Title: Comparing The Efficacy Of Topical Tazarotene Gel 0.1% Versus Microneedling in Atrophic Post-Acne Scars

NCT Number: under process

Date: 22 Aug 2020 to 21 Feb 2021

Study Protocol:
Objective: Comparison of tazarotene gel 0.1% versus microneedling in atrophic post-acne scars.
***Design*:** Randomized Control Trial.
Duration: Dermatology department, Jinnah Postgraduate Medical Centre (JPMC) Karachi, from August 22, 2020 to February 21, 2021.
Methodology: Patients aged 18-40 years were randomly divided into two groups having 101 patients in each group. Dermoscopic examination for scar type (such as icepick, rolling or boxcar) and scar severity assessed with Goodman and Baron acne scarring scale for every patient. In group A (tazarotene gel), patients were guided to put tazarotene gel 0.1% on scars everyday having pea-sized gel quantity with the help of finger tip on face. In group B, use a dermaroller (192 needles of length 1.5 mm), monthly for a period of 6 months. Saline pads were used post session. We recorded alteration from baseline in scar severity grade at follow up of 3 then 6 month. All collected data was entered into the proforma.
Results: Out of 202 patients, the mean age was 26.3±5.8 v.s 25.2±5.5 years, while 36 (35.6%) males and 65 (64.4%) females v.s 33 (32.7%) males and 68 (67.3%) females. Potency of gel 0.1% in 37 (36.6%) v.s microneedling in 31 (30.7%) patients (*p=0.372*).
Conclusion: Tazarotene gel 0.1% efficacy was comparable to microneedling in treating atrophic post-acne scars.

Key Words: Efficacy, Topical Tazarotene Gel, Microneedling, Acne Scars, Treatment.

INTRODUCTION

Acne vulgaris is a long term inflammatory disease of the pilosebaceous. It has high grade existence and is known to negatively influence quality of life [1]. It begins in adolescence with 30% to 100% popularity. Acne scarring is popular and well-recognized outcome of acne [2-3]. It may be either atrophic or hypertrophic, further categorized morphologically into boxcar, icepick or rolling with the option of treatment modalities often based on scar types [4]. Prior recognition and control of acne is necessary in averting scarring and resultant unfavorable social effects developed due to irritation and feeling of being ashamed [5]. Acne scars developed due to inadequate treatment or delayed healing of inflammatory acne lesions [6]. Gels of retinoids, like adapalene, raises collagen by stimulating fibroblast cells [7]. A home-based topical treatment is more accepted and would be suitable in treating scars [8].

Another research has shown the better results of tazarotene gel 0.1% with contrast to adapalene 0.1%, in controlling acne [9]. The aim of our study is comparison of daily use of tazarotene gel 0.1% in contrast to performing derma roller monthly sessions for controlling acne scars. Many previous studies reported, but there was lack of local researches in head to head

comparison between these two therapies, to improve outcome by adopting superior approach as first choice of treatment in future.

METHODOLOGY

This was a randomized Control Trial, done in Department of Dermatology, Jinnah Postgraduate Medical Centre (JPMC), Karachi from August 22, 2020 to February 21, 2021.

A total of 202 patients with 101 in each group. We estimated sample size using WHO calculator using statistics for efficacy in topical Tazarotene gel (group A) as 30.5% and micro-needling (group B) as 47.2%,80% power of test and 95% confidence level. Both genders, 18 to 40 years with atrophic post-acne scar patients of duration 4 to 8 years were included. Informed consent was obtained. Patients of grade 4 to 2 were estimated by Goodman and Baron scarring scale. While excluded pregnant/lactating woman, any prior allergy to given drug, known case of having likelihood of past keloid, active acne or post macules of variable colors, previous dermabrasion, laser resurfacing on face, other causes of scarring, collagen disorders, coagulation disorders, past retinoid exposure below 4 weeks, hydroxy acids, microdermabrasion session below 3 weeks and retinoids taken orally in past 6 months.

This study was conducted after approval from ethical review committee and CPSP. During the patient first visit, baseline photographs were captured with informed consent. Dermoscopic examinations of predominant scar type (such as icepick, rolling or boxcar) and the scar intensity estimated by using Goodman and Baron scarring scale for every patient. Before the start of the work , a digital number was allotted from computer randomly to divide them into two groups . In group A, patients were guided to use a gel on scars everyday by putting a pea-sized quantity on index finger to conceal. Patients who complained dryness were instructed to use a moisturizer in morning but avoid any other medication on face. In group B, microneedling was carried out with dermaroller (192 needles and length 1.5 mm) by the similar doctor, one time in a month in total 6 monthly sessions. Before conducting dermaroller session , local anesthesia was put on scars containing lignocaine and prilocaine.

Microneedling was conducted by dermaroller in constant rolling motion with slight pressure in variable paths (i.e, diagonal and right angled direction) with upward motion till pinpoint bleeding was seen . After session, the saline soaked gauze were put on that area. The patients were also directed for precise use of sunblock having sun protective factor 30 on full area of face. All patients were followed up at 3 month and then at 6 month from the initial visit. Data stored in the form of pictures. Excellent score was labelled to those patients who uplift by 2 grades, while good for 1 and poor for 0 grade. The results were noted from alterations of initial scar grade first at 3 then at 6 month appointment. All data was entered in a predesigned proforma.

Biasness and confounder were controlled by strictly following the inclusion criteria.
SPSS 21 analysed the data. Frequencies and percentages were enumerated for qualitative data like gender, scar type, treatment, scar severity grade at baseline, after 3 and 6 months and efficacy. Quantitative variables were presented as mean ± SD like age and duration of acne. Comparison between both groups for efficacy was done by using Chi square test. Modifier like age, gender and time span of disease were organised through stratification. Post stratification, Chi square test was used for categorical variables. Consider P $\leq$0.05 as significant.

STATISTICAL ANALYSIS

In this randomized control trial, the total of 202 patients 101 in each group were included to compare the efficacy between topical tazarotene gel 0.1% versus Microneedling in treatment of atrophic post-acne scars and results were analyzed as:

Mean±SD of age in group A (topical tazarotene gel 0.1%) was 26.3±5.8 with C.I (25.15----27.44) and group B (Microneedling) was

25.2±5.5 with C.I (24.11----26.28) years, as shown in **TABLE 1**.

Mean±SD for duration of acne in group A (Topical tazarotene gel

0.1%) and group B (Microneedling) was 6.5±3.1 and 6.1±2.6 with C.I

(5.88----7.11) and (5.88----7.11) years, respectively as shown in **TABLE 2**.

In group wise distribution of gender, 36 (35.6%) male and 65 (64.4%) females were enrolled in group A (Topical tazarotene gel 0.1%) while 33 (32.7%) male and 68 (67.3%) females were included in group B (Microneedling) as shown in **TABLE 3**.

In distribution for type of scar icepick was noted in 36 (35.6%) patients, rolling 14 (13.8%), boxcar 12 (11.9%) and mixed 39 (38.7%) patients in group A (Topical tazarotene gel 0.1%) while in in group B (Microneedling) icepick was noted in 40 (39.7%), rolling 15 (14.6%), boxcar 20 (19.9%) and mixed 26 (25.8%) patients as shown in **TABLE 4**.

Baseline scar severity grades 1,2,3,4 was noted in 0 (0%), 0 (0%), 20 (19.8%), 81 (80.2%) and 0 (0%),0 (0%), 20 (19.8%), 81 (80.2%) in group A and group B respectively. While at 3 and 6 months it was noted as 03 (3%), 12 (11.9%), 26 (25.7%), 60 (59.4%), 22 (21.8%),

67 (66.3%) and 03 (3%), 23 (22.8%), 26 (25.7%), 49 (48.5%), 03 (3%), 14 (13.9%), 24 (23.8%), 50 (59.4%) in group A and group B respectively as shown in **TABLE 5**.

Excellent grade was noted in 12 (11.9%) and 10 (9.9%) patients in group A and group B, respectively. Good grade was noted in 25 (24.8%) and 21 (20.8%) in group A and group B while poor grades was documented in 64 (63.4%) and 70 (69.3%) patients in group A and group B, respectively as shown in **TABLE 6**.

Topical tazarotene gel 0.1% was found to be effective in 37 (36.6%) patients while microneedling, was found to be effective in 31 (30.7%) patients with non-significant P value i.e. (P=0.372) as shown in **TABLE 7**.

Stratification of age group (18---25) and >25 years, gender (male & female) and duration of acne (4----6) > 6years were done to assess the significant difference between both groups from **(TABLE 8-10)**.

TABLE # 1
DESCRIPTIVE STATISTICS OF AGE
n=202

AGE [Years]		**n**	**MINIMUM**	**MAXIMUM**	**MEAN**	**±SD**	**95% C. I**
GROUP	Group A	101	18	40	26.3	5.8	25.15----27.44
	Group B	101	18	40	25.2	5.5	24.11----26.28

TABLE # 2
DESCRIPTIVE STATISTICS FOR DURATION OF ACNE n=202

DURATION [Years]		**N**	**MINIMUM**	**MAXIMUM**	**MEAN**	**±SD**	**95% C. I**
GROUP	Group A	101	4	8	6.5	3.1	5.88----7.11
	Group B	101	4	8	6.1	2.6	5.88----7.11

TABLE # 3
DISTRIBUTION OF GENDER n=202

GROUP	GE NDER	
	Male	**Female**
Group A	36	65
	35.6%	64.4%
Group B	33	68
	32.7%	67.3%

TABLE # 4
DISTRIBUTION OF SCAR TYPE n=202

GROUP	SCAR TYPE			
	Icepick	**Rolling**	**Boxcar**	**Mixed**
Group A	36	14	12	39
	35.6%	13.8%	11.9%	38.7%
Group B	40	15	20	26
	39.7%	14.6%	19.9%	25.8%

TABLE #

5

DISTRIBUTION OF SCAR SEVERITY GRADE n=202

GROUP	GARDE	SCAR SEVERITY GRADE		
		At Baseline	After 3 Months	After 6 Months
GROUP A	1	0 (0%)	3 (3.0%)	03 (3.0%)
	2	0 (0%)	12 (11.9%)	23 (22.8%)
	3	20 (19.8%)	26 (25.7%)	26 (25.7%)
	4	81 (80.2%)	60 (59.4%)	49 (48.5%)
GROUP B	1	0 (0.0%)	3 (3.0%)	03 (3.0%)
	2	0 (0.0%)	9 (8.9%)	14 (13.9%)
	3	20 (19.8%)	22 (21.8%)	24 (23.8%)

TABLE #

	4	81 (80.2%)	67 (66.3%)	60 (59.4%)

TABLE # 6
DISTRIBUTION OF OUTCOME LEVEL n=202

GROUP	)UTCOME LEVEL		
	Excellent	**Good**	**Poor**
Group A	12	25	64
	11.9%	24.8%	63.4%
Group B	10	21	70
	9.9%	20.8%	69.3%

TABLE #

TABLE # 7

COMPARISON OF EFFICACY BETWEEN BOTH GROUPS n=202

GROUP	EFFICACY		P-VALUE
	Yes	No	
GROUP A	37 (36.6%)	64 (63.4%)	0.372
GROUP B	31 (30.7%)	70 (69.3%)	

Applied Chi-Square test

STRATIFICATION OF AGE GROUP WITH EFFICACY BETWEEN GROUPS n=202

AGE GROUP [In Years]		**EFFICACY**		**P-VALUE**
		Yes	**No**	
18 - 25	Group A	16 (39%)	25 (61%)	0.739
	Group B	20 (35.7%)	36 (64.3%)	
>25	Group A	21 (35%)	39 (65%)	0.245
	Group B	11 (24.4%)	34 (75.6%)	

Applied Chi-

STRATIFICATION OF GENDER WITH EFFICACY BETWEEN GROUPS n=202

GENDER		EFFICACY		P-VALUE
		Yes	No	
Male	Group A	10 (27.8%)	26 (72.2%)	0.738
	Group B	8 (24.2%)	25 (75.8%)	
Female	Group A	27 (41.5%)	38 (58.5%)	0.359
	Group B	23 (33.8%)	45 (66.2%)	

Applied Chi-

STRATIFICATION FOR DURATION OF ACNE WITH EFFICACY BETWEEN GROUPS n=202

DURATION [In Years]		**EFFICACY**		**P-VALUE**
		Yes	**No**	
4 – 6	Group A	13 (24.5%)	40 (75.5%)	0.725
	Group B	17 (27.4%)	45 (72.6%)	
>6	Group A	24 (50%)	24 (50%)	0.187
	Group B	14 (35.9%)	25 (64.1%)	

DISCUSSION

Acne vulgaris is a frequent issue which might give scarring of different intensity and apppearance which compromise the patients self-esteem and lead to insecurity, suspicion of inadequacy, social confinement, anxiety and depression [10]. So, it is necessary to control the scars. Acne scars divided into plain macules (erythematous or hyperpigmented), raised (keloids or hypertrophic scars) and reduced (icepick, boxcar, and rolling subtypes) [11]. Patients having scars gained from different treatment modalities corresponding to skin Fitzpatrick type, gender, age, health, mental and public component and scarring characteristics (type, site, and severity) [12,13]. Recent therapies include (chemical peeling, retinoid creams, corticosteroids, or 5-FU injectables), procedures (excision, subscision), non-invasive therapies (cryotherapy sessions and electro-surgery) and energy-based modalities (lasers, radiofrequency devices) [13]. Such modalities have different mode of actions, outcome and complications. The more intrusive therapies seldom demand trouble (e.g the necessity to keep away from sunlight), hyper - or hypopigmentation and lengthy recover time. Further new modality (e.g lasers) are generally costly, and the pharmacological modalities can lead to regional and extensive toxicities.

The US Food and Drug Administration accepted tazarotene, a topical third degeneration acetylenic retinoid, for acne control in June 1997 [14]. Tazarotene in the form of cream or lotion is equally beneficial [15-17]. It has also been shown to

remarkably control the macules of acne scarring in contrast to adapalene 0.3% gel [18].

In our research, the mean age in group A and group B was noted as 26.3±5.8 v.s 25.2±5.5 years, respectively. A study done by Afra TP, et al [8] reported a mean age of 23.4±2.9 years. Another study noted age as 28±6.8 years [19]. The mean duration of acne was 6.5±3.1 v.s 6.1±2.6 years. Males were 36 (35.6%) and 65 (64.4%) females were enrolled in group A while 33 (32.7%) males and 68 (67.3%) females were in group B. Afra TP, et al [8] described that males were 43.5% and females were 56.5% . The present study also noted the scar type as icepick 36 (35.6%), rolling 14 (13.8%), boxcar 12 (11.9%) and mixed 39 (38.7%) in group A while icepick 40 (39.7%), rolling 15 (14.6%), boxcar 20 (19.9%) and mixed 26 (25.8%) were reported in group B. The study of Afra TP, et al [8] also noted to have scar type as icepick 05 (13.9%), rolling 20 (55.6%), boxcar 06 (16.7%) and mixed 05 (13.9%). Tazarotene gel was found to be effective in 37 (36.6%) patients while microneedling, was effective in 31 (30.7%) patients ($p=0.372$). Afra TP, et al [8] noted the efficacy in tazarotene group as 17.6% and 29.4% in microneedling alone group. In stratification of age group with respect to efficacy between groups, insignificant association was noted in both age groups 18-25 and >25 as $p=0.739$ and $p=0.245$, respectively. In stratification of gender with respect to efficacy between groups, insignificant association was noted in male and female genders as $p=0.738$ and $p=0.359$, respectively. In stratification of duration of acne with respect to efficacy between groups, insignificant association was noted in duration (4-6) and (>6) as $p=0.725$ and $p=0.187$, respectively.

CONCLUSION

It is to be concluded that efficacy of daily home based tazarotene gel application was comparable with monthly sessions of microneedling therapy in treating atrophic post-acne scars.

CONFLICT OF INTEREST: None.

ETHICAL APPROVAL: Ethical approval was taken from Institutional Review Board Jinnah Postgraduate Medical Center Hospital, Karachi prior to the initiation of the study.

PATIENT'S CONSENT: Informed consents were obtained from patients to publish the data concerning this case.

AUTHOR'S CONTRIBUTION:

FS: Contributed to the design research, ethical approval, patient consent, data collection, analysis of the results and writing of the manuscript.

RG: Involved in planning, supervised the work and provided feedback.

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Figure 1: Left sided before and Right sided after Tazarotene gel 0.1%

Figure 2: Left sided before and Right sided after Microneedling

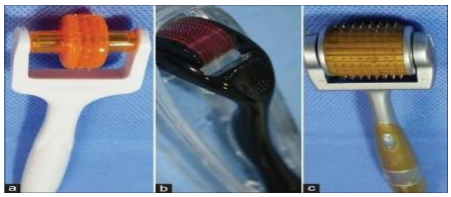

Figure 3: Different variety of Dermarollers (a) Dermaroller with narrow width of drum for smaller areas such as eyelids and nose (b) Dermaroller with 540 needles (c) Standard dermaroller with 192 needles.