Journal of Research in Clinical Medicine

J Res Clin Med, 2020, 8: 32
doi: 10.34172/jrcm.2020.032
https://jrcm.tbzmed.ac.ir

TUOMS PRESS

Original Article

Treatment of erythrasma: A double-blinded randomized controlled trial on the clinical application of clotrimazole and sertaconazole

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Article info

Article History:
Received: 27 Apr. 2020
Accepted: 30 June 2020
e-Published: 18 Aug. 2020

Keywords:
- Clotrimazole
- Erythrasma
- Exfoliation
- Gram-positive bacterial infections
- Sertaconazole

Abstract

Introduction: Topical clotrimazole and sertaconazole may be effective in the treatment of erythrasma, a superficial skin infection developed by a group of aerobic microorganisms. This study aimed to compare the effect of clotrimazole and sertaconazole on erythrasma.

Methods: In this double-blinded randomized controlled trial, 40 age-matched patients with confirmed erythrasma diagnosis were divided into two equal groups; one treated with topical 2% sertaconazole and the other with topical 1% clotrimazole. The clinical features of erythrasma were monitored for two weeks (baseline, day 7, and day 14) and compared. Data were analyzed using SPSS v16 software.

Results: On day 7, in clotrimazole group, reduction in erythema and pigmentation were more prominent in comparison to the sertaconazole group ($P=0.02$ and $P=0.005$, respectively), but there was no difference considering scaling reduction between groups. On day 14, in terms of erythema reduction, the clotrimazole group performed better compared to the sertaconazole group ($P=0.04$). Both groups had a significant reduction in erythrasma symptoms during their treatment period ($P<0.001$).

Conclusions: Regarding the results, both clotrimazole and sertaconazole are effective medications for erythrasma treatment. Still, clotrimazole has a faster recovery process in comparison to sertaconazole, but no significant difference is observed in outcomes after two weeks of treatment.

Introduction

Skin diseases contain a broad spectrum of disorders, varying from pyogenic skin infections to malignant melanomas.[1,2] The lack of hygiene, along with other predisposing factors like genetics and climatic characteristics, can intensify the spread of skin disorders, especially in public environments like schools and prisons.[3,4] For example, opportunist fungi such as *Malassezia, Candida, Trichosporon* and *Aspergillus* can result in skin and superficial fungal infections. The prevalence and the manifestations of these diseases are dependent on environmental conditions, patients' lifestyle and socio-economic status of the community.[5] Hence, they can be considered limited and preventable disorders.[6]

Erythrasma is a mild skin infection which is identified as red, flat and without secretion spots. It is mainly observed in the skin of wrinkled and creased parts of the body, like the groin, armpit and fingers, usually as a result of *Corynebacterium minutissimum* infection.[7-9] The etiology of erythrasma is not entirely clear, but the involved microorganisms – especially in toe cleft infections – are supposed to be part of the normal body flora.[10] Azole antifungal drugs, such as clotrimazole and sertaconazole, usually take significant steps towards the treatment of erythrasma.[11,12] Erythromycin and tetracycline are other acknowledged alternative treatments.[8,13]

Regarding the progressive quiddity of skin diseases like erythrasma, choosing the right treatment strategy can lead to lower costs for the health system and faster resolution for the patients.[14] On the other hand, eradicating infectious skin diseases from a community is only possible under the circumstances of rapid and firm therapeutic confrontation.[15] Concerning the full range of treatment options, there is no general agreement on the treatment protocol of erythrasma.[16] Therefore, this study was conducted to discuss and compare the effectiveness of clotrimazole and sertaconazole as the available drug choices in the treatment of erythrasma.

Methods

Study design and population

In this double-blinded randomized controlled trial, 40 patients among the patients referred to the dermatology

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department during a one-year period, with a confirmed clinical and bacteriological diagnosis of erythrasma, were included in the study. Patients with predisposing systemic disorders (such as diabetes), treatment history during the past one month, allergy to sertaconazole and clotrimazole, and patients experiencing adverse drug effects were excluded from the study. Included patients were allocated to two equal groups using the simple random method.

In one group, topical 2% sertaconazole cream (Ferrer Pharma, Spain) and in the other group, topical 1% clotrimazole cream (Sobhan Darou Pharmaceutical Co., Iran) was administered two times per day for two weeks. The patients were examined in three time-points; baseline, day 7 and day 14. The examination in these time points included assessment of erythema, scaling and pigmentation. The changes in these features were evaluated in comparison to the baseline condition (i.e., baseline vs. day 7 and baseline vs. day 14), which were categorized into no change, partial resolution or complete resolution. This examination was performed by two dermatologists separately, and any disagreement was solved by discussion. At last, the resolution of disease was compared among different time points, and also between the groups.

Statistical analysis

Data were analyzed using SPSS v16 Statistics software and reported as mean ± standard deviation, frequency and percentage. Quantitative and qualitative variables were analyzed using independent *t* test, paired *t* test and chi-square test respectively. A *P* value of less than 0.05 was considered significant.

Results

All the 40 patients enrolled in the study were divided into equal two groups, each one consisted of 19 women and one man. The mean age for the group receiving sertaconazole and clotrimazole was 40.4 ± 11.55 (minimum = 22, maximum = 63) years old and 34.95 ± 10.86 (minimum = 16, maximum = 56), respectively. There was no significant difference between the mean age of the groups ($P = 0.13$). The remission process was observed through two weeks by monitoring the changes in erythema, pigmentation and scaling. The changes after one week of following the treatment protocols are summarized in Table 1 and the changes after two weeks of treatment are available in Table 2.

When each group was investigated individually to compare the assessment in different time points, both sertaconazole and clotrimazole groups performed well in reducing erythema, pigmentation and scaling through time (day 0 vs. day 7, day 0 vs. day 14, and day 7 vs. day 14; $P = 0.001$)

Discussion

General hygiene is considered the most crucial factor in the prevention and treatment of dermatologic conditions. Lack of hygiene in developing communities can result in the higher development of skin diseases, depending on the region and time. Thus, most of the therapeutic

Table 1. Changes of skin manifestations after one week of following the treatment protocols

Manifestation	Resolution status	Sertaconazole (n = 20)	Clotrimazole (n = 20)	*P* value
Erythema	No change	12 (60%)	5 (25%)	0.02
	Partial resolution	8 (40%)	15 (75%)	
	Complete resolution	-	-	
Pigmentation	No change	16 (80%)	7 (35%)	0.005
	Partial resolution	4 (20%)	13 (65%)	
	Complete resolution	-	-	
Scaling	No change	9 (45%)	4 (20%)	0.17
	Partial resolution	11 (55%)	15 (75%)	
	Complete resolution	-	1 (5%)	

Table 2. Changes of skin manifestations after two weeks of following the treatment protocols

Manifestation	Resolution status	Sertaconazole (n = 20)	Clotrimazole (n = 20)	*P* value
Erythema	No change	1 (5%)	1 (5%)	0.04
	Partial resolution	9 (45%)	2 (10%)	
	Complete resolution	10 (50%)	17 (85%)	
Pigmentation	No change	2 (10%)	1 (5%)	0.15
	Partial resolution	16 (80%)	12 (60%)	
	Complete resolution	2 (10%)	7 (35%)	
Scaling	No change	1 (5%)	1 (5%)	0.25
	Partial resolution	10 (50%)	5 (25%)	
	Complete resolution	9 (45%)	14 (70%)	

protocols are based on suppression and eradication of the acting microorganisms, leading to a fewer spread of the disorder through the community. Notwithstanding that erythrasma is no exception either, the available pieces of evidence on treatment protocols are incomplete and very few studies have compared the effects of available drugs.

In a double-blinded trial designed to compare the effect of clotrimazole, Whitfield's ointment and nystatin ointment on the treatment of several skin disorders, clotrimazole was observed as a suitable treatment option for erythrasma, with the same efficacy as Whitfield's ointment.[17] Other studies have also supported the results.[18] Another research with the same design suggests that miconazole is a potential treatment for erythrasma with the same efficacy of clotrimazole.[19] Another study to assess the clinical efficacy of clotrimazole demonstrated that both cream and solution forms of this drug are useful on skin infections. Also, the best results were observed in patients suffering from erythrasma.[20] A study on efficacy and safety of both clotrimazole ointment and solution, with a sample of 1361 patients reported side effects in 2.7% of patients, but a significant efficacy on the treatment of several skin disorders.[21]

Although a review published on the management of cutaneous erythrasma describes the effect of clotrimazole on erythrasma as "poor and inconclusive",[8] many other studies support the point that clotrimazole can be considered as a drug of choice for treating erythrasma.[22-25]

On the other hand, sertaconazole has been used less as a drug of choice for treatment of erythrasma, but potent pieces of evidence support this opinion. For example, a study conducted on dermatitis features and treatments suggests that applying sertaconazole on the inflamed area twice a day for 14 days causes more than 50% decrease in clinical signs.[26] However, some studies rule this drug out by reporting low or no efficacy on treating erythrasma with sertaconazole.[12,27] This can be due to the late manifestation of drug effects, as a two-month window is usually considered to be necessary for sertaconazole to present the remission.[28]

Other drugs are useful at the treatment of erythrasma either, as many studies support the prescription of systemic tablets or local ointments.[29] In a double-blinded, placebo-controlled, randomized trial conducted on a group of 151 patients, the effects of treatment with clarithromycin and erythromycin were compared, and the results showed that clarithromycin was significantly more effective than erythromycin in 48 hours. Still, no significant difference was reported after 7 and 14 days.[16] Tetracycline and chloramphenicol are other available drug choices, but the effect of chloramphenicol on bone marrow, which could lead to various blood disorders, narrows down the usage of this drug.[8,30]

In overall, current study data supported the previous idea that both clotrimazole and sertaconazole are useful in the treatment of erythrasma. This study, discussing a novel topic on the treatment of erythrasma, had a proper sample size, and unlike previous studies, the changes were reported precisely at the end of each step. However, more up-to-date studies with proper sample size are needed to discuss the explicit results. Further studies may be conducted on lesion progression and changes in drugs' efficacies, with a longer duration of study or higher sample size, relying on the survey of drugs' clinical application.

Conclusion

The results of the current study showed that both clotrimazole and sertaconazole are effective in the treatment of erythrasma, but clotrimazole had a faster and more prominent therapeutic effect on erythrasma compared to sertaconazole. However, the ultimate decision is made upon the costs and availability of the drugs. It is suggested that further studies be conducted in higher populations and more extended follow-up period.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethics Approval

The study design was approved by the Ethics Committee of Tabriz University of Medical Sciences and according to the Declaration of Helsinki. The information of patients was anonymous, and the patient could abandon the study on personal desire at any stage. This study is registered at the Iranian Registry of Clinical Trials (identifier: IRCT201202142581N3). Written consent was obtained from all patients included in the study.

Authors' contribution

HHG and SH designed the study; SH, ASM and MSH gathered and analyzed the data; ASM and MSH drafted the manuscript; HHG and SH revised the manuscript; HHG supervised the study. All authors have read and approved the final version of the manuscript.

Acknowledgements

We would like to appreciate the contribution of Reza Piri M.D. in drafting the manuscript. This study is based on a thesis registered at Medical faculty of Tabriz University of Medical

Study Highlights

What is current knowledge?

- There is no uniform protocol available on the treatment of erythrasma. Azole antifungals are potentially effective agents in the management of erythrasma.

What is new here?

- Clotrimazole and sertaconazole are both effective in the treatment of erythrasma, but compared to sertaconazole, clotrimazole has a faster and more significant therapeutic effect.

Sciences, Tabriz-Iran.

Funding
This study was funded by Tabriz University of Medical Sciences.

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