ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.5336/dermato.2024-105134

Comparison of Topical Terbinafine vs Topical Mometasone Furoate and Terbinafine Use in Dermatophyte Infections: A Retrospective Study

Yüzeyel Mantar Enfeksiyonlarında Topikal Terbinafin ve Mometazon Furoat-Terbinafin Kullanımının Karşılaştırılması: Retrospektif Çalışma

Esra ARI[a], Deniz EVLİYAOĞLU[a]

[a]Alanya Training and Research Hospital, Clinic of Skin and Venereal Diseases, Antalya

ABSTRACT Objective: Superficial fungal infections of the skin are common infections worldwide, especially in the regions with humid climates. Topical antifungals are the 1st choice treatment in uncomplicated cases. Combinations with topical corticosteroids may be an option to reduce the rate of side effects due to irritant or allergic contact dermatitis caused by carriers and alcohol in the drug content and to rapidly control symptoms in cases where itching and inflammation are severe. We planned to investigate the contribution of short-term topical corticosteroid use to treatment and its side effects by comparing patients using topical terbinafine and patients using mometasone furoate-terbinafine combination in terms of symptoms and examination findings in dermatophyte infections. **Material and Methods:** In our study, 62 adult patients who were clinically diagnosed with tinea corporis, tinea pedis, tinea manuum, and tinea cruris were retrospectively evaluated. Patients who used topical terbinafine cream as monotherapy and patients who continued treatment with topical terbinafine, following the mometasone furoate-terbinafine combination were compared. The effectiveness of the treatment was evaluated according to symptoms and findings. **Results:** When comparing the duration of control of symptoms in patients, the median value was 14 days in the monotherapy group and 7 days in the combination therapy group ($p<0.001$). No side effects were observed in any of the patients during the treatment. **Conclusion:** As a result, a faster clinical response was achieved in the group receiving combination therapy compared to the group receiving monotherapy. Rapid improvement of symptoms will increase confidence in treatment, increase the duration of treatment, and reduce the complications.

Keywords: Terbinafine; dermatomycoses; mometasone furoate

ÖZET Amaç: Derinin yüzeysel mantar enfeksiyonları dünya çapında yaygın olarak görülen, özellikle nemli iklime sahip bölgelerde sık görülen enfeksiyonlardır. Topikal antifungaller komplike olmamış durumlarda ilk seçenek tedavidir. İlaç içeriğinde bulunan taşıyıcılar ve alkolden kaynaklanan irritan ya da alerjik kontakt dermatite bağlı yan etki oranını azaltmak, kaşıntı ve inflamasyonun şiddetli olduğu durumlarda semptomları hızlı kontrol altına almak için topikal kortikosteroid ile kombinasyonları bir seçenek olabilir. Dermatofit enfeksiyonlarında topikal terbinafin kullanan hastalar ile mometazon furoat-terbinafin kombinasyonu kullanan hastaları semptom ve muayene bulguları açısından karşılaştırarak, kısa süreli topikal kortikosteroid kullanımının tedaviye katkısı ve yan etkilerini gözlemlemek amacı ile araştırmayı planladık. **Gereç ve Yöntemler:** Çalışmamızda, klinik olarak tinea corporis, tinea pedis, tinea manuum, tinea cruris tanısı almış, 62 erişkin hasta retrospektif olarak incelenmiştir. Monoterapi olarak topikal terbinafin krem kullanmış hastalar ve mometazon furoat-terbinafin kombinasyonunu takiben tedaviye topikal terbinafin ile devam eden hastalar karşılaştırılmıştır. Klinik olarak dermatofit enfeksiyonu tanısı alan hastalarda, tedavinin etkinliği semptomlar ve klinik bulgulara göre değerlendirildi. **Bulgular:** Hastaların semptomlarının kontrol altına alınma süresi karşılaştırıldığında, monoterapi alan grupta ortanca değer 14 gün, kombinasyon tedavisi alan grupta ortanca değer 7 gündür. ($p<0,001$) .Tedavi sürecinde hastaların hiçbirinde yan etki gözlenmemiştir. **Sonuç:** Çalışmamızın sonucunda kombinasyon tedavisi alan grupta, monoterapi alan gruba göre daha hızlı klinik yanıt elde edilmiştir. Semptomların hızlı düzelmesi tedaviye güveni artırarak, tedavide kalım süresini artıracak ve komplikasyon gelişme ihtimali azalacaktır.

Anahtar Kelimeler: Terbinafin; dermatofit; mometazon furoat

Correspondence: Esra ARI
Alanya Training and Research Hospital, Clinic of Skin and Venereal Diseases, Antalya
E-mail: esra88ari@hotmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Dermatology.

Received: 20 Aug 2024 ***Received in revised form:*** 31 Dec 2024 ***Accepted:*** 02 Jan 2025 ***Available online:*** 28 Feb 2025

Superficial fungal infections of the skin are common infections around the world, especially in the regions with humid climates. It is estimated that a person's lifetime probability of superficial fungal infection is approximately 10-20%.[1] Dermatophytoses are infections caused by 3 different types of fungi that have the ability to invade and proliferate in keratinized tissue (skin, hair, nails). Trichophyton rubrum, Epidermophyton floccosum, Trichophyton mentagrophytes are the most common species that cause infection. The severity of the disease is affected by the fungus species and the characteristics of the host. The number and activity of sebaceous glands in a certain part of the body, disruption of the skin barrier, macerated skin, and the immunological state of the host are effective in the formation and severity of the disease. Additionally, temperature and humidity are also effective in the development of dermatophyte infection.

The 1st symptoms of superficial fungal infections of the skin are usually erythema and itching. The characteristic lesion is plaque lesions with sharp borders, scaly, active margins that may contain pustules or vesicles.[2]

Topical antifungals are the 1st-line treatment for uncomplicated superficial fungal infections such as tinea corporis, tinea pedis, and tinea cruris. The most important side effect is irritant or allergic contact dermatitis caused by the carriers and alcohol contained in the drug. Combinations with topical corticosteroids may be an option to reduce the rate of side effects and quickly control symptoms, especially in cases where itching and inflammation are severe.[3]

Potential side effects of topical steroids such as skin atrophy, striae, telangiectasia, folliculitis, acne, and development of tinea incognito limit their use.[4] The effectiveness of the combination of topical steroids with topical antifungals has been demonstrated in some studies.[5,6] We planned to research by comparing patients using topical terbinafine for dermatophyte infections with patients using mometasone furoate-terbinafine combination in terms of symptoms and examination findings, and to observe the contribution and side effects of short-term topical corticosteroid use to the treatment.

MATERIAL AND METHODS

In our study, 62 adult patients over the age of 18, who were clinically diagnosed with tinea corporis, tinea pedis, tinea manuum, and tinea cruris and who applied to the dermatology outpatient clinic of Alanya Training and Research Hospital between May 2023 and December 2023, were retrospectively examined. Patients who had not received any previous treatment for the current dermatophyte infection and had no complications (cellulitis, tinea incognito, etc.) were included in the study. Patients who used topical terbinafine 1% cream twice a day as monotherapy for 3 weeks were assigned to be group 1 (monotheraphy group) . Patients who continued treatment with topical terbinafine twice a day for 2 weeks; after applying the mometasone furoate-terbinafine combination twice a day for 10 days were assigned to be group 2 (combination group).

The effectiveness of the treatment in patients clinically diagnosed with dermatophyte infection was evaluated according to symptoms (itching, burning) and clinical findings (erythema, scale, exudation, vesicle, pustule). Symptoms and findings were evaluated with four point scale: 0=None, 1=Mild, 2=Moderate, 3=Severe. Data were analyzed with IBM SPSS V23. Compliance with normal distribution was examined with the Shapiro-Wilk Test. Mann-Whitney U Test was used to compare variables that did not comply with normal distribution according to groups. Yates correction, Fisher's exact test, Pearson chi-square test were used to compare categorical variables according to groups. Wilcoxon test was used to compare symptoms and findings before and after treatment. Analysis results were presented as frequency (percentage) for categorical variables, and as mean±standard deviation and median (minimum-maximum) for quantitative variables. The significance level was taken as $p<0.05$.

The approval of our study was obtained from the Clinical Research Ethics Committee of Alanya Alaadin Keykubat University Faculty of Medicine (date: December 13, 2023; no:18-02). Declaration of Helsinki, the Patient Rights Act, and ethical norms. Informed consent form was taken from all patients participating in the study.

RESULTS

62 adult patients (39 females, 23 males) over 18 years of age were included in the study. 36 patient was treated with combination therapy and 26 patient was treated with monotheraphy. There was no statistically significant difference between the average age values of the participants according to groups (p=0.909). While the average age of treated with monotherapy group is 41, the average age of treated with combination therapy group is 41.31. The distribution of dermatophyte infection types according to groups did not show a statistically significant difference (p=0.306). The severity of burning and itching symptoms before treatment was not statistically different between groups. While no statistically significant difference was observed between the groups treated with monotherapy and combination therapy in terms of the severity of scale, exudation, vesicle, and pustule before treatment, erythema was higher in the group treated with combination therapy before treatment than in the group receiving monotherapy. These findings are summarized in the Table 1. When the symptoms of the patients were evaluated after treatment, no significant difference was found in itching and burning scores between the 2 groups. Symptoms were controlled after treatment in both groups (Table 2). When post-treatment findings were evaluated, no difference was found in pustule, vesicle, scale, erythema, and exudation scores. Clinically, both groups achieved well-being (Table 3).

When the time to control the symptoms of the patients during the treatment is compared, the median time for symptoms to go away in the group treated with monotherapy is 14 days, while the median time

TABLE 1: Signs and symptoms before treatment.

	Group		
	Monotheraphy (terbinafine)	Combination (terbinafine+ mometasone furoat)	p value*
Erythema			
None	8 (30.8)	1 (2.8)	<0.001*
Mild	9 (34.6)	4 (11.1)	
Moderate	5 (19.2)	21 (58.3)	
Severe	4 (15.4)	10 (27,8)	
Scale			
None	4 (15.4)	11 (30.6)	0.159*
Mild	10 (38.5)	13 (36.1)	
Moderate	6 (23.1)	10 (27.8)	
Severe	6 (23.1)	2 (5.6)	
Exudation			
None	17 (65.4)	23 (63.9)	0.989*
Mild	5 (19.2)	7 (19.4)	
Moderate	3 (11.5)	5 (13.9)	
Severe	1 (3.8)	1 (2.8)	
Vesicle			
None	19 (73.1)	29 (80.6)	0.604*
Mild	4 (15.4)	2 (5.6)	
Moderate	1 (3.8)	1 (2.8)	
Severe	2 (7.7)	4 (11.1)	
Pustule			
None	22 (84.6)	32 (88.9)	0.492*
Mild	4 (15.4)	3 (8.3)	
Severe	0 (0)	1 (2.8)	
Burning			
None	11 (42.3)	11 (30.6)	0.607*
Mild	6 (23.1)	14 (38.9)	
Moderate	5 (19.2)	6 (16.7)	
Severe	4 (15.4)	5 (13.9)	
İtching			
None	3 (11.5)	3 (8.3)	0.599*
Mild	8 (30.8)	12 (33.3)	
Moderate	9 (34.6)	8 (22.2)	
Severe	6 (23.1)	13 (36.1)	

*Pearson chi-square test.

TABLE 2: Post-treatment symptoms.

	Monotheraphy (terbinafine)		Combination (terbinafine+mometasone furoat)		
	None	Mild (1 puan)	None	Mild (1 puan)	p value**
İtching	21	5	33	3	0.262**
Burning	24	2	36	0	0.172**

**Fisher's exact test.

TABLE 3: Findings after treatment.

		Monotheraphy (Terbinafine)	Combination (Terbinafine+ mometasone furoat)	p value**
Erythema	None	23 (88.5)	31 (86.1)	1.000**
	Mild	3 (11.5)	5 (13.9)	
Scale	None	24 (92.3)	36 (100)	0.172**
	Mild	2 (7.7)	0 (0)	
Exudation	None	26 (100)	36 (100)	---
Vesicle	None	26 (100)	36 (100)	---
Pustule	None	26 (100)	36 (100)	---

**Fisher's exact test.

TABLE 4: Duration of symptom resolution.

	Monotheraphy (Terbinafine)		Combination (Terbinafine+mometasone furoat)		
	Median	X̄±SD	Median	X̄±SD	p value***
Duration of symptom resolution (itching and burning) (days)	14 (10-16)	13.69±1.74	7 (3-14)	8.72±3.4	**<0.001**

***Mann-Whitney U Test. SD: Standard deviation.

for symptoms to go away in the group treated with combination therapy is 7 days ($p<0.001$) (Table 4).

No side effects were observed in any of the patients during the treatment process.

DISCUSSION

Terbinafine is an allylamine antifungal with fungicidal effect. It inhibits ergosterol synthesis by inhibiting squalene epoxidase. Topical terbinafine treatment is used effectively as monotherapy in dermatophyte infections. It has also been effective in treating Candida infections. In studies, over 80% mycological and clinical response was achieved when topical terbinafine was used once or twice a day as monotherapy for 2 weeks.[7]

Mometasone furoate is a high-potency topical corticosteroid. Although it has high anti-inflammatory activity and a long duration of effect, it has a low rate of systemic side effects and skin atrophy. Studies have shown that no side effects such as skin atrophy and telangiectasia have been observed in long-term use without occlusion once a day. Short-term use is recommended to reduce risk.[4]

The use of topical steroids in superficial fungal infections is a controversial issue due to misuse by patients. Many clinicians avoid using corticosteroid combinations. Insufficient information about the use of corticosteroids may result in patient abuse of the drug and excessive or misuse of the drug. In contrast, in Europe, where laws and regulations controlling the production and sale of drugs are strictly enforced, expert opinion strongly supports the use of antifungal-corticosteroid combinations for the treatment of inflammatory superficial fungal infections. It is recommended to apply an antifungal-corticosteroid combination for 1-2 weeks at the beginning of treatment, followed by a suitable antifungal alone (except for immunosuppressed patients). When topical corticosteroids are used correctly and according to recommendations and guidelines, side effects are rare. Misuse and overuse of corticosteroid combinations can be avoided by educating patients, physicians and pharmacists who play a role in treatment.[1-3]

Patients expect a rapid clinical response due to the severe erythema and itching in tinea cruris and tinea pedis infections. Findings such as erythema, vesicles, exudation, maceration and symptoms such as itching and burning are the most common complaints of patients. This condition not only causes serious discomfort to patients, but also causes deterioration in the skin barrier, leading to the development of secondary bacterial infection, the spread of fungal infection through contamination of the hands, and also reduces the patient's compliance with treatment. Short-term combination therapy provides control of inflammatory symptoms in a short time, increases confidence in the treatment and the clinician, and prolongs the duration of treatment. Breaking the itch-scratch cycle will also prevent the spread of infection through contamination. Severe inflammatory conditions cause delayed healing of the infection, its spread, and the development of complications such as secondary bacterial infections.

In our study, clinical signs and symptoms of all patients in both groups completely improved, and mild erythema and squama were detected in a small number of patients at the end of treatment. In direct microscopic examination with potassium hydroxide in these patients, fungal hyphae were not detected. We think that the scales were detected due to xerotic skin. We think that erythema may have developed due to the shoes used by the patient, activity before the examination, or sweating.

CONCLUSION

As a result of our study, a faster clinical response was obtained in the group receiving combination therapy than in the group receiving monotherapy. By reducing inflammation and itching, topical corticosteroids can prevent the spread of infection and reduce the risk of secondary infection, ultimately leading to faster and more desirable clinical outcomes.

Our study is a single-center and retrospective study. It needs to be supported by multicenter and prospective studies with a higher number of patients. There are no clinical studies with the new combination mometasone furoate-terbinafine. Terbinafine is an effective option for superficial fungal infections. However, we think that short-term combination therapy will be beneficial in patients with severe itching and inflammation symptoms. Afterwards, treatment can be continued with topical terbinafine. Rapid improvement of symptoms increases confidence in treatment and increases the duration of treatment. According to the results of our study, mometasone furoate-terbinafine combination can be used as a fast, effective and safe alternative in superficial fungal infections.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Authorship Contributions

Idea/Concept: *Esra Arı, Deniz Evliyaoğlu;* ***Design:*** *Esra Arı;* ***Control/Supervision:*** *Deniz Evliyaoğlu;* ***Data Collection and/or Processing:*** *Esra Arı, Deniz Evliyaoğlu;* ***Analysis and/or Interpretation:*** *Esra Arı;* ***Literature Review:*** *Esra Arı;* ***Writing the Article:*** *Deniz Evliyaoğlu, Esra Arı;* ***Critical Review:*** *Esra Arı, Deniz Evliyaoğlu;* ***References and Fundings:*** *Esra Arı.*

REFERENCES

Havlickova B, Friedrich M. The advantages of topical combination therapy in the treatment of inflammatory dermatomycoses. Mycoses. 2008;51 Suppl 4:16-26. Erratum in: Mycoses. 2009;52(1):96. PMID: 18783560.

2. Gül Ü. Derinin Yüzeyel dermatofit enfeksiyonlari [Superficial dermatophyte infections]. Ankara Med J. 2014;14(3):107-13. https://doi.org/10.17098/amj.08193

3. Schaller M, Friedrich M, Papini M, Pujol RM, Veraldi S. Topical antifungal-corticosteroid combination therapy for the treatment of superficial mycoses: conclusions of an expert panel meeting. Mycoses. 2016;59(6):365-73. PMID: 26916648.

4. Spada F, Barnes TM, Greive KA. Comparative safety and efficacy of topical mometasone furoate with other topical corticosteroids. Australas J Dermatol. 2018;59(3):e168-e174. PMID: 29411351; PMCID: PMC6099284.

5. Veraldi S, Persico MC, Schianchi R. Isoconazole nitrate vs isoconazole nitrate and diflucortolone valerate in the treatment of tinea inguinalis: results of a multicenter retrospective study. J Drugs Dermatol. 2012;11(11):e70-3. PMID: 23135097.

6. Olkhovskaya KB, Perlamutrov Y. Step-wise treatment of athlete's foot (tinea pedis) using isoconazole combined with a corticosteroid followed by isoconazole alone. Mycoses. 2008;51 Suppl 4:50-1. PMID: 18783571.

7. Krishnan-Natesan S. Terbinafine: a pharmacological and clinical review. Expert Opin Pharmacother. 2009;10(16):2723-33. PMID: 19874252.