Comparison between the therapeutic effect of microneedling versus tretinoin in patients with comedonal acne: a randomized clinical trial

Golnaz Mehran, MD
Saba Sepasgozar, MD
Masoomeh Rohaninasab, MD
Azadeh Goodarzi, MD
Mohammadreza Ghassemi, MD
Mahrokh Fotooei, MD
Elham Behrangi, MD

Department of Dermatology, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

Corresponding Author:
Elham Behrangi, MD
Department of Dermatology, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
Email: behrangi.e@iums.ac.ir

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Background: Microneedling has been shown to be a clinically effective and safe treatment for comedonal acne vulgaris. The aim of the present study was to compare the clinical effect of microneedling and the most commonly used topical drug, tretinoin, in the treatment of comedonal acne.

Methods: Patients with comedonal acne (n = 82) were randomized to receive topical tretinoin (n = 41) or 6 sessions of microneedling (n = 41) over a period of 3 months. Objective assessments such as changes in acne severity score by global acne grading system (GAGS) and patients' subjective satisfaction were investigated at the baseline, at the end of the treatment period, and at the 3-month follow up.

Results: GAGS was significantly reduced in both microneedling (7.8±3.8 to 3.5±2.6) and tretinoin (8±3.8 to 6.6±3.2) groups at the end of the treatment course compared with the baseline. The overall acne severity index reduction in microneedling group was significantly higher than that of the tretinoin group (P<0.001). Improvement in acne severity was also more permanent by microneedling. The severity of acne in tretinoin recipients was increased to 8.2±3.2 at the follow-up visit, while it remained nearly unchanged in the microneedling group. (3.3±2.4). Patients' subjective assessment concerning acne improvement was significantly more satisfactory in microneedling group (P<0.001).

Conclusion: Compared with tretinoin, microneedling seems to be a more effective, permanent and satisfactory treatment in the treatment of comedonal acne.

Keywords: acne, comedone, microneedling, tretinoin

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INTRODUCTION

Acne is a common skin condition, yet complex in terms of pathophysiology. It mostly presents as non-inflammatory (comedone) and inflammatory (papules and pustules) lesions on the face, chest and back, caused by the closure of skin pores with fat, dead cells, and bacteria. The inflammatory manifestation of acne is partly due to the colonization of *Propionibacterium acnes* [1]. The pathophysiology of acne is multifactorial because of bacterial colonization within the pilosebaceous units, follicular desquamation, inflammation, and excess sebum production. High levels of Interleukin 1 alpha (IL-1α) and pre-inflammatory cytokines found in skin contributes to comodogenesis.

Tretinoin, a vitamin A derivative, is the first therapeutic alternative for most forms of acne with a comedolytic effect. It regulates the proliferation and differentiation of epidermal cells in stratum corneum,

changes the abnormal follicular keratinization, and exerts anti-inflammatory effects through inhibiting toll like receptors. However, it may irritate the skin, ensuing redness, dryness, burning sensation, or aggravate eczema, particularly atopic dermatitis [2]. Designed by Fernandes to pierce the skin by fine stainless steel needles, microneedling, particularly employed as fractionated microneedle radiofrequency, is reported as a possible treatment for acne vulgaris and can reduce sebum level and sebum excretion rate [3-8]. It alleviates post-inflammatory erythema, a common result of acne inflammation, with anti-inflammatory and antiangiogenic properties [9]. Microneedling treatment creates deep dermal injury in the peri-hair follicle collagen, inducing collagen fiber synthesis that is expected to be beneficial in the treatment of acne vulgaris [10]. Lee et al. revealed that fractionated microneedle radiofrequency in two sessions with 1-month interval exerted therapeutic effects on inflammatory acne vulgaris [7]. Later, Kim et al. found that although microneedling significantly reduced both inflammatory and non-inflammatory acne lesions, the former had a better response. Additionally, sebum excretion, subjective satisfaction and patients' quality of life were significantly improved [4,5]. When the needle enters the skin, it causes local damage, entailing a minimum amount of bleeding by tearing the small blood vessels. Needles penetrate the epidermis, but do not detach it, hence the fact that microneedling can be safely repeated without causing serious or permanent side effects [11]. There is no direct comparison regarding therapeutic effects of tretinoins and microneedling in a controlled fashion. Therefore, we aimed to evaluate the efficacy and safety of these two therapeutic options in terms of comedonal acne treatments through a prospective, randomized controlled study.

PARTICIPANTS AND METHODS

Participants and Study Design

This study is a randomized controlled phase III clinical trial. The study population were patients of any age with comedonal acne, who were referred to Rasoul Akram Hospital, Department of Clinical Dermatology, within two consecutive years (2017-2018). Excluded from the study were subjects with inflammatory and severe acne, active herpes labialis or other local infections within the treatment area, keloidal predisposition, and immunosuppression, or those being treated with systemic anti-acne drugs.

Simple random sampling method was employed to include 82 patients. Sample sizes of 41 in microneedling group and 41 in tretinoin group were sufficient to achieve a 80% power to detect a difference of 0.29 (0.5 vs.0.79) concerning the group mean difference of post-treatment acne severity score. The employed test statistic was the 2-sided Z test with pooled variance. Computer-based random number generators were used to create a random allocation sequence to assign a treatment modality to each side. Randomization codes were secured over the entire course of the study. Patients were randomly assigned to receive the treatments, and were not allowed to use any other systemic, topical, or light-based acne treatments over the course of the study. Investigators, blinded to the randomization method and assigned treatments, collected and analyzed the data.

Data Collection and Outcome Measures

The Primary endpoint was the changes in acne severity at three time points in microneedling (Amiea Med 2016, Germany, needle: 1.5 mm) group: every two weeks during the treatment time-course, and three months after the treatment; tretinoin (Cream 0.05%, Iran Daru Company) group: every month during treatment, and three months following the treatment). A dermatologist blinded to treatment assignments, determined the acne severity by assessing the Visio face (VisioFace® 1000 D, Courage - Khazaka Electronic, Köln) images according to the global acne grading system (GAGS) [12]. In this quantitative scoring system, a factor of 1-3 is given to six acne prone areas based on its size (forehead, each cheek, nose, chin, chest and upper back). Then, a factor of 0-4 (no lesion = 0, comedone = 1, papule = 2, pustule = 3, and nodule = 4) is allocated to each region according to the most severe lesion type found in the assessed area. Finally, a score between 1 to 39 is calculated by the sum of all areas' scores after the multiplication of two factors in each area. A score of 1–18 shows mild acne, 19–30 indicates moderate acne, 31–38 is severe acne, and >39 shows very severe acne.

The other end point, patients' assessments of

the treatment outcomes, was further conducted at each evaluation visit. Accordingly, patients were asked to rate the improvements in their acne as mild, moderate or excellent.

Sample Size and Analysis Method

Data analysis in this study was carried out in two sections. First, the demographic and descriptive information, the samples and the results of the indicators were interpreted using one and two variables tables and charts. In the second section, the analysis part, normal variables distribution, t-test, analysis of variance and repeated measures for quantitative variables were conducted. Chi-square test was used for qualitative variables. Non-parametric tests were used in case the distribution of data was not normal. In this study, the data distribution was normal and the variance of the two groups was the same; data analysis was carried out using SPSS 23 software, where a P-value < 0.05 was significant.

Ethical Considerations

The ethical code of this trial is IR.IUMS.FMD.REC.1395.9411166001 and the IRCT number is IRCT2014040624018210N7.

RESULTS

In this study, 82 patients with a mean age of 24.5 years (standard deviation (SD) = 4.6 years) were entered. Of the patients, 12 (14.6%) were male and 70 (85.4%) were female. Demographic data is summarized in Table 1.

Table 1. Demographic data of participants

Variables	Microneedling	Tretinoin	*P*-value
Age	24.9±5.3	23.8±3.7	0.3
Men	6 (14.6%)	6 (14.6%)	0.6
Women	35 (85.4%)	35 (85.4%)	

Table 2 shows the changes in the severity of acne in the microneedling and tretinoin groups according to the location of the acne. In the first visit, there was no significant difference between the two groups concerning the severity of acne. However, the final and follow-up visits were significantly different. In both groups, an increase in acne severity index was observed in follow-up visit (especially in tretinoin group), but still there was a significant difference regarding acne severity score in both groups, before and after therapy. Interestingly, the increase of the acne severity index in tretinoin group, signifies its positive therapeutic effects during study.

Finally, the overall difference regarding the reduction of acne severity index in the microneedling group was significantly higher than that of the tretinoin group (Figure 1).

The patients' response to the intensity of the changes encountered in each group is illustrated in Table 3.

DISCUSSION

As far as the authors are concerned, this is the first study directly comparing tretinoin and microneedling concerning comedonal acne treatment. The current results are indicative of the efficiency and effectiveness of microneedling as a treatment for comedonal acne. The findings

Table 2. The changes in the acne severity index. * P-value is calculated for the final and follow up visit. The significance level is <=0.05

Treated location	Treatment method	First visit	Final visit	Follow-up visit	*P*-value*
Forehead	Microneedling	1.1±0.8	0.34±0.6	0.6±0.7	0.001
	Tretinoin	1.3±0.9	0.98±0.7	1.1±0.6	
Right cheek	Microneedling	1.1±0.9	0.61±0.8	0.6±0.7	0.001
	Tretinoin	1±0.7	0.9±0.7	1.1±0.6	
Left cheek	Microneedling	1.3±0.8	0.6±0.7	0.6±0.6	0.001
	Tretinoin	0.95±0.7	0.8±0.6	1.2±0.7	
Nose	Microneedling	0.5±0.7	0.1±0.4	0.15±0.4	0.001
	Tretinoin	0.6±0.6	0.4±0.5	0.5±0.5	
Chin	Microneedling	0.8±0.7	0.3±0.6	0.17±0.4	0.001
	Tretinoin	0.9±0.8	0.9±0.7	1.0±0.8	
Total	Microneedling	7.8±3.8	3.5±2.6	3.3±2.4	0.001
	Tretinoin	8±3.8	6.6±3.2	8.2±3.2	

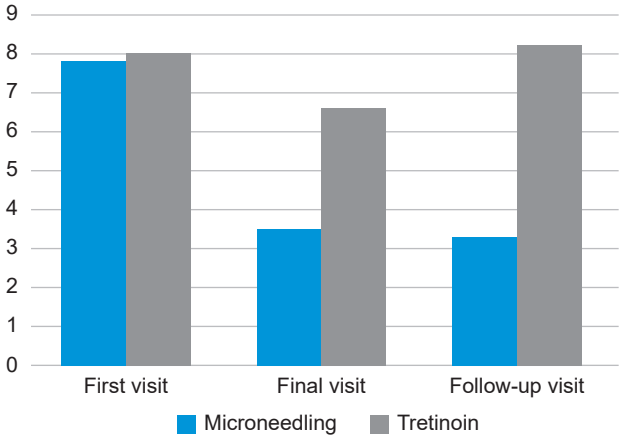

Figure 1. Acne severity index in three visits

Table 3. Patients'assessments of the efficacy of the treatment

Answer	Microneedling	Tretinoin	*P*-value
Excellent	13 (37.7%)	0 (0%)	0.001
Moderate	24 (58.5%)	3 (7.3%)	
Mild	4 (9.8%)	38 (92.7%)	
Total	41 (100%)	41 (100%)	

also showed that microneedling is more effective in reducing the severity of acne compared with tretinoin. Additionally, the severity of acne returned to the baseline in most patients of the tretinoin group in the 3 months of follow-up, while the improvement in acne was more permanent by microneedling. Our data showed that with regards to forehead, cheek, chin, and nose, the severity of acne in tretinoin recipients increased at the follow-up visit, compared to the final visit at the end of the treatment course. In the microneedling group, the severity of acne in the nose and forehead was slightly augmented, while it was reduced in the chins. Patients' subjective assessment of acne improvement was significantly more satisfactory in the microneedling group.

Microneedling is found to be an effective and safe treatment for acne vulgaris. Compared with previous studies, about 57% reduction in acne severity (from 7.8 to 3.3) was observed in the current study following 6 sessions of treatment, which is satisfactory. Kwon et al reported that microneedling reduced the non-inflammatory acne lesion count by around 33.2% (from 23.1 to 15.4) and acne grade by 55% [6]. Pai et al. found that most acne patients (42.1%) treated with 2-4 sessions of bipolar radiofrequency microneedles had 51-75% improvement in acne severity at two months after the final treatment session. About 26.6% and 24.7% of patients showed near total (> = 75%) and moderate (26-50%) improvement in acne severity [8]. Lee et al. reported a retrospective case series that examined 18 patients with moderate to severe acne treated with two, 1-month apart, sessions of microneedling. Improvement was reported to be >75% in 2, 50% to 75% in 8, and 25% to 50% in 6 patients [7]. On the other hand, Kim et al, observed more effectiveness in microneedling treatment of acne. They reported that the mean percentage of non-inflammatory acne lesions was reduced by 40.86%, 55.16%, 70.82% and 76.46% at one month after the first, second and third treatments, and at 3 months following the last treatment, respectively. However, it was evident that non inflammatory lesions respond better to microneedling treatment. They further revealed a significant improvement in sebum excretion, subjective satisfaction, and patients' quality of life [5]. Lee et al. found that after one session of microneedling, the acne severity was 1.8, 1.3, and 0.6 at 2-, 4-, and 8-week follow-ups, respectively. Additionally, inflammatory acne lesion count showed maximum improvement at the second week, followed by a gradual flare-up [3]. Interestingly, Kaminaka et al reported a mild flare-up of inflammatory and non-inflammatory lesions in 10.0% of the study population after the end of a 5-session microneedling [4]. Similarly, we observed a mild increase in the acne severity of the nose and forehead, while a decrease in the chins. However, improvement in acne was more permanent by microneedling compared with the tretinoin, which is reported to be effective in reducing the number of comedones in mild-to-moderate facial acne in a dose-dependent manner [13]. In the two previous studies, 12 weeks of tretinoin therapy at doses of 0.025% and 0.1% reduced microcomedones by 35% and 80%, respectively [14,15]. Our findings regarding tretinoin were not as satisfactory as the previous reports, which may be related to the shorter period of the present study.

There were some limitations in this study. First, our research lacked histological assessment. Second, topical tretinoin has dose-dependent effects, necessitating further studies with a higher range of dosage to compare with microneedling for a longer follow-up period. Additionally, further studies are required to search for optimized treatment parameters of microneedling and its combination

with other anti-acne medications.

CONCLUSION

Microneedling is a more effective and permanent treatment option for comedonal acne compared with tretinoin. Patients' satisfaction with the improvement in acne severity is also higher with microneedling procedure.

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Conflict of Interest: None declared.

REFERENCES

1. Cordain L, Lindeberg S, Hurtado M, et al. Acne vulgaris: a disease of Western civilization. Arch Dermatol. 2002;138(12):1584-1590.
2. Chandrashekhar BS, Anitha M, Ruparelia M, et al. Tretinoin nanogel 0.025% versus conventional gel 0.025% in patients with acne vulgaris: a randomized, active controlled, multicentre, parallel group, phase IV clinical trial. J Clin Diagn Res. 2015;9(1):WC04.
3. Lee KR, Lee EG, Lee HJ, et al. Assessment of treatment efficacy and sebosuppressive effect of fractional radiofrequency microneedle on acne vulgaris. Lasers Surg Med. 2013;45(10):639-47.
4. Kaminaka C1, Uede M, Matsunaka H, et al. Clinical studies of the treatment of facial atrophic acne scars and acne with a bipolar fractional radiofrequency system. J Dermatol. 2015;42(6):580-587.
5. Kim ST, Lee KH, Sim HJ, et al. Treatment of acne vulgaris with fractional radiofrequency microneedling. J Dermatol. 2014;41(7):586-591.
6. Kwon HH, Park HY, Choi SC, et al. Novel device-based acne treatments: comparison of a 1450-nm diode laser and microneedling radiofrequency on mild-to-moderate acne vulgaris and seborrhoea in Korean patients through a 20-week prospective, randomized, split-face study. J Eur Acad Dermatol Venereol. 2018;32(4):639-644.
7. Lee SJ, Goo JW, Shin J, et al. Use of fractionated microneedle radiofrequency for the treatment of inflammatory acne vulgaris in 18 Korean patients. Dermatol Surg. 2012;38(3):400-405.
8. Pai GS, Kashmar M, Kim YK, et al. The efficacy and safety of bipolar radiofrequency treatment with non-insulated penetrating microneedles for acne vulgaris and acne scars. Med Lasers. 2015;4(1):10-15.
9. Min S, Park SY, Yoon JY, et al. Fractional microneedling radiofrequency treatment for acne-related post-inflammatory erythema. Acta Derm Venereol. 2016; 96(1):87-91.
10. Kaminaka C, Uede M, Nakamura Y, et al. Histological studies of facial acne and atrophic acne scars treated with a bipolar fractional radiofrequency system. J Dermatol. 2014;41(5):435-438.
11. El-Domyati M, Barakat M, Awad S, et al. Microneedling therapy for atrophic acne scars: an objective evaluation. J Clin Aesthet Dermatol. 2015;8(7):36-4.
12. Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. Int J Dermatol. 1997;36(6):416-418.
13. Leyden J, Stein-Gold L, Weiss J. Why topical retinoids are mainstay of therapy for acne. Dermatol Ther. 2017;7(3):293-304.
14. Lavker RM, Leyden JJ, Thorne EG. An ultrastructural study of the effects of topical tretinoin on microcomedones. Clin Ther. 1992;14(6):773-780.
15. Thielitz A, Helmdach M, Röpke EM, et al. Lipid analysis of follicular casts from cyanoacrylate strips as a new method for studying therapeutic effects of antiacne agents. Br J Dermatol. 2001;145(1):19-27.