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Original Article
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The Effects of Myrtle (*Myrtus communis*) and Clindamycin Topical Solution in the Treatment of Mild to Moderate Acne Vulgaris: A Comparative Split-Face Study

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Objectives: Although Acne vulgaris is a chronic skin disease, which its standard treatment causes therapeutic limitations and some common adverse effects, medicinal plants can be effective in treatment with low adverse effects as combination therapy. Myrtle (*Myrtus Communis*) has some beneficial properties, which has been administered topically and orally for some skin diseases in Persian medicine. This study aimed to compare the efficacy and safety of Myrtle formula and 1% clindamycin topical solution.

Methods: This was a split-face clinical trial that was done on 55 patients with mild to moderate acne vulgaris for 16 weeks. The patients received topical Myrtle solution to the right side of the face (group 1) and clindamycin solution to the left side (group 2) twice daily for 12 weeks. All participants were examined for the acne severity index (ASI) and total acne lesions counting (TLC) at certain times during the study. Then, they stopped using them for four weeks. They also did not take the drug in the final four weeks of the study.

Results: Forty-eight patients completed the study for 16 weeks; 40 (83.2%) patients were female and the rest of them were male. The mean age and standard deviation were 25.62 ± 7.62 years. After 12 weeks, the percentage changes of comedones, inflammatory lesions, ASI and TLC were significantly reduced in both groups ($p < 0.001$). The percentage change of inflammatory lesions and ASI decrease was significantly higher in the group 1 ($p = 0.03$). There was no significant difference in the incidence of side effects between the two groups. There was a more significant decrease in sebum percentage change in the group 1 ($p = 0.003$).

Conclusion: Myrtle lotion was effective and safe for the treatment of mild to moderate acne vulgaris.

Keywords: acne vulgaris, myrtus communis, persian medicine, split-face

INTRODUCTION

Acne Vulgaris is a chronic inflammatory disease of the sebaceous glands, which is one of the most prevalent skin diseases among adolescents and young people worldwide. Its prevalence varies between countries and ethnic groups and it is estimated to be from 35 to over 90 percent [1, 2]. Clinical types of acne include non-inflammatory lesions (e.g, sebum, black and white comedones) and inflammatory lesions (e.g, papules, pustules, and nodules) [3]. In mild and moderate acne vulgaris, topi-

cal drugs are most commonly used [4]. A number of patients, discountinue topical treatments owing to unresponsiveness and side effects such as irritation, erythema, scaling, itching, and stinging, which consequently, lead to treatment failure [5]. Therefore, consumption of natural remedies has been considered, it is believed that they are the safe source for finding new biologically active treatment and have low side effects as well. A variety of medicinal herbs are used orally, topical or together for acne treatment worldwide [6, 7]. Myrtle (*Myrtus Communis*) is herbal medicine and its topical and oral use has been recommended for some kinds of skin diseases in Persian medicine [8]. Myrtle shows antiproliferative, antibacterial, and antiinflammatory properties in different *in-vitro* and *in-vivo* studies [9, 10]. A clinical study indicated that Myrtle essential oil had antibacterial activity and also valuable effects on removal of sebum and dead skin cells, and reduction in erythema [11].

The present study was conducted to assess the effect of topical Myrtle solution compared to clindamycin 1% solution on decreasing mild to moderate acne lesions.

MATERIAL AND METHODS

This study was a triple blind, non-randomized, split-face clinical trial. All the patients were recruited from three university centers in Tehran, Iran, from June 2017 to April 2019. The inclusion criteria were both the men and women, aged between 12 to 45 years old, with mild to moderate acne vulgaris on their faces. The characteristics of the lesions also include TLC score: 20-140, non-inflammatory lesions: 10-50, inflammatory lesions: 10-50, and lack of sinus tract, cysts, and nodules. Patients were excluded if they had a contemporary skin disease such as scar, rosacea, psoriasis that interfere with the assessment of acne lesions, acute systemic diseases, pregnancy, breast-feeding, the consumption of local treatment of acne in two months before or during the study, taking oral retinoic acid in six months before the study, and allergy to the drugs or their compounds.

The Ethics Committee of Iran University of Medical Sciences approved this study (Ethics code: IR. IUMS FMD.REC 1396.9321309010). Informed consent was taken from each participant. The study was registered in the Iranian Registry of Clinical Trials (registration no. IRCT 20171122037581N1).

1. Plant material and drug preparation

The required amount of Myrtle dried leaves were purchased from the herbal market in Tehran, Iran. The herbarium code of PMP-447 was obtained from the botany lab and herbarium of faculty of pharmacy, Tehran University of Medical Sciences, Tehran, Iran. The plant leaves were ground to powder using an electric miller. The ethanolic extract of Myrtle was prepared by maceration method using ethanol/water solvent. For this reason, 100 g of grounded powder was macerated with 500 mL of EtOH: H_2O (80:20) for 48 h.

2. Sample size

To estimate the sample size, data were derived from a pilot study of 10 subjects. It was calculated using the comparison of the formula for the means between matched pairs groups, on the basis of following assumptions: $\alpha = 0.05$, p = 80%, effect size = 0.6 and the attrition rate of 20%, the sample size was calculated to be 55 patients.

3. Study design and population

Fifty-five patients who met the inclusion criteria were enrolled in this study. They received topical Myrtle solution on the right side and clindamycin 1% solution on the left side of their faces twice daily for 12 weeks. After completing active therapy, the patients were drug-free for four weeks to follow up. During the study, the patients, the researchers and the statistical analyzer were unaware of the contents of the treatment.

The Myrtle and clindamycin 1% solution were administered for each patient in two opaque containers, both drugs are the same in their shapes and odors. Patients were visited and the treatment sites evaluated at the beginning of the study and then after 6, 12 and 16 weeks.

In each visit, the number of inflammatory and non-inflammatory lesions, ASI and TLC were evaluated. ASI and TLC were calculated by the following formula [12]:

$$\text{Total lesion count (TLC)} = \text{papules} + \text{pustules} + \text{comedones} + \text{nodules}$$

$$\text{Acne Severity Index (ASI)} = \text{papules} + (\text{pustules} \times 2) + (\text{comedones} / 4) + (\text{nodules} \times 3)$$

At each visit adverse events (AEs) including erythema, burning, itching, dryness, scabbing, aggravation of lesion and edema were assessed through direct questions and clinical assessment by the investigator. The numeric rating scale represents 0 =

none, 1 = mild, 2 = moderate and 3 = severe.

The following skin biophysical characteristics were measured on both sides of the face at the baseline and the end of the study on 16th week: Fluorescence photography was conducted usingVisiopor® PP 34 camera (Courage-Khazaka, Germany) with narrow-band UVA light (375 nm) and image size of 6.4 × 8 mm. Photographs were taken from the left and right cheek. The number of orange-red fluorescence spots were assessed. The orange-red fluorescence indicates the presence of *Propionibacterium acne* (*P. acne*) within clinically non-evident (follicular impactions and microcomedones) and clinically evident lesions (comedones, papules and pustules). Four skin biophysical characteristics were measured using MPA-9 (Courage-Khazaka, Germany). The erythema index and melanin index were measured using Mexameter MX 18. Stratum corneum hydration and sebum content, were measured by Corneometer CM 825, Sebumeter SM 815, respectively. All measurements were performed on the left and right cheek in a room at 20-25℃ temperature and a relative humidity of treatment.

4. Endpoints

The efficacy end point was the comparison of the inflammatory, non-inflammatory, TLC and ASI and percent change of them at baseline and week 12. Patient's satisfaction was scored from 0-4 (i.e. 0 = worse, 1 = no response, 2 = poor response, 3 = good response, 4 = excellent). 50% recovery was compared on both sides; drugs safety was measured through evaluating side-effects. The evaluation of side effects was based on "common terminology criteria for adverse events V4. 0 2009".

5. Statistical analysis

Data were analyzed using SPSS software (SPSS Inc. Version 17.0. Chicago, IL, USA). Variables were described by the mean, standard deviation. Normal distribution of variables was evaluated using Kolmogorov-Smirnov and Shapiro-Wilk tests. Friedman's test was used to determine the changes in the variables during the study. Wilcoxon matched-pairs signed ranks test was used to compare the variables between the right and left side of the face and pairwise comparisons on each side. The qualitative variables were compared between two sides of the face using McNemar's test. The p-value of less than 0.05 was considered statistically significant.

RESULTS

1. Baseline characteristics

A total of 83 individuals with mild to moderate acne vulgaris were interviewed in 3 university centers of whom, 55 subjects were enrolled to the study. These patients referred to one cen-

Table 1. Changes in non-inflammatory and inflammatory lesion, ASI and TLC scores

Variables	Formulation	Baseline Mean (SD)	6th week Mean (SD)	12th week Mean (SD)	p value*	16th week Mean (SD)	p value*
Comedones	1	24 (15.11)	19.22 (16.2)	17.58 (14.08)	< 0.001	17.06 (10.54)	< 0.001
	2	23.66 (12.71)	19.68 (14.56)	18.58 (14.49)	0.002	20.33 (13.94)	0.002
p value**		1	0.54	0.27		0.016	
Inflammatory lesions	1	10.10 (7.10)	5.2 (4.7)	4 (3.82)	< 0.001	4.2 (3.38)	< 0.001
	2	8.16 (6.05)	5.77 (5.14)	4.58 (4.59)	< 0.001	4.72 (3.97)	< 0.001
p value		0.004	0.56	0.35		0.10	
TLC	1	34.1 (17.48)	24.43 (18.24)	21.58 (15.65)	< 0.001	21.27 (11.45)	< 0.001
	2	31.83 (13.04)	25.45 (14.65)	23.16 (14.93)	< 0.001	25.06 (14.76)	< 0.001
p value**		0.28	0.31	0.07		0.01	
ASI	1	18.33 (9.6)	11.24 (8.6)	9.16 (6.67)	< 0.001	9.34 (5.03)	< 0.001
	2	15.77 (8)	11.88 (7.35)	10.39 (7.44)	< 0.001	11.02 (6.48)	< 0.001
p value**		0.02	0.3	0.21		0.02	

Formulation 1 = *Myrtus Communis*, Formulation 2 = clindamycin 1%. SD, standard deviation; TLC, total lesion count; ASI, acne severity index. *Friedman Test, **Wilcoxon matched pairs signed ranks test.

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ter. Clinical examinations and skin biophysical characteristic measurements were performed by one person. The study began with a total of 55 patients and seven persons dropped-out the study. Finally, 48 patients completed the study during 16 weeks. Forty subjects (83.2%) were female and the rest of them were male. The mean age and standard deviation were 25.62 ± 7.62 years.

At baseline, there were no significant differences among the subjects in terms of the mean TLC ($p = 0.28$) and comedone score ($p = 1$), but the mean number of inflammatory lesions ($p = 0.004$) and ASI ($p = 0.02$) was significantly higher on the right side compared to the left ones. Table 1 presents a comparison of the skin lesions, TLC, ASI and their changes in two sides.

Fig. 1 presents percent changes in comedones, inflammatory lesions, TLC and ASI at 16th week compared to the baseline.

2. Efficacy on total lesion scores (TLC)

At the beginning of the study, the mean scores of TLC on the right and left sides of the face were 34.1 ± 17.48 and 31.83 ± 13.04, respectively (Table 1). There was no significant difference between two sides in terms of decrease in the mean TLC in the 6 and 12 weeks ($p = 0.31$ and $p = 0.07$, respectively). In the 16th week, the subjects were reported increased TLC on both sides of the face compared to the 12th week of the study, however, percentage changes were significantly higher on the right side ($p = 0.01$). In both sides there was a significant decrease in TLC at the 12th and 16th weeks. Percentage change in TLC showed no significant difference at 12th week compared to baseline between the two sides ($p = 0.1$).

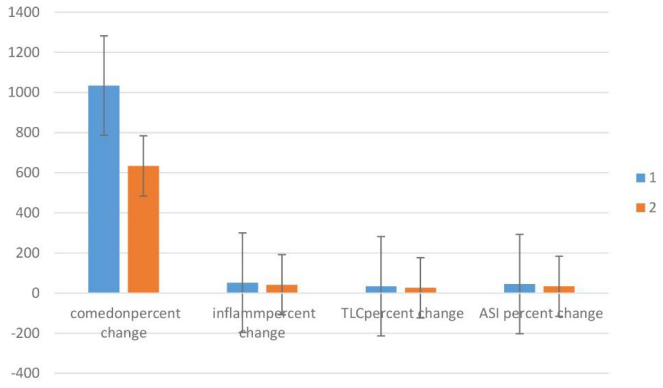

Figure 1. Percent changes in comedones, inflammatory cells, TLC and ASI at 16 weeks compared to baseline; 1 = *Myrtus Communis*, 2 = clindamycin.

3. Efficacy on non-inflammatory lesion (comedone) scores

In the 6th and 12th weeks of the study, the number of comedones were significantly decreased on both sides compared to the baseline ($p < 0.001$). In the 12th week, there was no significant difference in percentage changes of comedones between the two sides compared to the baseline ($p = 0.64$). In the 16th week, the mean number of comedones was higher on the left side ($p = 0.01$).

4. Efficacy on inflammatory lesion scores

At baseline, the mean number of inflammatory lesions was significantly higher on the right side ($p = 0.004$). In the 12th week, there was a significant decrease in the mean number of inflammatory lesions on both sides ($p < 0.001$), but on the right side, the inflammatory lesion percentage was significantly decreased more than the left side ($p = 0.03$).

5. Efficacy on acne severity index (ASI)

ASI was significantly higher on the right side compared to the left side at baseline conditions ($p = 0.02$). In the 6th and 12th weeks, the decreasing of ASI was equal on both sides ($p < 0.001$). The significant change in ASI seems obscure. Thus, it is necessary to compare the percentage changes of ASI in both sides in order to properly explain the results. After 12 weeks, there was a significant decrease in ASI percentage change for both sides compared to the baseline, but ASI percentage decrease on the right side was significantly higher ($p = 0.03$).

The percent changes of TLC and ASI in the 6th and 12th weeks are shown in Table 2.

6. Skin biophysical characteristics

There was a significant difference in melanin levels between the two sides at baseline ($p = 0.04$), and their percentage changes were not significant after 16 weeks ($p = 0.49$).

At 16th week, there was a significant increase in moisture level with clindamycin, while it was decreased with Myrtle, nevertheless, there was no significant difference in percentage change ($p = 0.07$).

After 16 weeks, sebum level was significantly lower with Myrtle ($p = 0.009$). Also, the percentage decrease with Myrtle was significantly higher than clindamycin ($p = 0.003$).

Erythema increased on the side treated with Myrtle, how-

Table 2. Percent changes in comedones, inflammatory lesions, TLC and ASI at 12 and 16 weeks compared to baseline

Variable	Formulation	12-0 week Mean (SD)	16-12 week Mean (SD)
Comedones percent change	1	21.55 (40.02)	–25.96 (74.54)
	2	13.21 (59.15)	–43.33 (102.09)
p value		0.64	0.39
Inflammatory lesions percent change	1	52.36 (50.30)	–41.94 (131.25)
	2	41.80 (48.03)	–24.86 (98.06)
p value		0.03	0.56
TLC percent change	1	34.13 (34.51)	–23.74 (63.49)
	2	26.47 (34.80)	–27.96 (072.40
p value		0.1	0.69
ASI percent change	1	45.08 (38.97)	–39.14 (94.87)
	2	34.15 (33.93)	–32.51 (93.87)
p value		0.03	0.71

Formulation 1 = *Myrtus Communis*, Formulation 2 = clindamycin 1%. SD, standard deviation.

Table 3. Skin biophysical characteristics

Variables	Formulation	Baseline Mean (SD)	16th week Mean (SD)	p value*	Percent change Mean (SD)
Melanin	1	197.01 (40.82)	199.70 (43.03)	0.5	–2.29 (14.56)
	2	206.83 (53.15)	202.69 (38.20)	0.95	–0.19 (13.63)
p value*		0.04	0.4		0.49
Skin moisture	1	37.47 (11.38)	33.82 (12.67)	0.04	5.53 (36.49)
	2	37.47 (11.38)	37.61 (12.85)	0.69	–7.46 (49.99)
p value*		1	0.03		0.07
Sebum ($\mu g/cm^2$)	1	87.85 (58.89)	73.42 (47.30)	0.02	1.18 (64.22)
	2	87.85 (58.89)	82.61 (49.14)	0.58	–15.13 (77.55)
p value*		1	0.009		0.003
Erythema	1	387.89 (72.22)	392.63 (91.22)	0.44	–2.21 (20.07)
	2	377.06 (74.06)	376.34 (80.68)	0.66	–0.84 (16.48)
p value*		0.16	0.02		0.46
P. acne count	1	18.58 (13.02)	16.06 (11.81)	0.02	6.74 (59.10)
	2	17.52 (13.40)	14.39 (11.09)	0.01	11.20 (57.11)
p value*		0.16	0.11		0.82

Formulation 1 = *Myrtus Communis*, Formulation 2 = clindamycin 1%. SD, standard deviation.

ever, it decreased with clindamycin at 16th week, which the difference was significant (p = 0.02). However, the percentage changes of erythema between both formulations were not significant (p = 0.46).

The percentage changes of *P. acne* (Visiopor) decreased for both products, but their differences were not statistically significant (p = 0.8). Table 3 demonstrates skin biophysical characteristics in the study population.

7. Recovery

The recovery was considered a 50% decrease in ASI at 6th and 12th weeks. It was observed at 6th week with Myrtle in 22 patients (45.8%) and with clindamycin in 13 patients (27.1%),

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which was significantly higher for Myrtle (p = 0.04), but at 12th week, the rate of recovery was not significantly different between both sides of the face (p = 0.14).

8. Adverse events

Table 4 shows the number of patients experiencing any AEs. Eighteen patients (37.6%) with Myrtle and 21 subjects (43.8%) with clindamycin reported at least one AEs after six weeks. It was decreased to 13 patients (26.2%) for Myrtle and 19 subjects (39.7%) for clindamycin at 12th week. The severity of symptoms on both sides of the face were mild to moderate, and none of them was severe. Scabbing, was the most common AEs for both Myrtle and clindamycin at the 6th and 12th weeks with no significant difference (p = 1 and p = 0.65, respectively). The second common AEs for both products were an aggregation of lesion (p = 0.73) in the 6th week and dryness (p = 0.08) in the 12th week.

The results showed no significant difference in the incidence of side effects between the two formulations.

9. Patient's satisfaction

The participants reported satisfaction with treatment as follows: median interquartile range (IQR) was between 3 (2-3.75) and 2 (2-3) for Myrtle and clindamycin respectively. The satisfaction was significantly higher for Myrtle (p = 0.02).

10. Recurrence

In both formulations, the percent changes of TLC, ASI, inflammatory and non-inflammatory lesion were increased at 16th week compared to 12th week. The recurrence rate was not significantly different between them (Table 2).

Fig. 2 and 3 show photograph of one subject who received the Myrtle (right side of the face) and clindamycin (left side of the face) in the baseline and end of the study (at 16th week).

DISCUSSION

The aim of this split-face study was to compare the efficacy and safety of Myrtle and clindamycin solution in patients with mild to moderate acne vulgaris on their faces. In this study, the decrease in the inflammatory and non-inflammatory lesions, ASI and TLC percentage changes were significant on both sides of the face at 12th week. There was a significant difference in the reduction of inflammatory lesions and ASI percentage changes for Myrtle compared to clindamycin. The significant decrease of sebum, as a precursor of acne, was one of the most outstanding features of Myrtle lotion. The patient's satisfaction for Myrtle was significantly higher than the clindamycin and the incidences of AEs between both formulations were similar.

Acne vulgaris is a multifactorial skin disease and some of its aspects remain unknown yet. Four key factors have been identified in the pathogenesis of acne, including increased sebum production, follicular hyperkeratinization, colonization of the pilosebaceouse unit with *P. acnes* and inflammation [13]. Its medical treatment is based on the effect of one or several factors to prevent the development of the lesion by inhibiting sebum growth, normalizing follicular hyperkeratinization, decreasing *P. acnes* colonization and inhibition of inflammation [14]. Releasing free radicals and inflammatory mediators reflect the presence of oxidative stress state in parts of the pathogenesis of acne, therefore, the use of antioxidant and anti-inflammatory agents has been considered along with usual medication for the

Table 4. Summary of AEs based on number (%) of patients

Adverse events	6th week		p value	12th week		p value
	Myrtle No. (%)	Clindamycin 1% No. (%)		Myrtle No. (%)	Clindamycin 1% No. (%)	
Scabbing	10 (20.8%)	9 (18.8%)	1	7 (13.6%)	8 (16.7%)	0.65
Dryness	3 (6.3%)	4 (8.3%)	0.65	3 (6.3%)	5 (10.4%)	0.08
Aggregation	4 (8.4%)	5 (10.4%)	0.73	2 (4.2%)	1 (2.1%)	0.56
Burning	1 (2.1%)	2 (4.2%)	0.31	0 (0%)	1 (2.1%)	0.31
Itching	0 (0%)	1 (2.1%)	0.31	1 (2.1%)	2 (4.2%)	0.31
Edema	0 (0%)	0 (0%)	1	0 (0%)	1 (2.1%)	0.31
Erythema	0 (0%)	0 (0%)	1	0 (0%)	1 (2.1%)	0.31

AE, adverse event.

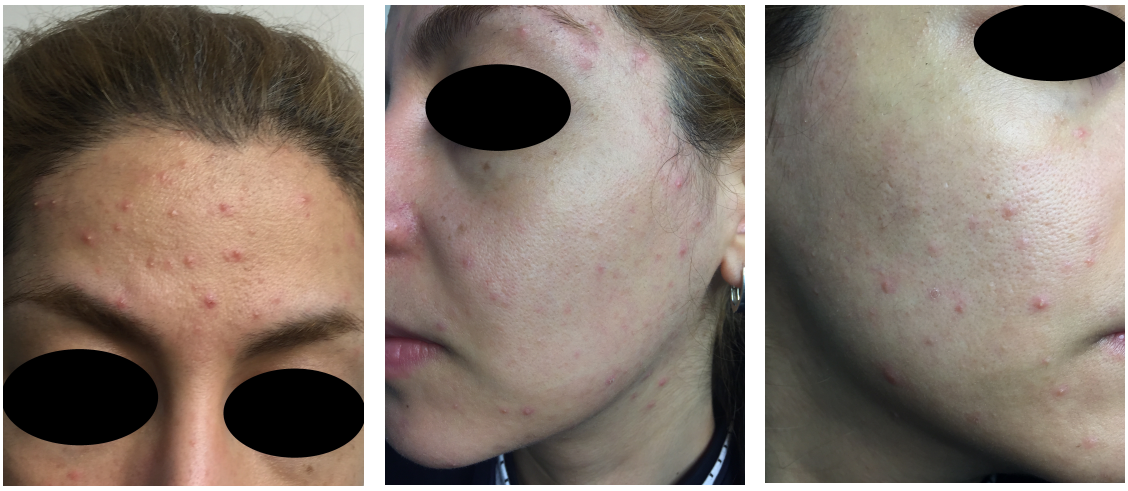

Figure 2. Photographs of one subject, right and left half the face before treatment.

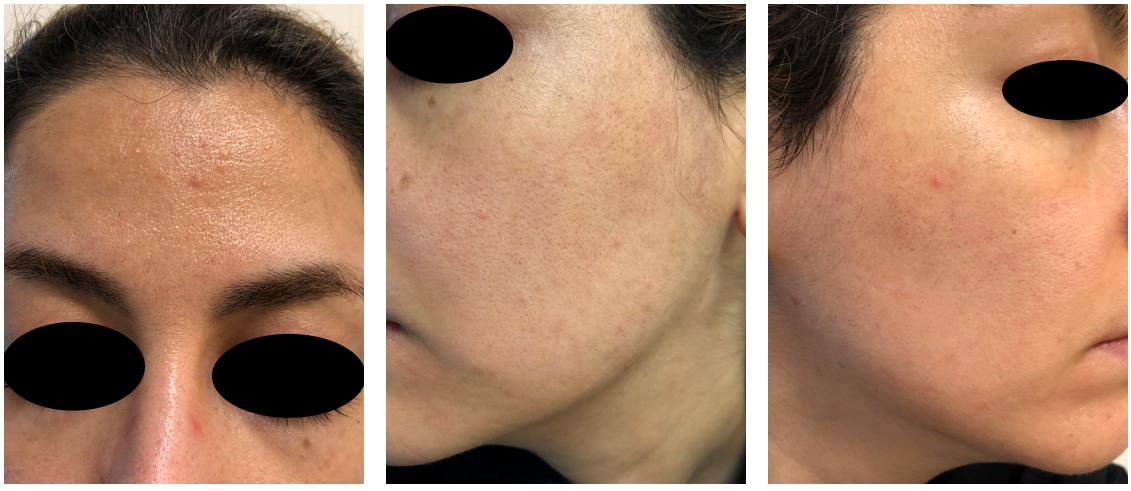

Figure 3. Photographs of one subject in myrtle (right half the face) and clindamycin (left side of the face) after treatment (16th weeks).

treatment of acne vulgaris [15].

It is believed that increased production of keratinocytes and subsequent retention can be considered a comedogenic factor [16]. An *in vitro* study conducted on ethanol product of Myrtle leaves (Myrtacin) have demonstrated anti-proliferative activities on human keratinocytes. Myrtacin inhibits keratinocyte proliferation by 27% and 76% at 1 and 3 μg/mL, respectively. The effective antiproliferative compounds of Myrtacine were Myrtucommulone A and B [9].

Colonization of the pilosebaceouse unit with *Staphylococcus aureus*, *Staphylococcus epidermidis* and *P. acnes* is another key factor in the pathogenesis of acne [17]. Myrtle has strong antimicrobial activity because of high content of monoterpene hydrocarbons such as α-pinene, limonene, linalool, eucalyptol and terpineol [18-20].

An *in vitro* study showed active compounds of Myrtle inhibited *P. acnes* growth. Three compounds, including 5-acetoxy-4-hydroxy-4-isobutyl 2, 2, 6, 6-tetramethylcyclohexan-1,3-dione and isomyrtucommulone-B demonstrated the highest antibacterial effect and strong inhibition against *P. acnes* [21].

The bactericidal activity of the ethanol product of Myrtle leaves (Myrtacin) and myrtucommulone A and B against erythromycin-sensible and resistant *P. acnes* strains was determined by measuring the MIC and D value. The extracts inhibited *P. acnes* strains growth with MICs of 4.9 μg/mL and 2.4 μg/mL, respectively. Myrtucommulone A and B also showed inhibitory activity against both strains (MICs of 1.2 μg/mL and about 0.5 μg/mL, respectively). The extract also exhibited a concentration-dependent antilipase activity [9]. *P. acnes* produces lipases, proteases, and hydrolases, contributing to inflammation [22].

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Several studies showed anti-inflammatory properties of essential oil, aqueous and ethanolic extract of Myrtle in animal model [23]. Anti-inflammatory effect of Myrtle also related to the Myrtucommulone (MC) and a lesser extent of Semi-Myrtucommulone (S-MC) and nonprenylated acylphloroglucinols. This is due to their ability to suppress the biosynthesis of eicosanoids by direct inhibiting cyclooxygenase-1 and 5-lipoxygenase *in vitro* and *in vivo*. They also have a restraining effect on synthesis of ROS species and release of elastase as the initiating factor of inflammation [24].

Releasing free radicals and inflammatory mediators reflect the presence of oxidative stress state in parts of the pathogenesis of acne, Oxidative stress is initiated by reactive oxygen species (ROS). Three free radicals (hydroxyl, superoxide and nitrous oxide) are responsible for the occurrence of irritation during the acne infection; therefore, the use of antioxidant and anti-inflammatory agents has been considered along with usual medication on the treatment of acne vulgaris [15, 25, 26]. Antioxidant activity and total phenolic compounds of four extracts (water, methanol, ethanol, and ethyl acetate) of Myrtus communis were measured. The methanol and water extracts possess significant antioxidant activities. This order is observed in both leaf and berry extracts. They showed that it is a rich source of phenolic content, which has been reported as an active antioxidant component. There is also a linear correlation between the phenolic content and antioxidant activity [27-29].

Clinical studies have also been performed to evaluate the effect of different topical Myrtle products in patients with acne, which confirm the results of *in vitro* and *in vivo* studies.

A prospective, randomized, parallel-group study was conducted on 164 patients with mild to moderate acne, who previously developed a retinoid dermatitis, in which, one group of patients received 0.2% Myrtacine and 4% nicotinamide, and the second group treated with a moisturizer. Patients treated with the Myrtacine / nicotinamide combination showed a statistically significant improvement in symptoms (pruritus, stinging and burning sensation) and signs (erythema, dryness and oedema). This good result also observed in patient with nodular acne [30].

A clinical study was performed with products containing Myrtacine on erythromycin-resistant strains of *cutibacterium. acnes*. Sixty patients with global acne severity evaluation (GEA) scale who had GEA grades 2 and 3 acne were treated with Myrtacine-based dermocosmetic twice daily for 8 weeks. At baseline, antibiotic-resistant strains of *cutibacterium. acnes* were detected in 38 patients. Global *cutibacterium. acnes* population counts were stable at the end of the study, however, there was a significant reduction of erythromycin-resistant strains of *cutibacterium. acne*. There was also a significant reduction of inflammatory and non-inflammatory lesions and acne severity after 8 weeks [31].

In another study on 20 Korean women with acne vulgaris for 6 weeks, it is clinically proved Myrtle essential oil has beneficial effects. The acne grades significantly decreased in the Myrtle group. The pore index, the erythema index, the sebum index, microorganism index and the desquamation index also decreased in the group in a statistically significant manner. In the control group with no Myrtle, the acne grades and the microorganism index a little decreased, but was not statistically significant, while the pore, erythema, sebum and desquamation indices rather increased to some extent [11].

Our results are consistent with those of those previous clinical trials on Myrtle products. In our study, erythema index was not reduced, which differed from the latest study findings. This difference may be related to the duration of the study (12 weeks versus 6 weeks) and the type of Myrtle product (ethanolic extract versus essential oil). We believe our study duration was more appropriate. One of the common findings between our study and the latest study is a decrease in sebum index. The number of *P. acne* that measured by Visiopor showed a significant decrease in our study. The effectiveness of Myrtle formula was significant on the assessment of ASI, TLC, inflammatory and non-inflammatory lesion. No withdrawals owing to adverse effect of Myrtle were reported in our trial. The efficacy and good tolerance of Myrtle formula demonstrated in our study were consistent with the results of previous studies.

The small sample size was the main limitation of this study. Other studies with larger sample size and higher dosage of Myrtle can be designed to investigate its effects on acne treatment.

CONCLUSION

This study showed a significant decrease in the inflammatory and non-inflammatory lesions, ASI and TLC percentage changes on both sides of the face at 12th week. There was a significant difference in the reduction of inflammatory lesions and ASI percentage changes for Myrtle compared to clindamycin. The results showed that Myrtle is as effective as clindamycin in treating mild to moderate acne. The significant decrease of sebum, as a precursor of acne, was one of the most outstanding features of Myrtle lotion. The patient's satisfaction for Myrtle

was significantly higher than the clindamycin and the incidences of AEs between both formulations were similar.

Myrtle can be used as a natural drug beside other standard topical drug in the treatment of acne vulgaris to improve clinical efficiency and reduce possible side effects.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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