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Comparing the Clinical Efficacy of Topical Application of Virgin Coconut Oil and 1% Clotrimazole Cream as an Adjuvant to Systemic Antifungal in Chronic Dermatophytoses- a Randomized Controlled Trial

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Abstract

Background: Dermatophyte infections have become a common entity with a prevalence ranging from 36.6-78.4%. Majority of the patients are from low socioeconomic background who favour topical treatment. High treatment costs of antifungal medication and consequent poor compliance have given rise to the need of an effective and economical topical preparation.

Objectives: To compare efficacy of topical 1% clotrimazole versus virgin coconut oil application as an adjuvant to systemic antifungals in dermatophytosis.

Materials and Methods: A total of 100 patients presenting to the dermatology outpatient department and diagnosed with tinea infection clinically and by potassium hydroxide mount were taken up for the study. The patients were randomized into two groups with 50 patients in each group. One group received virgin coconut oil while the other group received 1% clotrimazole cream twice daily application as the topical preparation. Mycological cure was assessed by potassium hydroxide mount and clinical improvement was assessed objectively by severity score for itch, changes in clinical signs and symptoms and subjectively by Dermatology Life Quality Index questionnaire. Statistical analysis was analyzed using SPSS software version 17.

Results: Virgin coconut oil and 1% Clotrimazole had equivocal response after 12 weeks of treatment with respect to potassium hydroxide mount positivity, itch severity, clinical improvement and changes in Dermatology Life Quality Index scores when used along with systemic antifungal.

Conclusion: Virgin coconut oil can be easily used as a topical emollient and antifungal preparation along with systemic antifungals in the treatment of dermatophytosis.

Key words: Clotrimazole; Dermatophyte; Dermatophytoses; Tinea; Virgin coconut oil

Introduction

Dermatophytosis has assumed big significance in developing countries like India, where prevalence for dermatophytosis now ranges from 36.6–78.4%.[1]
A shift in the clinical presentation has been observed due to increase in the use of over-the-counter medication which mostly consists of topical corticosteroid creams alone or in combination with an antifungal agent. This has resulted in chronicity and unusual morphology of presenting lesions.

Expensive prolonged treatment of dermatophytos is in resource poor settings like that of India, usuallyleads to poor compliance. This further propagates the vicious cycle of recurrentand recalcitrant tinea infection. The treatment recommended in standard textbooks

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appears to be out of sync to current clinical scenario. It has become essential to research for moreeffective, practical and affordable treatment modalities that are research and evidence based.1 1% Clotrimazole has been used in past studies as a comparative agent for newer topical antifungal molecules.[2-5]

Hence this study was planned to compare the efficacy and safety of topical virgin coconut oil against 1% clotrimazole in cases of dermatophytosis. Virgin coconut oil has a long been used as a treatment modality in traditionaland ayurvedic medicine. It is easily accessible, cheap and effective against.[6] Thus, virgin coconut oil may provide dual benefit of being an emollient as well as an antifungal agent.

Materials and Methods

The present study was conducted in the Department of Dermatology and Microbiology, of Shri Ram Murti Smarak Medical College in northern India adjoining Nepal, over a duration of one and half year from June 2020 to November 2021. This was an open label hospital-based randomised study on patients presenting with dermatophytos is to the Department of Dermatology.

Patients of either gender, aged 18 years and above, clinically diagnosed with dermatophytos is by a dermatologist and in whom potassium hydroxide (KOH)mount demonstrated septate fungal hyphae were included in this study.

Informed written consent and willingness for follow up were other prerequisites for inclusion in this study. Pregnant and lactating females were excluded. Patients were randomly divided into two groups; group A patients were given topical 1% clotrimazole cream and group B patients were given virgin coconut oil as the topical preparation. Patients were randomized using random number generator available online7 into two sets – set A and set B. Patients were allotted a number consecutively as and when they presented to the dermatology OPD. If a patient dropped out from the study due to any reason, another patient was recruited till 50 patients from both the groups completed the study.

Institution ethical committee gave the ethical clearance for the present study. Trial was registered with Clinical Trials Registry India(CTRI) (reference number: CTRI/2020/05/025375). The sample size was calculated according to prevalence (p) of 27.6 %.8Using the formula n (sample size) = (1.96)^2 x p x (1-p)/E^2 and absolute error of E= 10% minimum sample size came out to be 76.73~77. After adding 10% for non response we got sample size of 86 which was divided into two groups with 43 each.

Patients were evaluated at baseline, 4, 8 and 12 weeks of treatment. Changes in clinical signs and symptoms and tolerability to treatment were recorded. The total study period encompassed 12 weeks. Mycological diagnosis by KOH mount was performed at baseline and repeated at each subsequent visit i.e., 4,8,12 weeks. All the study patients were given the assigned topical preparation along with same systemic treatment consisting of, terbinafine 250 mg single daily dosing and levocetirizine 5mg single daily dosing at night. Terbinafine was selected as the drug for systemic treatment as it was considered as first line of treatment in major standard textbooks at the time of this study, besides itraconazole is known to have more drug interactions.[9]

Clinical efficacy was monitored and recorded on each subsequent visit i.e., baseline, 4, 8, and 12 weeks. Tolerability to treatment was recorded subjectively and was graded as 1: very good, 2: good, 3: acceptable, 4: bad.[10] Mycological cure was assessed by KOH mount at baseline and then at week 12 of treatment. Dermatology Quality Of Life (DLQI) questionnaire was used at first visit and then repeated at 12 weeks to assess effect of disease on patient's quality of life and consequent change after treatment if any.

Statistical analysis was done through the SPSS software for windows, version 17.0(SPSS, Chicago, Illinois). Continuous variables were presented as mean ± SD, and categorical variables were presented as absolute numbers or percentage. Data was checked for normality. Unpaired t-test was used for assessingnormally distributed continuous variables and Mann-Whitney U test for not normally distributed variables. Paired t-test was used for the comparison. Categorical variables were analysed using either the chi-square test or Fisher's exact test as appropriate and proportion test for the comparison of pre to post categorical data. A p value of less than 0.05 was taken to signify a significant difference.

Results

A total of 100 patients i.e., 50 in each group were included in the final analysis for this study. Minimum age of the patient was 18 years as per the inclusion criteria and maximum age recorded was 65 years. As per Table 1 group A and B were comparable at baseline, on various demographic and clinical parameters. All the patients of superficial fungal infection complained of itching (100% in both groups) followed by redness (98% and 96%), scaling (98% and 100%) burning sensation (80% and 62%) and lastly pigmentation (42% and 48%) in group A and B respectively(Table 2)(Figure 1- 4).

A progressive decline in erythema, scaling, itching and peripheral active margin was seen within group A ($p<o.oo1$) as well as within group B($p<0.001$), which was statistically significant. However, no significant difference was seen within group A ($p = 0.095$) in case of papules, pustules, and vesicles. Now, when both the groups were compared to each other no significant difference was seen in the above-mentioned clinical parameters(Table 2). Similarly, at 12 weeks KOH mount positivity (septate fungal hyphae seen on microscopy) declined significantly in both group A and B separately ($p<0.001$ and $p<0.001$). However intergroup

comparison revealed no significant difference (p = 0.487)(Table 3).

Maximum of the patients had good tolerability for the treatment in both the groups with 66% and 52% patients recording tolerability score of 1 (very good) at week 12 for group A and B respectively. No side effects were reported by the patients in group A. Burning sensation, erythema and/or pustules were reported as the side effects among 10% patients in group B of this study. All of these side effects were tolerable as none of the patients in group B stopped treatment despite the side effects.

As per table 4, both study groups showed a very large effect on the patient's quality of life. Post treatment at week 12 DLQI scores showed an improvement of more than 2 bands (from very large effect to no effect). The decline was statistically significant at week 12 of treatment within each group ($p<0.001$). Again, no statistically significant difference was seen between the two groups ($p= 0.419$).

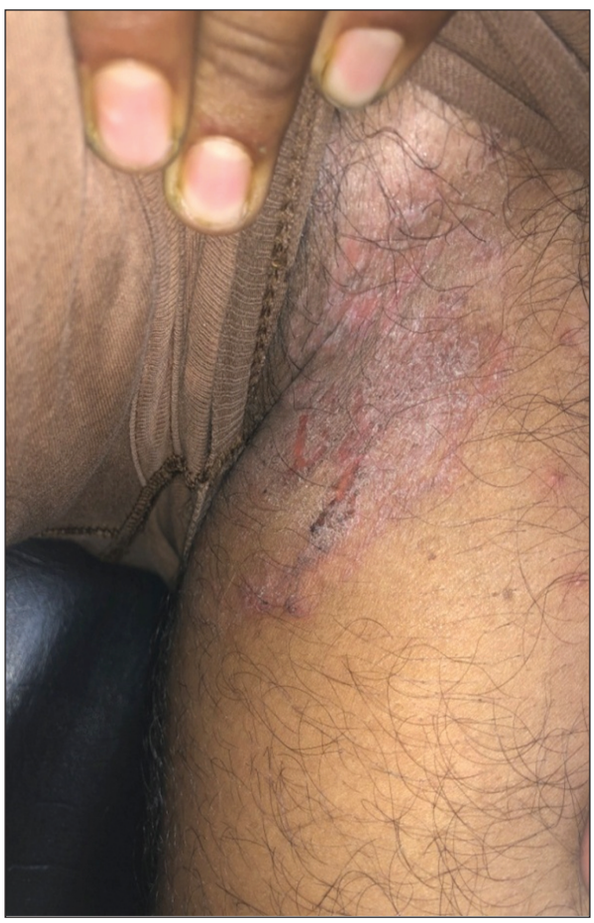

Figure 1 : Pre-treatment 1% clotrimazole group A at baseline

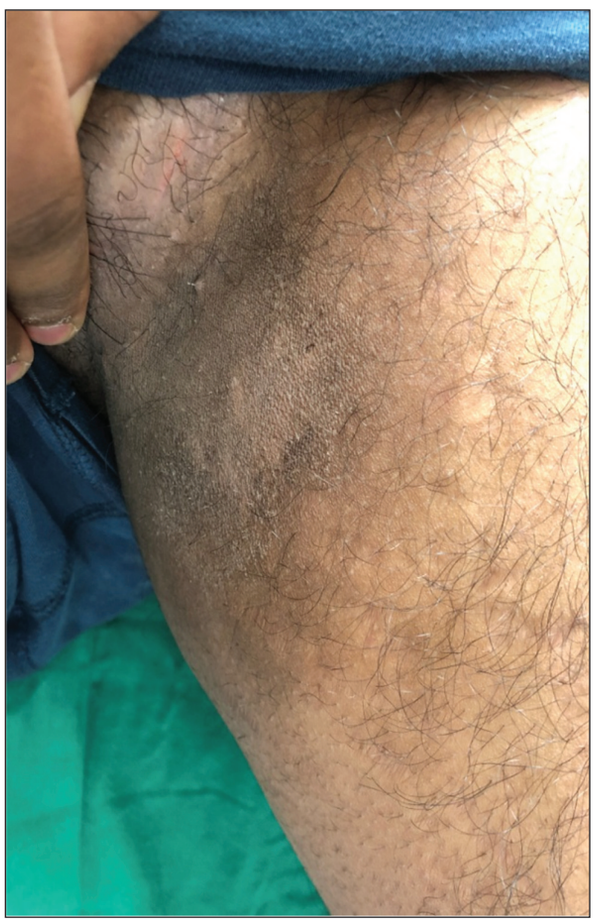

Figure 2 : Post-treatment 1% clotrimazole group A after 12 weeks of treatment

	GROUP A	GROUP B	P VALUE
Age	30.08 ± 11.08	30.20 ± 13.07	0.961
Weight (kg)	66.10 ± 9.70	65.62 ± 11.47	0.822
Height (cm)	165.02 ± 7.89	165.72 ± 16.83	0.791
BMI	24.35 ±5 3.76	24.43 ± 3.61	0.918
Gender Female	19	17	0.677
Male	31	33	
Duration months	4.57 ± 3.33	5.02 ± 6.06	0.961
Family History	44.0%	40.0%	0.534
Animal Contact	48.0%	54.0%	0.548

History of medication	96.0%	100.0%	0.495
Topical corticosteroid use	92.0%	84.0%	0.678
Married	60.0%	58.0%	0.360
Unemployed	52.0%	56.0%	0.060
Education status			
Illiterate	14.0%	4.0%	0.547
Primary	20.0%	20.0%	
Secondary	30.0%	36.0%	
Post High School	6.0%	10.0%	
Graduate	30.0%	24.0%	
Post Graduate	0.0%	6.0%	
Hygienic Status			
Average	38.0%	44.0%	0.750
Good	14.0%	10.0%	
Poor	48.0%	46.0%	
Body Surface Area (%)	4.74 ± 2.73	5.18 ± 2.30	0.386

Table 1 : Demographic features in Group A andGroup B

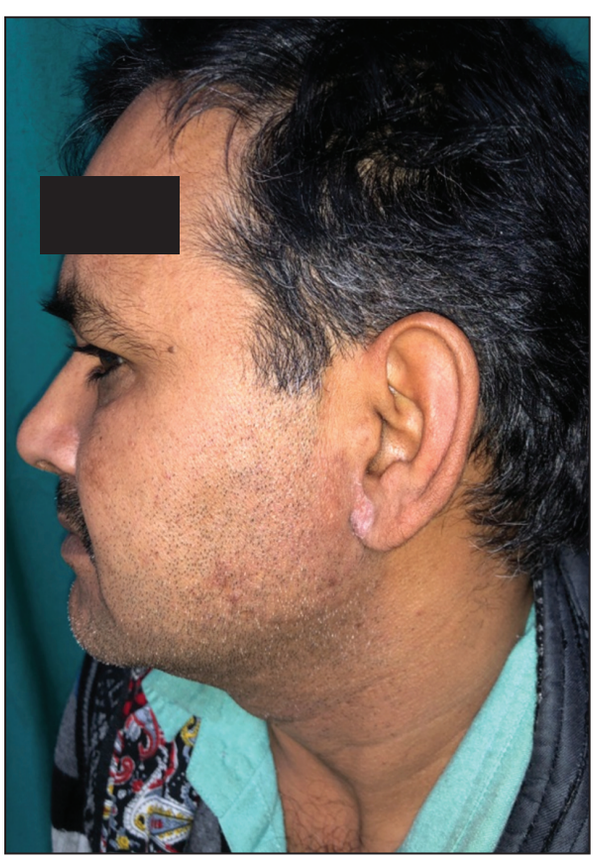

Figure 3 : Pre-treatment inCoconut oil group B at baseline

Figure 4 : Post-treatment Coconut oil group A after 12 weeks of treatment

Clinical feature	Baseline		P Value	Week 12		P Value
	Group A	Group B		Group A	Group B	
Erythema	98.0%	96.0%	1.000	12.0%	10.0%	1.000
Scaling	98.0%	100.0%	1.000	16.0%	24.0%	0.317
Papules/ Pustules/ Vesicles	16.0%	22.0%	0.444	4.0%	2.0%	1.000
Peripheral Active Margin	96.0%	98.0%	1.000	2.0%	4.0%	1.000
Pigmentation	42.0%	48.0%	0.546	94.0%	96.0%	1.000
Itching (scoring 1-10)	6.12 ± 1.96	6.38 ± 1.68	0.477	1.36 ± 1.01	1.64 ± 1.29	0.229

Table 2 : Clinical findings in Group A and Group B

KOH Mount (Positive)	Group A	Group B	P Value
	Frequency %	Frequency %	
Baseline	100.0%	100.0%	-
Week 12	6.0%	12.0%	0.487
Baseline - week 12(within group) p-value	<0.001	<0.001	

Table 3 : KOH mountin Group A and Group B

DLQI	Group A	Group B	P Value
	Mean ± SD	Mean ± SD	
Baseline	17.32 ± 4.99	15.56 ± 5.42	0.094
4 Weeks	8.10 ± 3.34	7.86 ± 3.70	0.734
12 Weeks	3.90 ± 2.53	3.46 ± 2.88	0.419
Baseline - week 12 (within group) p-value	<0.001	<0.001	

Table 4 : DLQI scoresinGroup A and Group B

Discussion

Dermatophytes cause superficial fungal infection of the skin and a steady rise in the prevalence has been noted in the recent years.[1] It is a sad scenario since most of the affected individuals do not have the knowledge or the resources for the correct treatment, and largely rely on over-the-counter topical formulations for quick relief. The local immune suppression from the use of topical steroids may promote widespread tinea infection with a chronic course and modified clinical presentation.[10, 11] The purpose of this study was to compare topical clotrimazole against virgin coconut oil in patients of dermatophytosis. The systemic treatment was kept same in both the groups as only the topical agents were being compared.

A progressive decrease in the score for itch from baseline score to 12th week of treatment in the present study was similar to that reported by Monica *et al*[12] in their study. Improvements were seen in erythema, scaling, papules, and vesiculation and peripherally active margin in the present study, with topical clotrimazole usage. These findings are similar to the findings reported by Del palacio *et al.*,[3] and Oyeka *et al*.[13] McVie *et al*[14] reported clinical improvement after 8 weeks of treatment with 1% clotrimazole in 96% of the study patients with respect to scaling, erythema, itching, and maceration. In the review by Sawyer *et al.*,[15] of various trials done with respect to clotrimazole use in dermatophyte infection, significant clinical improvement as well as mycological cure was seen.

However, in the present study topical application of virgin coconut oil showed comparable efficacy to 1% clotrimazole. These two compounds have not been

compared in the past, though S. Sheidaei *et al.*,[16] compared virgin coconut oil against clotrimazole cream topically in patients of candidiasis. Good response to itching and burning was seen clinically with both clotrimazole and coconut oil. The mycological cure rate was also comparable in both the groups. Their study showed similar findings to our study i.e. no significant difference was seen between the clotrimazole group and coconut oil group with respect to changes in clinical symptoms and mycological reports between the two groups.

Clotrimazole is a known antifungal with ability to mycologically cure dermatophytosis, as seen in the various trials and studies done by Del palacio *et al.*,[3] Verallo-Rowell*et al.*,[10] Oyeka *et al*.,[13], McVie *et al*.,[14] and S. Sheidaei *et al*.[16]

Verallo-Rowell *et al*.,[10] studied antibacterial and emollient effects of coconut oil. They reported a reduction in SCORAD scores, along with improvement in itching and skin desquamation in patient's of atopic dermatitis. These symptoms improved after virgin coconut oil application in the present study as well. Coconut oil has been proposed to have antifungal affects.[10] Coconut oil has saturated and unsaturated fatty acids which largely determine its toxicity against dermatophytes. Coconut oil coats the skin, slows down trans-epidermal water loss and increases hydration within the stratum corneum and top layers of the epidermis10. In the in vitro study done by A.P. Garg et al.,6 various organic oils were studied for their anti-fungal affects. In their study, growth and inhibition of four species of dermatophytes was evaluated which included *Microsporium canis, Microsporium gypseum, Trichophyton mentagrophytes* and *Trichophyton rubrum*. Amla oil followed by cantharidin and coconut oil was found to be toxic for *M.canis , M. Gypseum, and T. Rubrum*. Whereas in case of *Trichophyton mentagrophytes*, coconut oil was found to be the most toxic.[6]

Coconut oil contains more than 63% lauric acid and myristic acid, which are 12 carbon and 14 carbon fatty acids, respectively. Coconut oil in the study by A.P. Garg *et al*.,[6] showed maximum growth inhibition at low concentrations for *T.mentagrophytes*. Lauric acid and myristic acid show high toxicity and inhibition of growth of fungus in the cultures thus explaining the possible toxic effect of coconut oil on fungal growth.10In another study done to study antifungal effects of coconut oil on *Candidabiofilm* it was proposed that the medium chain fatty acids penetrate the cell wall of fungus and disrupt their cell membrane thus leading to toxic effects.[16]

Coconut oil contains monolaurin that may cause allergic contact dermatitis in certain individuals. But it is generally considered safe by the food and drug administration (FDA), very few side effects are reported if they occur at all, and mainly consist of eczema like symptoms.[17] Coconut oil using group in the present study reported mild symptoms like pustules ,erythema, etc that did not warrant removal from the study. These side effects could be due to withdrawal of topical corticosteroid before including patient in this study.

In the present study, most patients reported good tolerability to the treatment in both the groups. Our findings are concurrent with those reported by McVie *et al*.[14]

Verallo-Rowell*et al*.,[10] reported similar good acceptance with coconut oil for itching in patients with atopic dermatitis.

DLQI has shown to be useful in evaluating efficacy of treatment in chronic skin diseases, i.e. changes in DLQI scores correlate with changes in clinical parameters during course of treatment.18Assessment for DLQI scores revealed that both the groups were similar at baseline with DLQI scores falling in the "very large effect" band. Studies on the change in DLQI scores and its correlation with clinical efficacy give a minimum score change of more than equal to five or atleast one band shift for it to be called clinically significant.[19-20] Within the groups, after 12 weeks of treatment, a decline in score of more than 5 and a shift of more than 1 band was observed which was statistically significant. However, this difference was not statistically significant between group A and B. This particular trait with DLQI for coconut oil application has not been studied in the past. Kircik *et al*.,[21] used DLQI assessing efficacy of sertaconazole in tinea pedis. They reported similar findings to our study.

Mycological cure in our study was defined as the negative reports on KOH mount i.e. no fungal hyphae. Patients who achieved negative KOH microscopy after therapy were taken to be mycologically cured. Regular fungal culture could not be done due to paucity of financial aids in this study, which served as a limitation.

Conclusion

This study shows that virgin coconut oil and 1% clotrimazole cream has comparable efficacy and tolerability when used topically in combination with oral terbinafine in patients of dermatophytosis. The need of the hour is to find an economical and sustainable answer to circumvent the irrational and unmitigated use of cheaper topical corticosteroid and antifungal combination creams. Topical virgin coconut oil offers a cheaper easily available alternative that will provide the benefit of being an antifungal and an emollient which provides symptomatic relief and restores pH of the skin.

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References

1. Rajagopalan M, Inamadar A, Mittal A, Miskeen AK, Srinivas CR, Sardana K, et al. Expert consensus on the management of dermatophytosis in India (ECTODERM India). BMC Dermatol. 2018;18(1):6. https://doi.org/10.1186/s12895-018-0073-1
2. Clayton YM, Connor BL. Comparison of clotrimazole cream, Whitfield's ointment and Nystatin ointment for the topical treatment of ringworm infections, pityriasis versicolor, erythrasma and candidiasis. Br J Dermatol. 1973;89(3):297–303. https://doi.org/10.1111/j.1365-2133.1973.tb02978.x
3. Del Palacio A, Ortiz FJ, Perez A, Pazos C, Garau M, Font E. A double-blind randomized comparative trial: eberconazole 1% cream versus clotrimazole 1% cream twice daily in Candida and dermatophyte skin infections. Mycology. 2001;44(5):173–80. https://doi.org/10.1046/j.1439-0507.2001.00632.x
4. Singal A, Pandhi D, Agrawal S, Das S. Comparative efficacy of topical 1% butenafine and 1% clotrimazole in tinea cruris and tinea corporis: A randomized, double-blind trial. J Dermatolog Treat. 2005;16(5-6):331–5. https://doi.org/10.1080/09546630500375783
5. Banerjee M, Ghosh AK, Basak S, Das KD, Gangopadhyay DN. Comparative evaluation of effectivity and safety of topical amorolfine and clotrimazole in the treatment of tinea corporis.Indian J Dermatol. 2011;56(6):657. https://doi.org/10.4103/0019-5154.91823
6. Garg AP, Miiller J. Inhibition of growth of dermatophytes by Indian hair oils: Wachstumshemmung von Dermatophyten durch indische Haaröle. Mycology. 1992;35(11-12):363–9. https://doi.org/10.1111/j.1439-0507.1992.tb00895.x
7. Randomizer.org. 2022. Research Randomizer. [online] Available at: <https://www.randomizer.org/> .
8. Lakshmanan A, Ganeshkumar P, Mohan SR, Hemamalini M, Madhavan R. Epidemiological and clinical pattern of dermatomycoses in rural India. Indian J Med Microbiol. 2015;33:S134–6. https://doi.org/10.4103/0255-0857.150922
9. Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's textbook of dermatology. John Wiley & Sons; 2016 Feb 29.
10. Verallo-Rowell VM, Dillague KM, Syah-Tjundawan BS. Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis. Dermatitis. 2008;19(6):308–15. https://doi.org/10.2310/6620.2008.08052
11. George M, Chaudhary RG, Rana D, Kasundra D, Chaudhary AR, Malhotra SD. Comparative evaluation of efficacy of terbinafine and itraconazole in treatment of tinea cruris. Int J Basic Clin Pharmacol. 2019;8(7):1460. http://dx.doi.org/10.18203/2319-2003.ijbcp20192642
12. Monica M, Fauriah E, Budiardjo SB, Suharsini M, Sutadi H, Indiarti IS, et al. Antifungal effectiveness of virgin coconut oil mousse against Candida albicans biofilm in children with early childhood caries. Czas Stomatol 2018;71(3):259–62. https://doi.org/10.5114/jos.2018.80643
13. Oyeka CA, Gugnani HC. Isoconazole nitrate versus clotrimazole in foot and nail infections due to Hendersonula toruloidea, Scytalidium hyalinum and dermatophytes. Mycology. 1992;35(11-12):357–61. https://doi.org/10.1111/j.1439-0507.1992.tb00894.x
14. McVie DH, Littlewood S, Allen BR, Pollock AC, Wood P, Milne LJ. Sulconazole versus clotrimazole in the treatment of dermatophytosis. Clin Exp Dermatol 1986;11(6):613–8. https://doi.org/10.1111/j.1365-2230.1986.tb00518.x
15. Sawyer PR, Brogden RN, Pinder KM, Speight TM, Avery GS. Clotrimazole: a review of its antifungal activity and therapeutic efficacy. Drugs. 1975;9(6):424–47. https://doi.org/10.2165/00003495-197509060-00003
16. Sheidaei (MSc) S, Jafarnejad F, Rajabi O, Najaf Zadeh MJ. Comparison of vaginal cream of coconut oil and clotrimazole on candidal infection of vagina. J BabolUniv Med Sci. 2019;21(1):93–8.
17. Abbas AA, Assikong EB, Akeh M, Upla P, Tuluma T. Antimicrobial activity of coconut oil and its derivative (lauric acid) on some selected clinical isolates. Int J Med Sci ClinInvent. 2017;4(8):3173–7. https://doi.org/10.18535/ijmsci/v4i8.12
18. Kondoh A, Ohta Y, Yamamoto K, Iwashita K, Umezawa Y, Matsuyama T, et al. Feasibility of modified DLQI-based questionnaires for evaluation of clinical efficacy of herbal medicine in chronic skin diseases. Tokai J Exp Clin Med. 2005;30(2):97–102. PMID: 16146199
19. Krueger GG, Langley RG, Finlay AY, Griffiths CE, Woolley JM, Lalla D, et al. Patient-reported outcomes of psoriasis improvement with etanercept therapy: results of a randomized phase III trial. Br J Dermatol. 2005;153(6):1192–9. https://doi.org/10.1111/j.1365-2133.2005.06948.x
20. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994–2007: a comprehensive review of validation data and clinical results. Br J Dermatol. 2008;159(5):997–1035. https://doi.org/10.1111/j.1365-2133.2008.08832.x
21. Kircik LH. Observational evaluation of sertaconazole nitrate cream 2% in the treatment of pruritus related to tinea pedis. Cutis. 2009;84(5):279–83. PMID:20099622