ORIGINAL ARTICLE

The myrtus communis L. solution versus ketoconazole shampoo in treatment of dandruff: A double blinded randomized clinical trial

Mahsa Rostami Chaijan,[1] Farhad Handjani,[2] Mohammadmehdi Zarshenas,[3] Massih Sedigh Rahimabadi,[4] Ali Tavakkoli[5]

Abstract

Objective: To evaluate the efficacy and safety of myrtus communis L. solution in the treatment of dandruff and to compare it with ketoconazole.

Method: This double-blind randomised clinical trial was conducted at Shiraz University of Medical Sciences, Shiraz, Iran, from December 2015 to August 2016, and comprised patients with dandruff aged 18-60 years visiting the dermatology out-patient clinic. The subjects were randomised into two equal groups. The treatment group received myrtus communis L. solution and a placebo shampoo, while the control group received ketoconazole shampoo and a placebo solution. The total duration of the study for each subject was one month and subjects in both groups used their respective interventions 8 times during that period. The parameters studied were pruritus, erythema, severity of scaling, and the extent of scalp involvement. All subjects underwent scalp scaling tests at the beginning, after 10 days and at the end of the 30th day. SPSS 21 was used for data analysis.

Results: Of the 90 individuals, there were 45(50%) in each of the two groups. However, 74(82%) subjects completed the third visit and, of them, there were 37(50%) in each group. Both groups showed significant improvement in all outcome measures ($p<0.001$). There were no significant differences between the groups in terms of efficacy, satisfaction rate and side effects ($p>0.05$ for each outcome).

Conclusion: Myrtus solution was found to be effective in the treatment of dandruff.

Keywords: Dandruff, Myrtus communis L., Ketoconazole, Seborrheic dermatitis, Traditional Persian medicine.(JPMA 68: 715; 2018)

Introduction

Seborrhoeic dermatitis on the scalp can present as dry white fluffy scales known as pityriasis sicca, or as seborrhoea, greasy scales and crusting known as pityriasis steatoides. It is a non-fatal disease but strongly impairs the wellbeing of the patient.[1,2] A survey has shown that about 50 million people suffer from dandruff in the USA and nearly $300 million is spent on various products for dandruff treatment annually.[3] Many hypotheses have been put forward, but the cause of seborrhoeic dermatitis remains unknown. It is probably due to the over-growth of the yeast malassezia furfur and abnormalities of skin surface lipids.[2,4]

There are many modalities for the control of dandruff. Shampoos containing anti-yeast agents, such as ketoconazole or zinc pyrithione, are effective in most cases of pityriasis capitis. Shampoos containing selenium sulfide or tar have also been widely used and salicylic acid-containing preparations can be helpful for heavy scaling.[2] However, high resistance and recurrent rates, toxicity and the price of anti-fungal agents are some factors behind their limited usage.[5]

Traditional Persian medicine (TPM) is a popular complementary practice among Iranians and nowadays a tidal trend of studies are being undertaken to assess its therapeutic recommendations.[6] The main medical books of TPM, such as al-Hawi fi al-tibb by Rhazes, Kamil al-Sinayah al-Tibbiyah by Haly Abbas, al-Qanun fi al-tibb by Avicenna, and Zakhireye Kharazmshahi by Esama'il Gorgani, have separate chapters about the diseases of skin and hair. In TPM, dandruff is called; "abriyeh" or "Hozaz".[7-9]

There are many herbal products and remedies for treatment of dandruff of which a topical drug, which is safe, non-toxic, cheap and with available ingredients, would be a good candidate. A combination of myrtus communis L. and vinegar (Moord solution) that has been mentioned in TPM appears to have all of the above-

[1,5]Research Center for Traditional Medicine and History of Medicine,[2]Molecular Dermatology Research Center and Department of Dermatology, Shiraz University of Medical Sciences,[3]Medicinal Plants Processing Research Center, and Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz, Iran,[4]Department of Persian Medicine, Fasa University of Medical Sciences, Fasa, and Essence of Parsiyan Wisdom Knowledge - based Institute, Traditional Medicine and Medicinal Plant Incubator, Shiraz University of Medical Sciences, Shiraz, Iran. Correspondence: Farhad Handjani. Email: hanjanif@yahoo.com

mentioned features.[9-12]

Myrtus communis is an evergreen, bushy shrub or a small tree growing up to 5 meters high with opposite branches and quadrangular cane-shaped, initially delicately glandular, downy branches.[13] It grows from the Mediterranean region to the northwestern Himalayas[5,13] and is a well-known plant that has been used from ancient times as medication, food preparation and spice. Despite its pleasant odour, its bitter taste limits the oral administration of myrtus. However, it has been used vastly in perfume, cosmetics and food industries for flavouring.[5] Myrtus has anti-microbial, anti-fungal, anti-oxidant and anti-inflammatory effects.[5,14,15]

In TPM, myrtus communis L. is known as "Moord" or "As" and almost all parts of the plant, including fruits, leaves, roots, its essential oil and extracts, have been used in many medical or cosmetic conditions such as controlling bad body odour, hair loss, oral aphthous lesions, poor appetite, stomach ache, diarrhoea, infectious diseases, abnormal uterine bleeding, etc.[16]

Myrtus and vinegar are common remedies which are repeatedly recommended in TPM texts as anti-dandruff agents[7-9,16] and a combination of myrtus aqueous extract and vinegar have been suggested in the treatment of dandruff.[9,16] The current study, the first of its kind, was planned to evaluate a combination of this herb and vinegar as an anti-dandruff solution. Also part of the study was to assess its side effects and user-friendly application and to compare it with ketoconazole 2% shampoo for the treatment of dandruff.

Subjects and Methods

This 2-arm, double-blinded, blocked randomised comparative clinical trial using a parallel design with a 1:1 allocation ratio was conducted at Shiraz University of Medical Sciences, Shiraz, Iran, and comprised patients with dandruff attending Shahid Faghihi Department of Dermatology out-patient clinic affiliated with the university. Those included had presence of dandruff, were aged 18-60 years, and who agreed to sign the written informed consent. Those excluded were pregnant and lactating females, those with hypersensitivity to azole groups, history of liver disease, porphyria, skin cancer, use of immunosuppressives in the preceding 4 weeks, use of

Table-1: The quantitative and qualitative dandruff indices.

Index	Score	Definition
Itching	Yes	An irritating and uncontrollable sensation that makes you want to scratch to relieve the feeling
	No	
Excoriation pruritus grading (EPG)	0	Absence (0 lesion)
	1	1-2 lesions
	2	3-5 lesions
	3	6-10 lesions
	4	10< lesions
Adherent Scalp Flaking Score (ASFS)	0	Healthy scalp with no dryness or dandruff
	1	Fine dryness on scalp surface (slight scaling)
	2	Small powdery flakes partially adhering to scalp (some scaling)
	3	Moderately flaky scales loosely attached to scalp (moderate scaling)
	4	Large pronounced crusty scales adhering to scalp (heavy scaling)
	5	Very large pronounced crusty scales congealed into plates adhering to scalp (very heavy scaling)
Redness of scalp skin	0	Absence
	1	Very slight erythema
	2	Well-defined erythema
	3	Moderate to severe erythema
	4	Severe erythema
Grading of scalp skin involvement	0	Not assessable
	1	10-25% of the total scalp area
	2	25-50% of the total scalp area
	3	50-75% of the total scalp area
	4	75% < of the total scalp area

steroids in any form in the preceding 2 weeks or had addiction to alcohol. The subjects were allocated randomly to intervention and control groups. Quantitative and qualitative indices were used to assess dandruff (Table-1).

After obtaining permission from the institutional review board, the sample size was calculated using Power Statistical Consulting Centre (SCC) software. Considering 1-sided significance level of 0.05, and a power of 0.90, the sample size was calculated to be 37 participants in each group. We considered an additional 20% to compensate for probable dropout.

A package labelled as A or B and consisting of 3 bottles was given to each participant. The intervention group received myrtus communis solution, placebo shampoo and daily shampoo, while the other group received ketoconazole 2% shampoo, placebo solution and daily shampoo.

Meanwhile, a 50ml mini cup and an applicator were handed to all the participants. The patients were instructed to use the solution and shampoo once every 3-4 days. They used them 3 times before the second visit and 5 times between their 2nd and 3rd visits. Also, they were asked to massage the antidandruff solutions on the scalp 3-5 minutes before going for a shower and then to wash their hair with the antidandruff shampoo. In addition, they were instructed to allow the shampoo foam to stay on their scalp for 5 minutes and after that to rinse it. The daily shampoo of both groups were the same, but the ketoconazole group received a placebo solution as their antidandruff solution and ketoconazole shampoo as their antidandruff shampoo, whereas the myrtus group received a placebo shampoo as their antidandruff shampoo and a myrtus solution as their antidandruff solution. The daily and placebo shampoos were the same with no known effect on dandruff or inflammation of the scalp.

Questionnaires about patients' demographic data and disease evaluation criteria were filled out at baseline, 10 days (the 2nd visit) and 30 days (the 3rd or final visit) after initiation of treatment. At the final visit, questionnaires about patient's satisfaction and ease of usage were filled out and any adverse events were recorded. The scoring criterion to assess the severity of seborrheic dermatitis included pruritus, erythema, severity of scaling and the extent of scalp involvement. The patients' satisfaction and acceptance of the product were evaluated with a visual analogue scale (VAS) and ranged from 1 (least satisfactory or tolerable) to 5 (most satisfactory or acceptable).

All patients were examined by a dermatologist and the dermatology office secretary, dermatologist, medical researcher assistant, and statistician were blinded to the allocation of the patients.

For the preparation of antidandruff solutions, approximately 50g of myrtus communis fine powder was added to 500ml of distilled water. The mixture was decocted for 10 minutes. Subsequently, 50ml of industrial vinegar (Varda vinegar; operation license No. 1827) was added to the mixture and boiled for almost 1 minute. The solution was then filtered through Whattmann filter paper. Also, a traditional myrtus communis oil sample was prepared via macerating fine powder of leaves in a heated vessel (glycerin; Norton, Iran) up to 50°C. The proportion of powder to the vehicle was 1:10.

The final solution was prepared via diluting 1ml of the oil sample in the above solution up to 30ml. The remedy was then subjected to gas chromatography (GC) and microbial evaluation before intervention. This myrtus solution was a sample product just for use in the study. Because these solutions were not made in mass quantities and were prepared solely for research purposes, it was produced in small amounts to avoid the influence of time on it.

The placebo solution was made by distilled water and some natural dyes, like amitida liquid colour, to have the same colour as the myrtus solution.

A randomised list was generated using Microsoft Excel with a block randomisation method, and eligible participants sequentially were allocated into 2 parallel groups using the list. A separate randomised list was created for females and males. For example, the first two males were allocated to group A then the third one was allocated to group B and the fourth one was again allocated to the group A, and so on. The same action was performed for the female participants using a different randomisation list. The research assistant was responsible for the allocation of the participants to their respective groups and the dermatologist gave them the appropriate package.

The data were analysed using SPSS 21.0. The normal distribution assumption was checked by Kolmogorov-Smirnov test and Q-Q plot. The frequency (percentage), mean ± standard deviation (SD) and median were used for data description. Independent-samples t-test, Mann-Whitney, chi-square, and Fisher's exact tests were used for comparison of the difference between the 2 groups. Changes within an intervention group were evaluated with Wilcoxon signed rank test and paired sample t-test. Analysis of covariance was used for comparison of both

groups adjusted for the baseline variables. P<0.05 was considered statistically significant.

Results

Of the 90 individuals, there were 45(50%) in each of the two groups at the start of the study. However, 74(82%) subjects completed the third visit and, of them, there were 37(50%) in each group who formed the study sample. At baseline, the overall mean age was 51.33±6.75 years and mean dandruff duration was 9.96±6.23 years, and there was no statistically significant difference between the groups (Table-2).

After using the antidandruff products, all dandruff indices improved dramatically (p<0.001) in both groups at both follow-ups compared to the baseline (Table-3). At the end of 30 days, myrtus solution appeared to have a stronger effect compared to ketoconazole 2% shampoo, but none of these differences were statistically significant (p>0.05).

Comparing the results of the two follow-ups, it was only in the myrtus group that significant improvement in itching of participants was noted (p=0.004). In the ketoconazole group, despite some improvement in itching severity, comparing the first and second follow-ups was not statistically significant (p=0.058) (Table-4).

Adverse events were observed in 8(11%) patients but showed no significant difference between the groups (p>0.05).

Table-2: Demographic data (n=90).

Variables	measurement	Total	Group		P value
			Ketoconazole (n=45)	Myrtus(n=45)	
Age (years)	Mean ± SD	30 ± 9	31 ± 10	29 ± 8	0.19†
	Median (IQR)	29 (24 to 34)	29 (24 to 35)	27 (21 to 34)	
Gender	Female	44 (48.9%)	22 (48.9%)	22 (48.9%)	1.0*
	Male	46 (51.1%)	23 (51.1%)	23 (51.1%)	
Duration of dandruff (mon.)	Mean ± SD	89 ± 80	97 ± 84	81 ± 77	0.34†
	Median (IQR)	60 (36 to 120)	72 (42 to 120)	54 (30 to 120)	

IQR: inter quartile range. † Based on t-test. * Based on chi-square test.

Table-3: The differences of primary outcome measures between two intervention groups (n=74).

Parameter	Time	Group		95% CI		P value
		Ketoconazole (n=37)	Myrtus(n=37)	Lower	Upper	
EPG	Baseline	1.30 ± 0.94	1.49 ± 1.10	-0.28	0.66	0.56‡
	After 10d	0.54 ± 0.56	0.54 ± 0.73	-0.30	0.30	0.67§
	After 30d	0.16 ± 0.44	0.05 ± 0.23	-0.27	0.06	0.239§
ASFS	Baseline	2.92 ± 0.98	3.03 ± 0.83	-0.31	0.53	0.59‡
	After 10d	1.89 ± 0.97	1.65 ± 1.01	-0.70	0.21	0.34§
	After 30d	0.86 ± 0.89	0.62 ± 0.72	-0.62	0.13	0.24§
Redness of scalp skin	Baseline	1.62 ± 0.76	1.68 ± 0.71	-0.01	0.66	0.77‡
	After 10d	0.89 ± 0.81	0.59 ± 0.73	-0.65	0.06	0.08§
	After 30d	0.24 ± 0.50	0.19 ± 0.46	-0.28	0.17	0.57§
Grading of scalp skin involvement	Baseline	2.97 ± 0.76	3.30 ± 0.66	-0.01	0.66	0.07‡
	After 10d	1.70 ± 0.81	1.59 ± 0.80	-0.48	0.27	0.71§
	After 30d	0.49 ± 0.84	0.41 ± 0.64	-0.43	0.27	0.91§

CI: Confidence Interval.
EPG: Excoriation pruritus grading.
ASFS: Adherent Scalp Flaking Score.
Pre: At the start of the study.
After 10d: Ten days after using solutions.
After 30d: Thirty days after starting the study (end point of the study).
‡ Based on Mann-Whitney test.
§ Adjusted for the baseline, based on Analysis of Covariance.

Table-4: The power of the outcome measures between and in each group after 30 days. (n=74).

Outcomes	P-Value		Power	
	Between groups	Within groups	Between groups	Within groups
EPG	0.23	0.001	26.8%	100%
ASFS	0.24	0.001	24.5%	100%
Redness of scalp skin	0.57	0.001	6.4%	100%
Grading of scalp skin involvement	0.91	0.001	6.7%	100%

EPG: Excoriation pruritus grading.
ASFS: Adherent Scalp Flaking Score.

Although patient satisfaction rates in both groups were almost the same (p=0.647), it was noted that using the ketoconazole shampoo was more acceptable and easier than the myrtus solution (p=0.003).

Discussion

There are many antidandruff products in the world which are either topically or orally administrated. Almost every year some new products with various antidandruff formulas are entering the market perhaps due to insufficient therapeutic effects of the existing drugs and increase in the incidence of dandruff all over the world.

The current study used myrtus communis that has a long history of traditional usage in cosmetics as well as hair repair and growth.[7,8,16] Using TPM references, a combination of myrtus and vinegar can have a powerful anti-dandruff effect.[8,16] Hair-protective or fortifying effects of myrtus communis have been shown in several studies,[17] yet there is no strong study about the efficacy of myrtus solution on dandruff.

The results of the current study showed that myrtus solution had a powerful and rapid effect on scaly scalps with no severe adverse events and all dandruff indices showed dramatic improvement at both interventional follow-ups (p<0.001) except in the excoriation pruritus grading (EPG) index on the 1st follow-up. Consequently, bearing in mind the type one and two errors of this study, one can assume that on the one hand both interventions had strong probability in the treatment of dandruff (p<0.001 and powers=100%) and on the other hand the similarities between these interventions may be altered in some studies by larger sample sizes. Comparing the effects of the myrtus solution and the ketoconazole shampoo on dandruff indices, it seems there is no significant difference between the two study groups at the end of the study (p>0.05), but a look at their respective powers reveals that the powers of these data are very low (powers <27%) (Table-4). This means that it is totally probable to drive the superiority of myrtus solution effects on observed outcomes compared to ketoconazole shampoo if we test these products in a study with a larger sample size.

The anti-bacterial, anti-fungal and anti-inflammatory effect of myrtus have been proven in many studies[15,18-21] and these are the main anti-dandruff mechanisms of our myrtus solution. On the other hand, myrtus has different components, such as polyphenols, myrtucommulone (MC), semi-myrtucommulone (S-MC), 1 and 8-cineole, alpha-pinene, myrtenyl acetate, limonene, linalool and alpha-terpinolene, which can explain the mentioned characteristics of this plant. Furthermore, considering the fortifying and protective properties of myrtus and its few side effects,[13,17,22-24] this solution may have a dual application and can be used for a long period of time, although these claims have to be evaluated in further studies.

The rather small number of cases and a short follow-up time were the main limitations of the current study.

Conclusion

Myrtus communis is used for seborrhoeic dermatitis in herbal medicine and was found to be effective in the treatment of dandruff with no severe adverse events. It can be an appropriate substitute for ketoconazole 2% shampoo but more studies with a larger sample size and longer follow-ups are recommended to better evaluate this natural product.

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Conflict of Interest: None.

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