

Efficacy and Safety of Oral Isotretinoin and non Insulated Fractional Microneedling Radiofrequency in Acne Treatment.

Saad Hashim Salman, Sattar Gaber Ajeel and Dina Nawfal Abid

Ibnsina Medical Collage/ Medicine Department

Abstract— Non insulated microneedling RF can be used for treatment of pilosebaceous unit disorders especially in age 11-30 years who have acne vulgaris with oral therapy of isotretinoin. The psychosocial impact of acne that have affected individuals have doubtless social bleakness and many psychological disturbance.

Aim: Efficacy and Safety of combined non insulated fractional microneedling radiofrequency (NIFMRF) with oral isotretinoin drug in treatment of acne.

Material and methods: A study that include Forty eight patients with acne (moderate to severe) were subjected to monthly sessions of fractional RF micro-needling device (4 times) and oral isotretinoin therapy 0.5–1 mg/kg for 5 five months.

Results: In this research, 48 acne vulgaris were evaluated for 6 months duration received 20–40mg of oral isotretinoin and 4 monthly session of NIFMRF.

Acne vulgaris patients were 20.6 ±3.3 years old, 55.85 ±5.6 kg, 40 females, and 8 males. After 12 weeks all patients shows better global acne assessment scale (GAAS) result. The global acne assessment scale change with every months of treatment.

Age or weight doesn't have difference and no permanent side effect of scarring or hypo and hyperpigmentation due to use of NIFMRF even in type III & IV skin type and patient have high satisfaction for this combination of treatment.

Conclusion: from the present study show that the combination of NIFMRF with concomitant use of oral therapy of isotretinoin in treatment of moderate to severe acne are highly effective with less scarring and high satisfaction result.

Index Terms—NIFMRF, fractionated microneedling, systemic isotretinoin, safety, pilosebaceous unite

I. INTRODUCTION

Pilosebaceous unit disorders especially in age 11-30 years have acne vulgaris disorder and the hall mark of acne are comedone [1]. Acne mainly classified to mild, moderate and severe, acne in the face can cause severe inflammatory response which may lead to scarring in the face making the patients looking for reasonable management and helping theme to overcome the psychosocial impact and psychological disturbance[4,5]. The pathogenesis of acne vulgaris is multifactorial. A four major factors are:

1. follicular epidermal hyperkeratinisation
2. increase sebum production
3. proinflammatory effects of normal skin flora and Propionibacterium acnes

4. Inflammation [6].

The cause primarily is unknown. Acne have some aggravating factors of [7, 8]: e.g corticosteroids, chloride, halothane, bromide, iodide, oral contraceptives, ACTH, isoniazid, thyroid hormone, progesterone, phenytoin, or lithium, coal tar. Excessive friction, rubbing as mechanical factors. Chemicals like chlorinated hydrocarbons, petrol can cause acneiform eruptions, and comedogenic cosmetics and skin care products [1].

Vitamin A analogue (isotretinoin), are readily isomerized to tretinoin [2, 9].

US Food and Drug Administration (FDA) in 1982 was approved to manage severe, resistant, nodular acne [10]. All of pathophysiologic factors in acne typically targeted producing excellent results [2, 9].

Acne scarring may lead to emotional encumbrance, so a lot of patients seek treatment to prevent of scarring [7].

Acne scars are usually treated with laser or light rather than active lesions, the safety and efficacy of various laser devices, including pulsed dye laser, nonablative 1,450-nm diode laser, and light like intense pulsed light, for the inflammatory acne vulgaris treatment have been reported.[11,12,13,14]. Non-surgical device like Radiofrequency is use a variety of energy source for acne vulgaris patients perhaps by decreasing the size of sebaceous glands [15]. Sever inflammation that cased by acne can be treated by Nonablative radiofrequency (RF) device effectively [16].

“Recently, Lee et al. [17] demonstrated a positive therapeutic effect of fractional microneedles radiofrequency on inflammatory acne vulgaris and related scars”.

We made this study to investigate the efficacy and safety of a fractional microneedling RF with oral Isotretinoin therapy in the acne vulgaris treatment utilizing objective parameters.

II. METHODS

Moderate to severe acne patients were included in this study (40 female, 8 male, mean age 20.6 ±3.3 years old, range 17-24 years old, Fitzpatrick skin type: III–IV). Character of patients are summarized in Table 1.

TABLE I
PATIENT DEMOGRAPHICS

| Variable | | number | percent |
|-----------------------|-----|--------------------------|---------|
| Sex | F | 40 | 83.3 |
| | M | 8 | 16.6 |
| Age, years | | 20.6 ± 3.3(range, 17–26) | |
| Fitzpatrick skin type | III | 18 | 37.5 |
| | IV | 30 | 62.5 |
| GAAS scale | 3 | 36 | 75 |
| | 4 | 12 | 12 |

GAAS scale

Excluded Patients from the study if they:

- Received intense pulsed light photodynamic therapy
- Had treated with 1,450-nm diode laser
- Had treated with 595-nm pulsed dye laser
- Nonablative erbium–glass fractional laser therapy
- Had carbon dioxide laser fractional type 10,600 within 6 months

- Incision and drainage, intralesional corticosteroid
- Received systemic and topical antibiotics with 1 month
- Patients with a high possibility of becoming pregnant
- A possibility for keloids
- immunosuppressed

Four sessions of fractionated non-insulated RF microneedling at 1-month intervals were used. Cleansing of the face with a 70% alcohol and mild soap and local anesthesia applied before the beginning of the session, a cream of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine was used under occlusion for 1 hour.

The treatment parameters were a microneedle depth of 1.5 mm for the face except the frontal area is 1 mm. The intensity was set at 3, and the RF conduct time was 100 ms off, 500 ms on, and 100 ms off. NIFMNR was applied to the entire face for one pass, with an extra pass targeted at severe pustular lesions. 49 needles are simultaneously injected into the skin with adjustable penetration depth ranging from 1mm to 1.5mm, accurate to 0.1mm. The needles are arranged in a sophisticated matrix network and follow a bipolar pattern.

The international acne appraisal measure was used to assess the severity of acne by physicians. At 0, 4, 8, and 12 weeks, microneedling sessions were conducted.

Patients were examined at weeks 4, 8, 12, 16, and 20, and subsequently at 6 and 12 months. Photographic picture was done by use camera (galaxy note 10) in baseline and every visit, by one person at base line and on every follow-up session. Acne lesions were manually tallied during the initial appointment and during subsequent visits. The assessment involved marking each lesion with a pen to verify its documentation. The global acne assessment scale was utilized as a 5-point measure at the beginning and conclusion of the research.

Patients underwent checkups at weeks 4, 8, 12, 16, and 20, followed by assessments at 6 and 12 months. A photograph was taken using a camera (Galaxy Note 10) at baseline and throughout each visit by one individual at baseline and at every

follow-up appointment. All acne lesions were manually tallied during the initial visit and during subsequent visits. The assessment involved coloring each lesion with a pen to verify that each lesion was documented. The global acne assessment scale was utilized as a 5-point measure at the beginning and finish of the research.

Patients with a prior herpes virus infection were given preventive oral acyclovir hydrochloride for 3 days. It is advised to apply a noncomedogenic moisturizer 2-3 times a day for a few days after each treatment to enhance wound healing and avoid dryness. Patients were advised to limit sun exposure and apply a broad-spectrum sunscreen once the post-therapy crusting had diminished.

Statistical analysis:

We performed statistical analysis using SPSS 24. For the assessment of categorical data, frequency and percentage were used, and for the assessment of continuous data, mean and SD. The T test is employed to evaluate mean differences. A P-value of less than 0.05 proved to be significant.

III. RESULTS

The study comprised 48 patients with acne vulgaris, with a mean age of 20.8 ± 3.2 years, consisting of 40 females and 8 males as shown in Table 1. There are notable variations in the mean of GAAS at 8 weeks (12.8), 12 weeks (1.25), 6 months (0.17), and 12 months from baseline. The most significant change is observed six months following the initial measurement, as shown in Table 2.

TABLE II
DIFFERENCE BETWEEN THE MEAN GAAS FROM BASELINE, GOOD RESPONSE AFTER 8 WEEKS, THEN VERY GOOD RESPONSE AFTER 12 WEEKS, AND LASTLY GREAT OUTCOME AFTER 6 MONTHS FOLLOWING THERAPY.

| Group | N | Mean | Std. deviation | P-value |
|--------------|----|-------|----------------|---------|
| GAAS: | | | | |
| Baseline | 48 | 3.25 | 0.438 | 0.0001 |
| 8 weeks | 48 | 12.31 | 0.870 | |
| GAAS: | | | | |
| Baseline | 48 | 3.25 | 0.438 | 0.0001 |
| 12 weeks | 48 | 1.25 | 0.887 | |
| GAAS: | | | | |
| Baseline | 48 | 4.05 | 0.60 | 0.0001 |
| 6 months | 48 | 0.17 | 0.467 | |

P-value ≤ 0.05 (significant).

Four treatment sessions spaced one month apart, with follow-up for a minimum of one year post-treatment.

Redness, swelling, and bleeding affect 60% of patients, 25% of those with scaling and swelling, and 12% of those with crusting. Immediate postoperative symptoms were heavy bleeding, edema, and redness; however, these symptoms improved within four days. As early as two days following the

surgery, crusts and scaling were visible, but these faded after a week. There were no signs of hyperpigmentation, hypopigmentation, burns, or scarring.

With each sessions the subjective satisfaction were increasing during treatment time especially after 3 months from start of treatment as show in figures 1,2,3.



Figure 1- Photographs taken (a) prior to and (b) following treatment of a female patient 19 years old.



Figure 2- Before fractional radiofrequency microneedling, (a) a 20-year-old male patient; (b) following three treatments; and (c) following five months of follow-up.

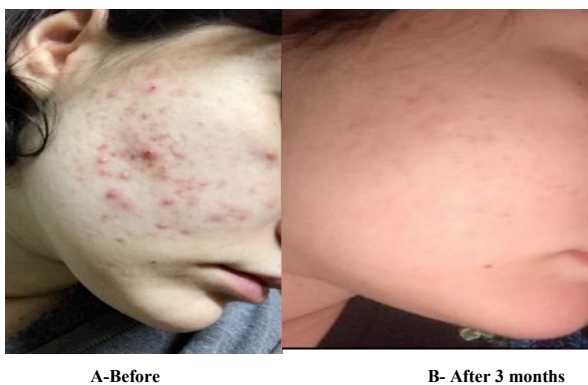


Figure 3. A female patient, age 18, is shown in (a) before therapy and (b) following fractional radiofrequency microneedling for five months.

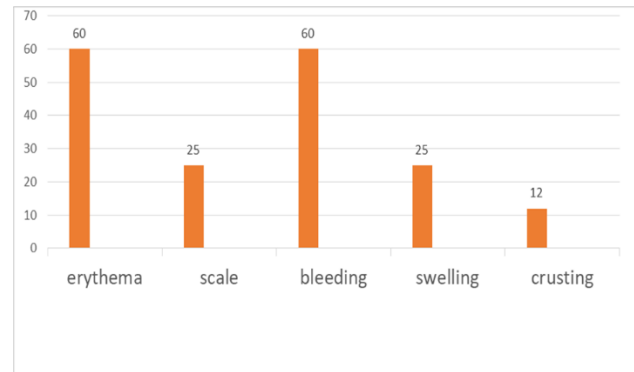


Figure 3. The frequency of each adverse event following fractional radiofrequency microneedling in treatment patients.

IV. DISCUSSION

Understanding the structure and function of the pilosebaceous unit is crucial for explaining how acne develops and creating successful treatment plans. Acne development is influenced by variables such as follicular hyperkeratinization, hormonal effects on sebum production and composition, and inflammation, partly caused by *P. acnes*. Standard treatments consist of topical benzoyl peroxide, retinoids, azelaic acid, and oral antibiotics.

However, It takes a long time for most of these therapies to work, and the current issue of bacteria developing resistance to antibiotics has led to the use of non-pharmacological methods in acne treatments, either on their own or in combination with pharmaceuticals.[3. 16].

Isotretinoin received FDA approval for patients with severe nodulocystic acne that does not respond to treatment, such as oral antibiotics. Isotretinoin has proven to be highly beneficial for many clinical kinds of acne throughout time. [30].

Many scar types, including atrophic and hypertrophic scars as well as inflammatory acne, are treated with radiofrequency devices [16, 31]. The dermis undergoes bulk heating due to the absorption of radiofrequency (RF) radiation by water, collagen, melanin, and dermal microvasculature; this, in turn, triggers the release of cellular mediators and growth factors, which facilitates the healing of wounds.

Hantash and colleagues- initially proved that a bipolar microneedle electrode system—a minimally invasive radiofrequency device—could have an effect on human skin. The scientists used pairs of microneedle electrodes to generate radiofrequency thermal zones in the dermis. [21].

Sang et al conducted the research on 18 individuals whose acne vulgaris was moderate to severe; they underwent two fractionated microneedle RF treatments spaced one month apart. Assessment of progress was done by considering the quantity of inflammatory acne lesions and improvement scores were calculated according to the severity of the lesions. Inflammatory acne lesions did not worsen in any patient. Inflammatory acne vulgaris and associated scars can be effectively treated with fractionated microneedle radiofrequency, according to their findings. Also, this method won't make an active acne lesion worse [22].

Kim et al; Another study demonstrated the use of microneedle

electrode pairs to create radiofrequency heat zones in the dermis. These zones were then utilized to treat inflammatory acne vulgaris and its associated dermatologic diseases, such as acne scars and inflated facial holes. [23].

Ganesh et al: set out to assess the safety and effectiveness of treating acne vulgaris and acne scars using bipolar radiofrequency energy delivered through non-insulated penetrating microneedles. The efficacy of bipolar non-insulated microneedle therapy RF in alleviating moderate to severe acne vulgaris and mild to severe acne scarring was assessed in 316 participants (195 males and 121 females; ages 18-34 years; Fitzpatrick skin types IV-V) treated with two to four sessions. Patients with Fitzpatrick skin types IV-V may safely and successfully treat acne vulgaris and acne scars with bipolar non-insulated microneedle radiofrequency therapy, according to the results. [24].

In this study, we utilized 49 non-insulated microneedles to administer high-intensity RF radiation in conjunction with oral isotretinoin. The device's large number of microneedles also helps to reduce the procedure time when compared to alternatives, such as the Kobayashi needle. Additionally, the use of microneedles reduces epidermal injury, crust formation, and reconstruction time. Skin healing is aided by this radiation's thermal effects, which reduce sebaceous gland activity while promoting cytokines and growth factors. Topical anesthetics are safe to use, as they cause only minor adverse effects like discomfort and bleeding, and they do not pose serious risks like scarring, depigmentation, or burns.

Researchers found that a combination of isotretinoin therapy with noninsulated microneedling radiofrequency did not exacerbate active acne and had a synergistic impact that reduced the likelihood of scarring and acne recurrence.

CONCLUSION

For moderate to severe acne vulgaris, it is safe and effective to combine fractional RF microneedling with oral isotretinoin. Fractionated microneedling is a safe and effective way to treat active acne; it speeds up the healing process, reduces scarring, and reduces the likelihood of recurrence. We suggest that future research with a comparable design use large samples and have extended follow-up periods to determine recurrence rates and avoid scare tactics.

REFERENCES

1. Akdogan N, Dogan S, Atakan N, Yalçın B. Association of serum hormone levels with acne vulgaris: low estradiol level can be a pathogenetic factor in female acne. *Our DermatolOnline* 2018; 9: 249-56.
2. Eichenfield LF, Krakowski AC, Piggott C, et al. Evidence-base recommendations for the diagnosis and treatment of pediatric acne. *Pediatrics* 2013; 131 Suppl 3: S163-86.
3. Friedlander SF, Eichenfield LF, Fowler JF Jr, et al. Acne epidemiology and pathophysiology. *Semin Cutan Med Surg* 2010; 29 (2 suppl 1): 2-4.
4. Lee YJ, Lee CY, Shin MK. A neglected acne scar type: papular acne scars and their correlations with keloid scars. *Dermatol Surg* 2021; 47: 1347-51.
5. Connolly D, Vu HL, Mariwalla K, Saedi N. Acne scarring – patho-genesis, evaluation, and treatment options. *J Clin Aesthet Dermatol* 2017; 10: 12-23.
6. Al-Hamamy HR, Sharquie KE, Noaimi AA, Hussein WN. Topical erythromycin-zinc acetate complex lotion versus topical erythromycin gel in treatment of mild to moderate acne vulgaris. *Our Dermatol Online* 2014; 5: 347-51.
7. Eichenfield DZ, Sprague J, Eichenfield LF. Management of acne vulgaris: a review. *JAMA* 2021; 326: 2055-67.
8. Sharquie KE, Noaimi AA, Al-Janabi EA. Treatment of active acne vulgaris by chemical peeling using 88% lactic acid. *Our Dermatol Online* 2014; 5: 337-42.
9. Li W, Liu Y, Luo Q, et al. Off-label uses of retinoids in dermatology. *Our Dermatol Online* 2012; 3 (Suppl. 1): 259-78.
10. Pile HD, Sadiq NM. Isotretinoin. [Updated 2022 May 8]. In: Stat Pearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK525949>.
11. Harper JC. An update on the pathogenesis and management of acne vulgaris. *J Am Acad Dermatol* 2004; 51:S36–8.
12. Seaton ED, Charakida A, Mouser PE, Grace I, et al. Pulsed-dye laser treatment for inflammatory acne vulgaris: randomized controlled trial. *Lancet* 2003; 362:1347–52.
13. Munavalli GS, Weiss RA. Evidence for laser- and light-based treatment of acne vulgaris. *Semin Cutan Med Surg* 2008; 27:207–11.
14. Rinaldi F. Laser: a review. *Clin Dermatol* 2008; 26:590–601.
15. Alster T. S. and Lupton J. R. (2007):"Non oblativ cutaneous remodeling radiofrequency devices" *Clinic in Dermatology*.25:487-91.
16. Ruiz-Esparza J, Gomez JB. Nonablative radiofrequency for active acne vulgaris: the use of deep dermal heat in the treatment of moderate to severe active acne vulgaris (thermotherapy): a report of 22 patients. *Dermatol Surg* 2003; 29:333–9.
17. Harper JC. An update on the pathogenesis and management of acne vulgaris. *J Am Acad Dermatol* 2004; 51: S36–S38.
18. Lee SJ, Goo JW, Shin J, Chung WS, Kang JM, Kim YK, ChoSB. Use of fractionated microneedle radiofrequency for the treatment of inflammatory acne vulgaris in 18 Korean patients. *Dermatol Surg* 2012;38:400–405.
19. Torzecka J, Dzikowska-Bartkowiak B, Gerlicz-Kowalczyk Z, Wozniacka A. The use of isotretinoin in low doses and unconventional treatment regimens in different types of acne: a literature review. *Adv Dermatol Allergol* 2017; 34: 1-5.
20. Kim H, Ahn KJ, Lee S, et al. Interactive thermal tissue reactions of 7-MHz intense focused ultrasound and 1-MHz and 6-MHz radiofrequency on cadaveric skin. *Skin Res Technol* 2019; 25: 171-8.
21. Hantash BM, Renton B, Berkowitz RL, Stridde BC, et al. Pilot clinical study of a novel minimally invasive bipolar

microneedling radiofrequency device. *Lasers Surg Med* 2009; 41:87-95.

22. Sang J. L., Ja W. G., Jaeyong S., Jin M. K., Won S. C., Young K. K., and Sung B. C. (2012): "Use of Fractionated Microneedle Radiofrequency for the Treatment of Inflammatory Acne Vulgaris in 18 Korean Patients". *Dermatological Surgery Journal* 38(3):400-405.

23. Kim H, Ahn KJ, Lee S, et al. Interactive thermal tissue reactions of 7-MHz intense focused ultrasound and 1-MHz and 6-MHz radiofrequency on cadaveric skin. *Skin Res Technol* 2019; 25: 171-8.

24. Ganesh S. P., Mouhamad K., Young K. K., and Jongju N.(2015): "The Efficacy and Safety of Bipolar Radiofrequency Treatment with Non-Insulated Penetrating Microneedles for Acne Vulgaris and Acne Scars" *Med Laser* 4(1): 10-15.

25. Kruglikov IL. Assessment of mechanical stress induced by radiofrequency currents on skin interfaces. *Biomed Res Int* 2021; 2021: 6623757.

26. Kositratna G, Hibert ML, Jaspán M, et al. Effects of deviation from focal plane on lesion geometry for ablative fractional photothermolysis. *Lasers Surg Med* 2016; 48: 555-61.

27. Wat H, Wu DC, Chan HH. Fractional resurfacing in the Asian patient: current state of the art. *Lasers Surg Med* 2017; 49: 45-59.

28. Azzopardi EA, Duncan RT, Kearns M, et al. Cutaneous laser surgery for secondary burn reconstruction: cost benefit analysis *Burns* 2020; 46: 561-6.

29. Kim ST, Lee KH, Sim HJ, et al. Treatment of acne vulgaris with fractional radiofrequency microneedling. *J Dermatol* 2014; 41: 586-91.

30. Pochi PE, Shalita AR, Strauss JS, et al. Report of the Consensus Conference on Acne Classification. Washington, DC, March 24 and 25, 1990. *J Am Acad Dermatol* 1991;24:495-500.

31. Elsaie ML, Choudhary S, Leiva A, Nouri K. Nonablative radiofrequency for skin rejuvenation. *Dermatol Surg* 2010;36: 577-89.