0- absent, 1- mild, 2- moderate, 3- severe.

Evaluation was based on the global clinical evaluation criteria, and response was accordingly noted as (A – complete improvement, B - marked improvement, C - lesions remaining (>50%), D - no change, or E – worsened)

A koh scan was performed at the time of patient enrolment and at the end of 4weeks

Liver function analyzes were performed at the beginning of treatment and after 4weeks of treatment

Patients were considered cured when there was an absence of scale , erythema, and pruritus, with KOH negative

Side effects of both treatments were evaluated.

3. RESULTS

3.1- Comparison of Basic Demographic Statistics

The vast majority of patients in the studied research sample 44.4% were within theage group 18-28 years and 20% were within the age group 38-48 years (table-1 Fig-1,). In the (itraconazole) group the mean age was 33.95 ± 16.1 years, while in the (terbinafine) group the mean age was 34.91 ± 14.9 years.(table -3)

Table 1: distribution of the research sample by age group.

Age	Number	Precentage
18-28	40	44.4%
28-38	12	13.3%
38-48	18	20%
48-58	10	11.1%
58-68	10	11.1%
Total	90	100%

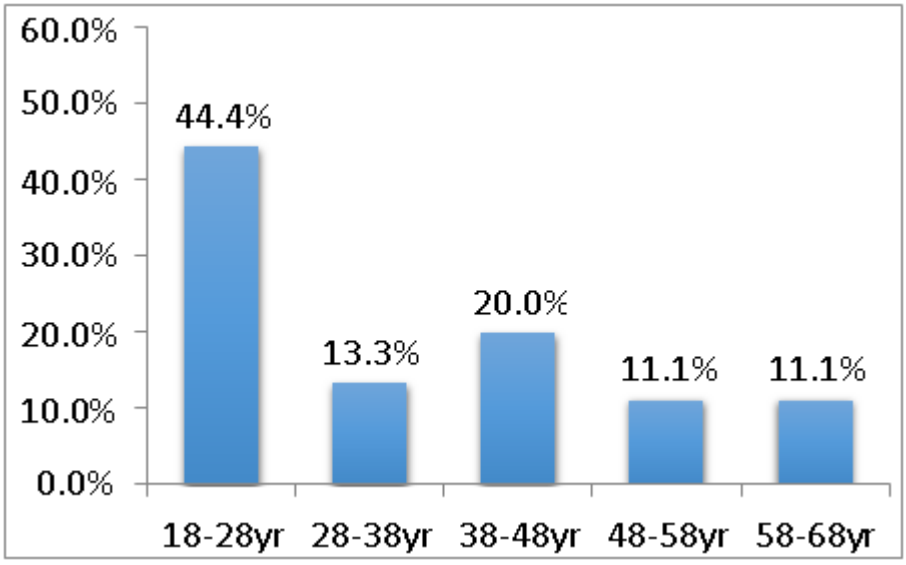

Fig 1: distribution of the research sample by age group.

We noticed that 68.9% of the subjects were males with Sex Ratio (M:F) = 2.2:1,(table -2, Fig-2) as the vast majority of cases in both groups were males, 60% in the (itraconazole) group and 77.8% in the (terbinafine) group, respectively. The proportion of females is 40% in the (itraconazole) group and 22.2% in the (terbinafine) group. There was no statistically significant difference between thetwo groups with respect to gender(table-3).

Table 2: distribution of the research sample by gender.

gender	number	Precentage
male	62	68.9%
female	28	31.1%
total	90	100%

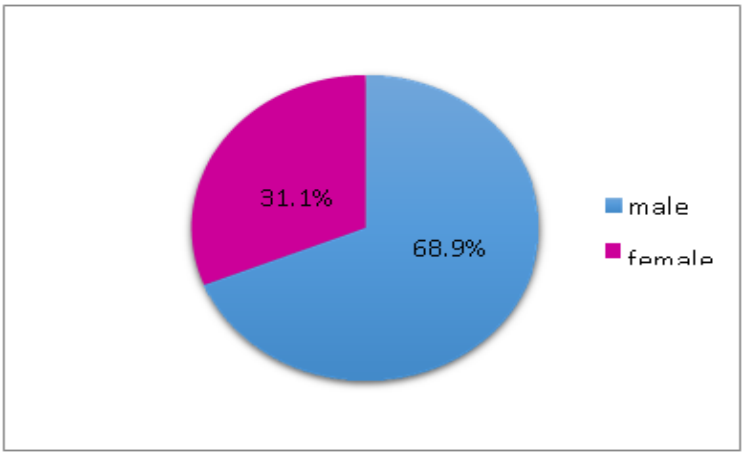

Fig 2: Distribution Of The Research Sample By Gender.

Table 3: Comparison Of Basic Demographic Statistics.

Demographic Statistics	Research group		P-value
	itraconazole	terbinafine	
gendermale female	27(60%) 18(40%)	35(77.8%) 10(22.2%)	0.06
Age(year)	33.95±16.1	34.91±14.9	0.7

3.1- Comparison of lesion position and Duration of Disease between Two Groups.

We noticed that 38.9% of the studied research sample had tinea cruris, followed by 34.4% of multiple (cruris and corporis) and 26.7% tinea corporis (table -4, Fig-3). And that 88.9% of the studied research sample had a duration of infection less than six months, and the duration of infection ranged with an average of 2.1 ± 1.99 months table-5.

Table 4: Comparison of Lesion Position.

lesion position	number	Precentage
tinea corporis	24	26.7%
tinea cruris	35	38.9%
multiple (cruris and corporis)	31	34.4%
Total	90	100%

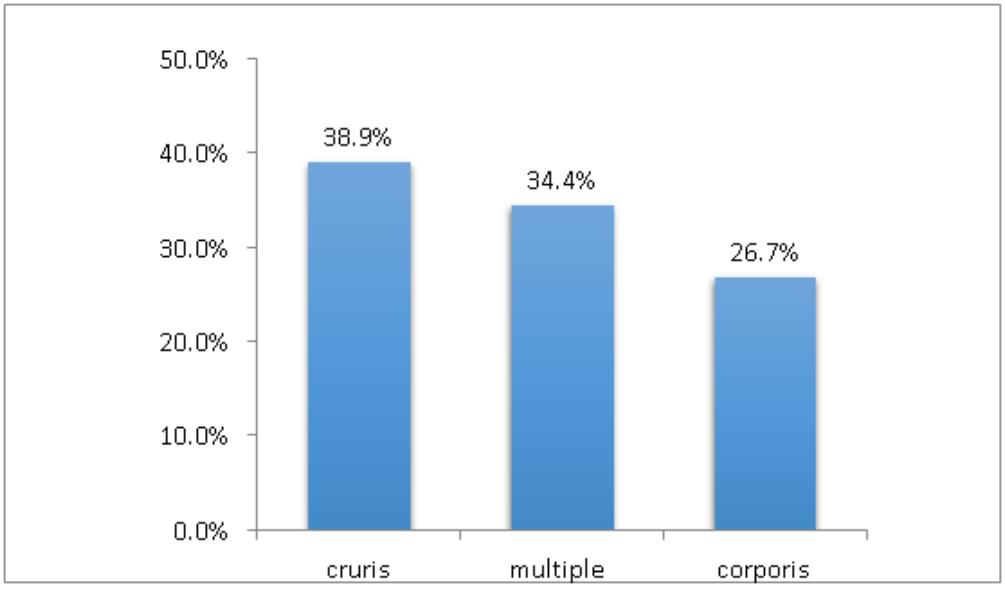

Fig 3: Comparison of lesion position.

Table 5: Comparison of Duration of Disease between Two Groups.

Duration of Disease(month)	number	Precentage
<6	80	88.9%
≥6	10	11.1%
total	90	100%

3.3- Comparison of Previous Treatment and Comorbidities History between theTwo Groups

We noticed that 15.6% of the research sample studied were previously treated with steroids, 10% antifungal creams, 6.7% unknown treatments(table -6), and that 7.8% of the research sample studied had diabetes and 5.6% had hypertension (table -7). We did not notice any statistically significant differences between the research groups with regard to age, gender, disease duration, medical history, and comorbidities.

Table 6: Comparison of Previous Treatment.

Previous Treatment	number	Precentage
steroids	14	15.6%
antifungal creams	9	10%
unknown treatments	6	6.7%

Table 7: Comparison of Comorbidities History between the Two Groups.

Comorbidities History	number	Precentage
diabetes	7	7.8%
hypertension	5	5.6%

3.4- clinical parameters and clinical evalution

We noticed that there were statistically significant differences with regard to the mean values of erythema in both research groups, where the percentage of decreaseat the end of the fourth week was 93.95% in the itraconazole group compared to 86.69% in the terbinafine group(table -8, Fig-4), we found statistically significant differences with regard to the mean values of

pruritus in both research groups, where the percentage of decline reached 95.71% compared to 93.51%(table -9, Fig- 5), respectively , and we also found statistically significant differences with regard to the mean values of scales in both research groups, where the percentage of decline reached 95.42% compared to 92.99%, respectively(table -10, Fig-6).

Table 8: Change in erythema in both research groups.

time	Research group	
	itraconazole	terbinafine
First visit	2.48±0.6	2.48±0.6
After 2 weeks	1.55±0.5	1.40±0.5
After 4 weeks	0.15±0.4	0.33±0.5
P-value	0.0001	0.0001

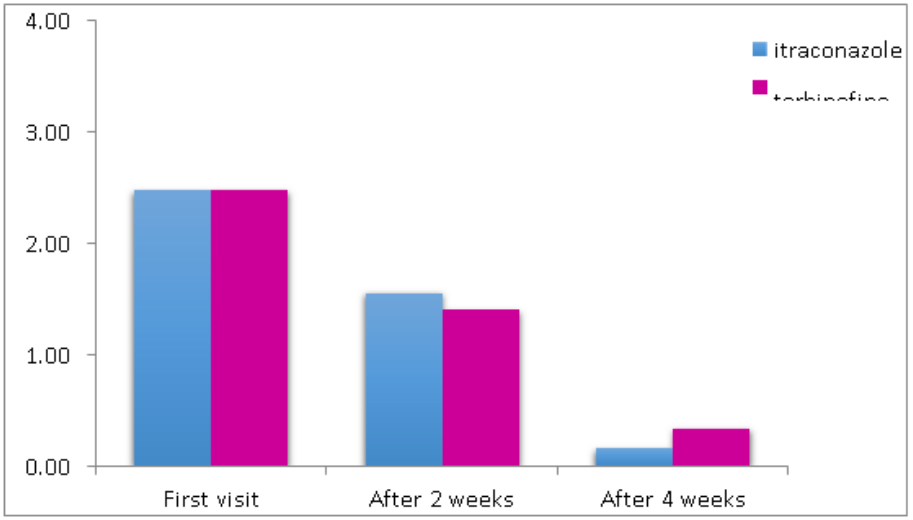

Fig 4: change in erythema in both research groups.

Table 9: change in pruritus in both research groups.

time	Research group	
	itraconazole	terbinafine
First visit	2.57±0.6	2.62±0.5
After 2 weeks	1.46±0.5	1.40±0.6
After 4 weeks	0.11±0.3	0.17±0.4
P-value	0.0001	0.0001

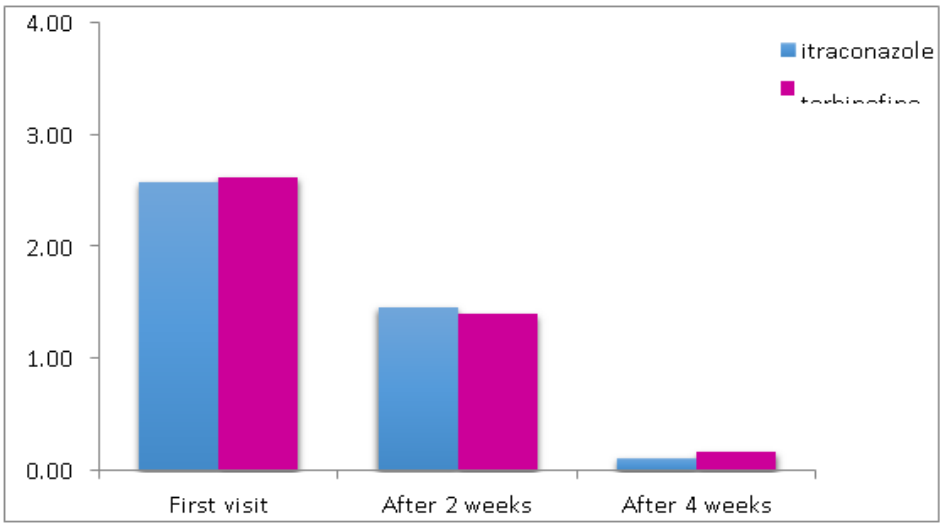

Fig 5: change in pruritus in both research groups

Table -10: change in scales in both research groups.

time	Research group	
	itraconazole	terbinafine
First visit	1.75±0.7	1.57±0.7
After 2 weeks	0.62±0.5	0.51±0.5
After 4 weeks	0.08±0.2	0.11±0.3
P-value	0.0001	0.0001

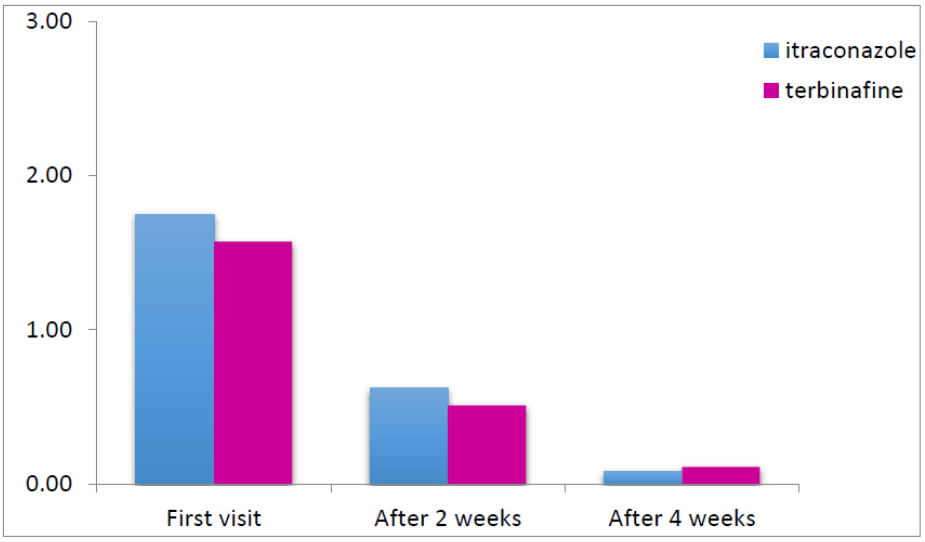

Fig 6: change in scales in both research groups,

In the end, there were statistically significant differences between the two research groups With regard to the evaluation of recovery between the two research groups, where we find that the cases of complete recovery (A) amounted to 86.7% in the oral itraconazole treatment group, compared to 72.7% in the terbinafine group, while the percentage of cases of significant improvement (B) was 8.9% and 15.6%, respectively, and The percentage of cases with an improvement of less than 50% (C) was 4.4% and 9.5%, respectively, and we did not notice in the itraconazole treatment group that there were no cases of no changes in treatment (D), and one case was seen in the terbinafine group 2,2 %. We did not notice any statistically significant differences between the research groups with regard to the occurrence of recovery, age, gender, disease duration, lesions, therapeutic antecedents and comorbidities (table -11,fig-7).

Table 11: evaluation of recovery between the two research groups.

Healed evalution	Research group		P-value
	itraconazole	terbinafine	
A	39(86.7%)	32(72.7%)	0.04
B	4(8.9%)	7(15.6%)	
C	2(4.4%)	5(9.5%)	
D	0(0%)	1(2.2%)	

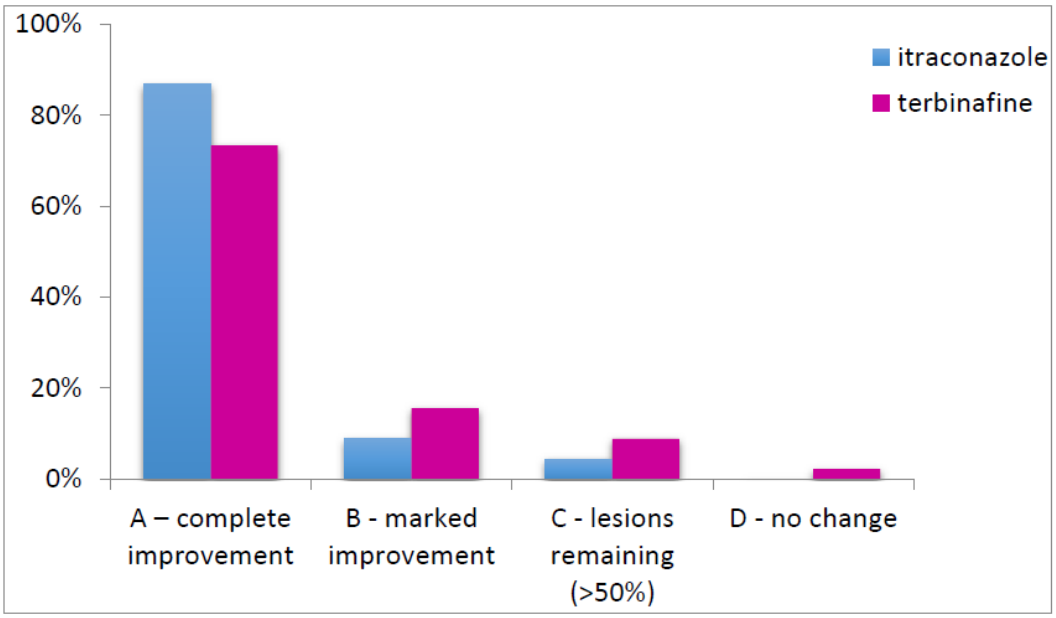

Fig-7 evaluation of recovery between the two research groups.

3.5-Side effects

In the itraconazole group, 2,3% developed digestive symptoms and 13,6% developed hyperpigmentation, and in the terbinafine group, 2,3% developed headaches, 6,5% developed digestive symptoms, and 15,2% developed hyperpigmentation. This was not clinically significant, and there was no discontinuation of treatment due to side effects. There was no statistically significant difference in side effects between the two groups(table-12)

Table 12: side effects between the two groups.

side effects	Research group		P-value
	itraconazole	terbinafine	
hyperpigmentation	6(13.6%)	7(15.2%)	0.5
headaches	0(0%)	1(2.3%)	
digestive symptoms	1(2.3%)	3(6.5%)	

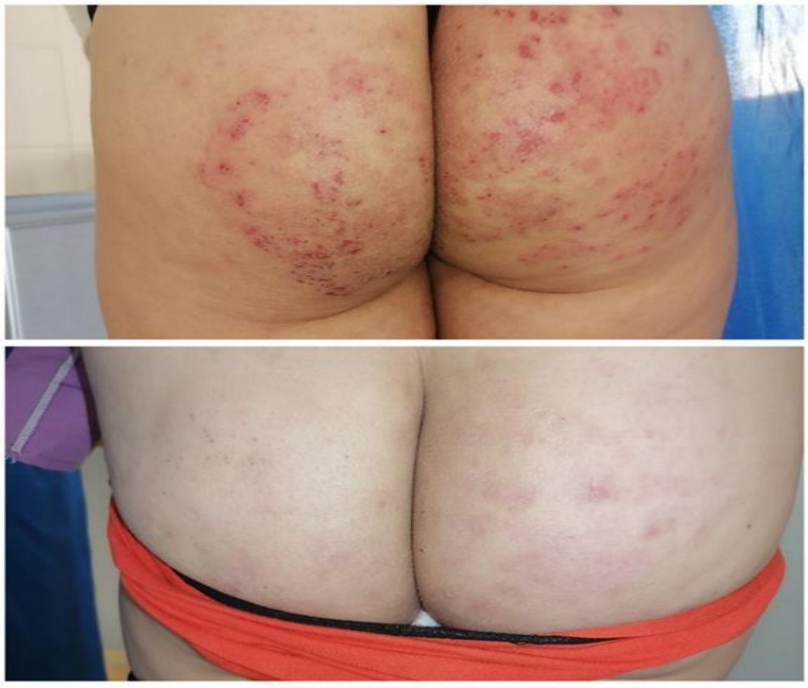

Fig 8: Terbinafine(before and after).

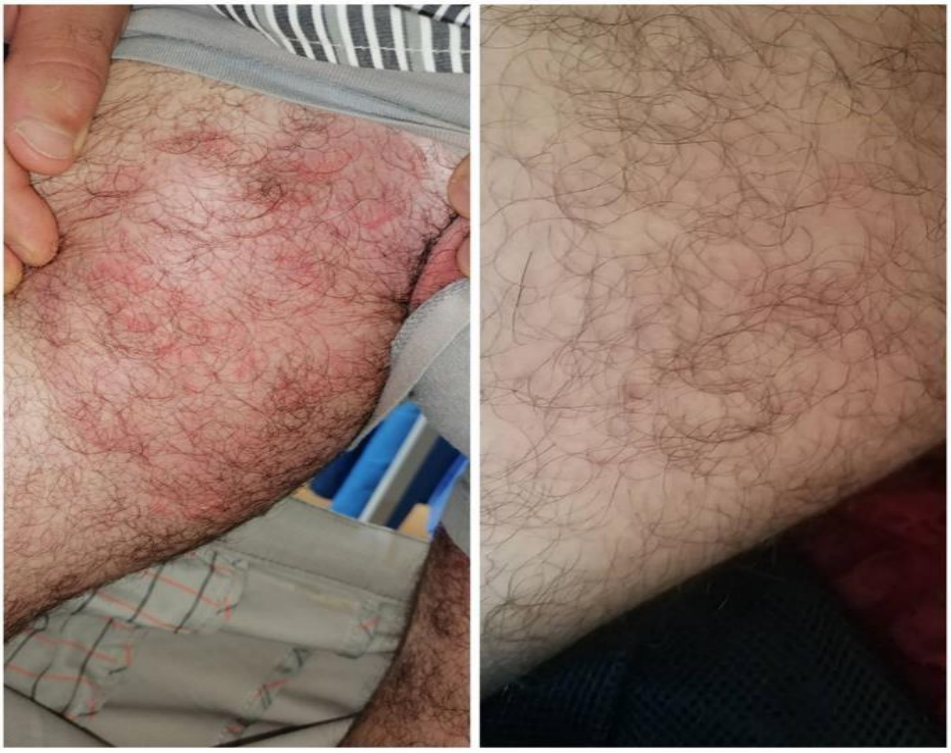

Fig 9: Itraconazole (before and after).

4- DISCUSSION

Comparison with global studies

Our study agreed with the study conducted by Anuradha Bhatia and et al in India in 2019, where 320 patients in two groups, the first group were treated with terbinafine at a dose of 500 mg for 4 weeks, and the second group was treated with itraconazole at a dose of 200 mg for 4 weeks, and the cure rate was 74.3% and 91.8%. respectively, but it differed in the number of patients whose lesion changed for the worse, as the percentage was 12.2% and 4.1%, respectively, while this did not happen in our study, perhaps due to the small size of the sample(3).

As for the study of S. Brigida and his colleague in India in 2021, the sample consisted of 100 patients distributed into two groups. The first group was treated with terbinafine at a dose of 500 mg for two weeks, and the second group was treated with itraconazole at a dose of 200 mg for two weeks. The cure rate was 70% and 88%, respectively, and an increase in liver enzymes occurred in 6%. And 2%, respectively, while this did not happen in our study except for one patient who received terbinafine treatment.[25]

As for the study by Ravindra Babu and others that they conducted in India in 2017, they evaluated the effectiveness of terbinafine only at a dose of 500 mg, where 440 patients were divided into three groups. They were treated: a group of 194 patients for two weeks, a group of 211 patients for a period of 4 weeks, and a group of 35 patients for a period of 6 weeks and two weeks, and the cure rate was 87% and 92%. And 80%, respectively, and 57 patients experienced side effects.[26]

As for the study of Priyanka Sharma and et al in India in 2020, 60 patients were divided into three groups who received treatment for a period of 3 weeks. The first group was treated with terbinafine at a dose of 250 mg, and the second group was treated with itraconazole at a dose of 200 mg and the third group received the two treatments together, and the cure rate was 35%, 50%, and 90% respectively.[27]

The last study, also in India, conducted by Monica George and her colleagues in 2019, differs from our study, where 60 patients were divided into two groups. The first group was treated with terbinafine at a dose of 250 mg for a period of 4 weeks, and the second group was treated with itraconazole at a dose of 100 mg for a period of two weeks. A topical treatment of 2% Sertaconazole was used in both groups, andthe result was that Both treatments are effective without statistically significant differences.[28]

5- CONCLUSIONS

Through this study, we reached the following conclusions:

* Itraconazole is better than terbinafine in the treatment of tinea cruris and tineacruris and may be considered as the first line
* The safety of both drugs, even after using higher concentrations and a longertreatment period.

6- Recommendations

*Start using the two medicines within a period of up to a

month
*Use topical antifungals in addition to systemic ones to get better results
*Carrying out studies in a larger number of patients and comparing both drugs with other available systemic drugs.

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