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Original Article

Comparison of outcome of Fractional Carbon dioxide Laser plus topical hyaluronic acid serum versus Fractional Carbon dioxide Laser alone in the treatment of post-acne scars

Huma Saleem, Wajieha Saeed, Faria Altaf*, Ghazala Butt, Sabahat Shehzadi, Anam Mehmood, Ijaz Hussain

Department of Dermatology, King Edward Medical University, Mayo Hospital, Lahore.
* Department of Dermatology, Services Institute of Medical Sciences, SIMS, Lahore.

Abstract

Objective The objective of the study was to compare the frequency of outcome of fractional carbon dioxide (CO_2) laser plus topical hyaluronic acid serum versus fractional CO_2 laser alone in the treatment of post-acne scars.

Methods 300 patients of both genders 18 to 40 years who presented with post-acne scars were enrolled. One side of patient's face was randomly allocated to treatment Group-A which received combination therapy of topical hyaluronic acid and fractional CO_2 laser while the other side of face was allocated to treatment Group-B which was treated with fractional CO_2 laser alone. Percent reduction in Goodman and Baron quantitative grading score from baseline was determined after 3 months of treatment and was graded as excellent, significant, moderate and slight improvement and was compared between the groups.

Results In this study, the mean age of the patients was 23.2±4.7 years. There were 90 (30.0%) male and 210 (70.0%) female patients with a male to female ratio of 1:2.3. Both the groups were comparable in terms of mean Goodman and Baron quantitative grading score at baseline (54.68±14.30 vs. 53.66±14.83; p-value=0.391). The mean score at follow-up was significantly lower in patients receiving combination therapy as compared to fractional CO_2 laser alone (22.66±12.46 vs. 24.85±13.85; p-value=0.042). The frequency of excellent (17.0% vs. 14.3%) and significant (53.3% vs. 44.0%) improvement was significant higher in patients receiving combination therapy consisting of fractional CO_2 laser plus topical hyaluronic acid as compared to fractional CO_2 laser alone.

Conclusion Combining topical hyaluronic acid with fractional CO_2 laser resulted in significantly better outcome as compared to conventional practice of fractional CO_2 laser alone in patients with post-acne scars which advocates preferred use of this novel combination therapy in the management of such patients in future practice.

Key words
Post-acne scars, Fractional CO_2 laser, hyaluronic acid.

Introduction

Acne is a frequently encountered skin condition affecting up to 80 percent of the adolescents.[1] Severely inflamed lesions of acne vulgaris may heal with permanent scars, which can be related to psychological pain, low self-esteem, and

Address for correspondence
Dr. Wajieha Saeed, Assistant Professor,
Department of Dermatology Unit I,
King Edward Medical University, Lahore
Ph: +923334210884
Email: jiya114@hotmail.com

reduced quality of life in these patients.[1] Clinical severity of the acne vulgaris doesn't correlate with the incidence or severity of scarring. Moreover, the clinical severity of acne scars is not an accurate measure of the patient's distress (i.e., mild scarring may lead to significant distress).[1,2] The pathogenesis of acne scarring is still not completely understood, but several hypotheses have been proposed. It is most likely associated with the inflammatory mediators, immuno-inflammatory cells and degradation of collagen fibers and subcutaneous fat by enzymes produced by fibroblasts and keratinocytes.[1]

Acne scarring, observed in 95 percent of all people with acne vulgaris, can be challenging to treat.[3-7] Because of the prevalence of acne scarring and the strong negative impact on patient's self-esteem, acne and post-acne scars are common presentation in dermatology outdoors.[3,4] The treatment options include a long list of procedures like chemical peeling, dermabrasion, needling, dermal and subcutaneous augmentation with fillers, punch techniques for sharply marginated scars, silastic sheeting, laser resurfacing and other energy-based devices, and use of intra-lesional cytotoxics.[3-7] However, none of these treatments is good enough to treat these scars and resolve the emotional and psychological distress of the patient.[5]

Fractional CO_2 laser works on the principal of photothermolysis. The benefits of using this high energy cool scanned laser is that it minimizes the conventional ablative laser-induced adverse events by causing less tissue damage, less edema and shorter recovery time.[6] Hyaluronic acid (hyaluronan, HA) is a mucopolysaccharide, occurring naturally in all living organisms. It regulates cellular responses to growth factors and plays a role in cell migration, particularly of fibroblasts and smooth cells. Topical application of HA may result in increased hydration of the stratum corneum, restoration of elasticity thus producing anti-wrinkling effect.[7]

Alsaedy *et al*. (2017) evaluated the results of fractional CO_2 laser plus Topical application of HA in Iraqi patients with post-acne scars and reported that the frequency of excellent (16.6% vs. 9.6%), significant (50.0% vs. 44.4%), moderate (27.7% vs. 27.7%) and slight (5.5% vs. 11.1%) improvement was higher with combination therapy than fractional CO_2 laser alone after 3 months of treatment.[8]

Thus fractional CO_2 laser plus topical application of HA can be helpful in treating the post acne scars and can bring a hope for distressed patients presenting in the dermatology outdoor. However, the evidence is limited to a single international research paper as for now and there is no other locally published evidence. Therefore the purpose of the current study is to compare the outcome of fractional CO_2 laser alone and in combination with topical HA in patients presenting with post-acne scars. The results of the current study will help in better management of such patients in future practice.

Materials and methods

The study was conducted at Department of Dermatology Unit 1, Mayo Hospital, Lahore. It was a randomized controlled trial of 6 months duration, from July 2018 to Jan 2019. After taking permission from ethical review board, sample size of 300 (split-face study) cases was calculated with 80% power of test and 95% significance level while taking expected frequency of slight response to be 5.5% vs. 11.1% in patients with post-acne scars treated with fractional CO_2 laser plus topical HA and fractional CO_2 laser alone, respectively.[8] Non-probability, consecutive sampling technique was used for patient selection. Patients aged 18-40

years, of both genders, presenting with post-acne scars (≤5 year duration) and those who consented, were included in the study. Exclusion criteria included; patients currently taking steroids or history of steroid therapy for more than 4 weeks in the preceding 6 months period, patients with history of retinoid use in the past 6 month's period, having active infection on affected site, patients with history of photosensitivity or Keloidal tendencies (previous traumatic or surgical scars) and patients taking photosensitizing drugs.

Written informed consent to participate in the study was taken from each patient. Patient's age, gender, duration and type of scar and baseline Goodman and Baron Score were noted. One side of patient's face was randomly selected for combination therapy and the other for fractional CO_2 laser monotherapy. All the patients were given fractional CO_2 laser treatment. Following laser settings were used with fluence of 150-200 mJ, with density of 5–6, spot size of 1.2-mm and pulse rate between 30-50 Hz. One pass per treatment area was given. The coolscan mode was used to generate microthermal treatment zones (MTZ) to avoid excessive heating of the treated area. After the procedure, treated skin was covered with an antibiotic ointment (Polyfax Plus) and sunscreen, and the patients were advised to use sunblock daily and to avoid unnecessary sun exposure for at least 1 month. Patient was advised to apply hyaluronic acid serum (1% sodium hyaluronate serum) to the side of face randomized for combination therapy for 1 month. 3 treatment sessions were done, 1 month apart. Patients were called for follow-up one month after the last session, in OPD and Goodman and Baron Score was recalculated. Percentage reduction was calculated and noted in the attached proforma. All the treatment sessions were done by a single doctor and all the pre and post session assessments were performed by a single dermatologist with 5 years' experience to minimize bias. Confounding variables have been controlled by exclusion. All this information was recorded in a proforma by the candidate. All the collected data was entered and analyzed through SPSS version 20.0. Quantitative variables; age, duration of scar, initial score, post-treatment score and % reduction have been presented by mean±SD. Categorical variables; gender, scar type and outcome (excellent, significant, moderate and slight) have been presented by frequency and percentage. Chi-square test has been applied to compare the frequency of outcome (excellent, significant, moderate and slight) between the two groups and $p \leq 0.05$ was taken as significant. Data has been stratified for age, gender, type & duration of scar and initial score. Post stratification, chi-square test has been applied taking $p \leq 0.05$ as significant.

Results

Patient's ages ranged from 18 years to 40 years with a mean of 23.2±4.7 years. There were 90 (30.0%) male and 210 (70.0%) female patients with a male to female ratio of 1:2.3. The duration of acne scars ranges from 1 to 5 years with a mean of 3.2±1.3 years. Rolling scars were most frequent and were observed in 119 (39.7%) patients followed by icepick (33.3%) and boxcar (27.0%) as shown in **Table 1**.

Table 1 Baseline characteristics of study sample.

Characteristics	*Participants n=300*
Age (years)	23.2±4.7
18-29 years	264 (88.0%)
30-40 years	36 (12.0%)
Gender	
Male	90 (30.0%)
Female	210 (70.0%)
Duration of acne scars (years)	3.2±1.3
1-2 years	85 (28.3%)
3-5 years	215 (71.7%)
Type of acne scar	
Icepick	100 (33.3%)
Rolling	119 (39.7%)
Boxcar	81 (27.0%)

Table 2 Comparison of Goodman and Baron quantitative Grading Score between the study groups.

Time Stamp	*Fractional CO_2 Laser + Hyaluronic Acid n=300*	*Fractional CO_2 Laser alone n=300*	*P-value*
Baseline	54.68±14.30	53.66±14.83	0.391
At 3 months	22.66±12.46	24.85±13.85	0.042*
Change	32.03±13.63	28.81±14.82	0.006*
% reduction from baseline	58.68±19.28	53.41±22.08	0.002*

Independent sample t-test, * observed difference was statistically significant.

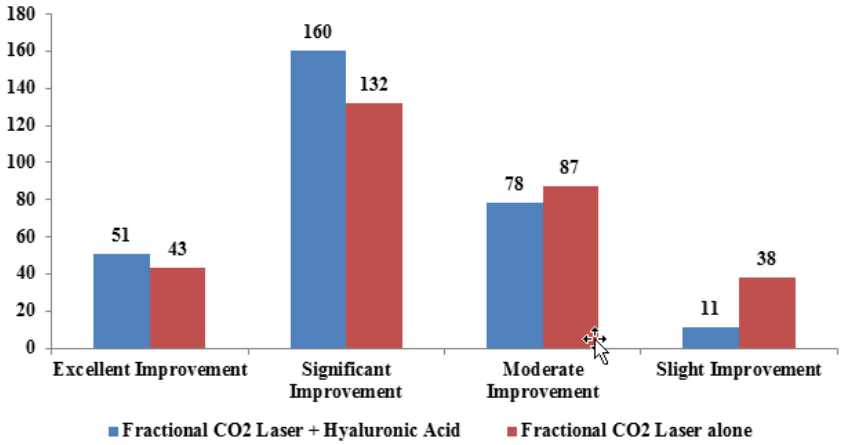

Figure 1 Comparison of Outcome between the study groups

Both the groups were comparable in terms of mean Goodman and Baron quantitative grading score at baseline (54.68±14.30 vs. 53.66±14.83; p-value=0.391). The mean score at follow-up was significantly lower in patients receiving combination therapy as compared to fractional CO_2 laser alone (22.66±12.46 vs. 24.85±13.85; p-value=0.042). The mean change (32.03±13.63 vs. 28.81±14.82; p-value=0.006) and mean of percent reduction (58.68±19.28 vs. 53.41±22.08; p-value=0.002) in baseline score was also significantly higher in patients receiving combination therapy as compared to fractional CO_2 laser alone as shown in **Table 2**. The frequency of excellent (17.0% vs. 14.3%) and significant (53.3% vs. 44.0%) improvement was significant higher in patients receiving combination therapy of fractional CO_2 laser plus topical hyaluronic acid as compared to fractional CO_2 laser alone as shown in **Figure 1**. Similar differences were observed among various subgroups based on patient's age, gender, duration and type of acne scars and initial score as shown in **Tables 3-5**.

Table 3 Comparison of Outcome between the study groups across different age groups. *n=300 (split-face).*

Age Groups	*n*	*Outcome*	*Fractional CO2 Laser + Hyaluronic Acid n=300*	*Fractional CO2 Laser alone n=300*	*P-value*
18-29 years	264	Excellent Improvement	45 (17.0%)	38 (14.4%)	0.002*
		Significant Improvement	141 (53.4%)	118 (44.7%)	
		Moderate Improvement	68 (25.8%)	75 (28.4%)	
		Slight Improvement	10 (3.8%)	33 (12.5%)	
30-40 years	36	Excellent Improvement	6 (16.7%)	5 (13.9%)	0.296
		Significant Improvement	19 (52.8%)	14 (38.9%)	
		Moderate Improvement	10 (27.8%)	12 (33.3%)	
		Slight Improvement	1 (2.8%)	5 (13.9%)	

Chi-square test, * observed difference was statistically significant.

Table 4 Comparison of Outcome between the study groups across gender.
n=300 (split-face)

Gender	*n*	*Outcome*	*Fractional CO2 Laser + Hyaluronic Acid n=300*	*Fractional CO2 Laser alone n=300*	*P-value*
Male	90	Excellent Improvement	15 (16.7%)	11 (12.2%)	0.046*
		Significant Improvement	46 (51.1%)	37 (41.1%)	
		Moderate Improvement	26 (28.9%)	29 (32.2%)	
		Slight Improvement	3 (3.3%)	13 (14.4%)	
Female	210	Excellent Improvement	36 (17.1%)	32 (15.2%)	0.011*
		Significant Improvement	114 (54.3%)	95 (45.2%)	
		Moderate Improvement	52 (24.8%)	58 (27.6%)	
		Slight Improvement	8 (3.8%)	25 (11.9%)	

Chi-square test, * observed difference was statistically significant.

Table 5 Comparison of outcome between the study groups across type of acne scars.
n=300 (split-face)

Type	*N*	*Outcome*	*Fractional CO2 Laser + Hyaluronic Acid n=300*	*Fractional CO2 Laser alone n=300*	*P-value*
Icepick	100	Excellent Improvement	17 (17.0%)	14 (14.0%)	0.041*
		Significant Improvement	50 (50.0%)	39 (39.0%)	
		Moderate Improvement	28 (28.0%)	30 (30.0%)	
		Slight Improvement	5 (5.0%)	17 (17.0%)	
Rolling	119	Excellent Improvement	21 (17.6%)	17 (14.3%)	0.043*
		Significant Improvement	66 (55.5%)	58 (48.7%)	
		Moderate Improvement	30 (25.2%)	32 (26.9%)	
		Slight Improvement	2 (1.7%)	12 (10.1%)	
Boxcar	81	Excellent Improvement	13 (16.0%)	12 (14.8%)	0.315
		Significant Improvement	44 (54.3%)	35 (43.2%)	
		Moderate Improvement	20 (24.7%)	25 (30.9%)	
		Slight Improvement	4 (4.9%)	9 (11.1%)	

Chi-square test, * observed difference was statistically significant.

Discussion

Acne is one of the most common skin disease, affecting more than 80% of adolescents and young adults. It is one of the commonly encountered dermatological conditions in outpatient department of Dermatology.[1] The prevalence of acne varies from 35 to 90% of adolescents at some stage in their life. Few studies reported the prevalence of comedones approximately 100% in both sexes during adolescence.[1-3] Acne appears earlier in females as compared to males, possibly reflecting the earlier onset of puberty.[1] It is also associated with a premenstrual flare.[9,10] Some studies, have notified seasonal variations in acne vulgaris, with exacerbation in winters and improvement in warmer months.[1] Several studies that have investigated the psychosocial impact of acne have had incongruous results.[11] The prevalence of severe acne has decreased in past 2 decades because of improved treatment.[11]

Acne is not life-threatening, but it has huge impact on the quality of life of the patient and imparts socioeconomic burden. The psychological effects can lead to problems like social isolation, lack of self-confidence, increased levels of anxiety, anger, frustration, unemployment and even suicidal ideation. Less than 15% of acne scar patients require medical treatment due to the severity of their scars, and 2-7% of them experience lifelong post-acne scarring.[11] None of the available treatment

options is good enough to treat these scars and thus resolve the emotional and psychological trauma to the patient.[1-3] A recent study claimed that addition of topical hyaluronic acid to fractional CO_2 laser improves the outcome as compared to conventional practice of fractional CO_2 laser done alone.[8] However, the available evidence is limited and there is no such local published data which necessitated the current study.

In our study, the mean age of the patients was 23.2±4.7 years. Same mean age of 18.7±4.5 years has been reported by Rajar *et al*. (2009) among patients presenting with post-acne scars at Isra University, Hyderabad.[12] Rana *et al*. (2017) reported comparable mean age of 23.3±4.4 years in such patients in India[13] while Saadawi *et al*. (2018) reported it to be 26.8±6.1 years in Egypt.[14] Shin *et al*. (2012) reported similar mean age of 23.5±5 years in Korea[15] while Lu *et al*. (2012) reported it to be 24.3±7 years in China.[16]

We observed that there was a female predominance with a male to female ratio of 1:2.3. Similar female predominance among patients with post-acne scarring has been reported by Rajar *et al*. who observed male to female ratio of 1:1.9 in patients presenting at Isra University Hospital, Hyderabad.[12] Puri *et al*. and Arora *et al*. reported this ratio to be 1:4 and 1:1.6 respectively among Indian patients.[17,18] Comparable female predominance with male to female ratio of 1:1.5 has been reported by Rongsaard *et al*. (2015) in Thailand[19] while Chae *et al*. (2012) documented this ratio to be 1:4 in Korea.[20]

In the current study, the mean duration of acne scars was 3.2±1.3 years. Rolling scars were most frequent and were observed in 119 (39.7%) patients followed by icepick (33.3%) and boxcar (27.0%). Our observation is in line with that of Rana *et al*. (2017) who noticed similar mean duration of disease on presentation in Indian patients with post-acne scars and reported it to be 3.1±1.9 years.[13] Arora *et al*. reported comparable distribution of icepick (29.9%), rolling (41.8%) and boxcar (28.3%) scars in Indian such patients.[18]

We recorded that the frequency of excellent (17.0% vs. 14.3%) and significant (53.3% vs. 44.0%) improvement was much higher in patients receiving combination of fractional CO_2 laser plus topical hyaluronic acid as compared to fractional CO_2 laser alone. Our results are in line with the previously published paper by Alsaedy *et al*. (2017) who evaluated the results of fractional CO_2 laser plus topical application of HA in Iraqi patients with post-acne scars and reported that the frequency of excellent (16.6% vs. 16.6%) and significant (50.0% vs. 44.4%) improvement was higher with combination therapy than fractional CO_2 laser alone after 3 months of treatment.[8]

The current study is unprecedented in local population and adds to the limited existing evidence on this research topic. In the present study, we found that combining topical hyaluronic acid with fractional CO_2 laser resulted in significantly better outcome as compared to conventional practice of fractional CO_2 laser alone in patients with post-acne scars which advocates preferred use of this novel combination therapy in the management of such patients in future.

A very important limitation in the current study was that we didn't compare various side effects between the two groups which are very important particularly in dermatologic practice as these may lead to poor patients' compliance and drop outs. There is need for such a study in future to establish the safety of this novel combination therapy among such patients.

Conclusion

Combining topical hyaluronic acid with fractional CO_2 laser resulted in significantly better outcome as compared to conventional practice of fractional CO_2 laser alone in patients with post-acne scars which advocates preferred use of this novel combination therapy in the management of such patients in future practice.

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