Original Article

A Comparative Study to Assess the Efficacy of Fractional Carbon Dioxide Laser and Combination of Fractional Carbon Dioxide Laser with Topical Autologous Platelet-rich Plasma in Post-acne Atrophic Scars

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Abstract

Context: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit prevalent in adolescent population. Atrophic acne scarring negatively affects the quality of life. Although challenging to treat, the introduction of fractional carbon dioxide (CO_2) laser and platelet-rich plasma (PRP) therapy for atrophic scars has opened up new avenues. **Aim:** The aim of this study was to evaluate and compare the efficacy of fractional CO_2 laser alone and in combination with topical PRP in treating post-acne atrophic scars. **Subjects and Methods:** A hospital-based prospective, double-blinded, randomized, and comparative study was conducted. A total of 33 cases with post-acne atrophic scars of moderate to severe grade were randomly allotted into Group A and Group B who were treated for three monthly sessions of fractional CO_2 laser followed by topical PRP and fractional CO_2 laser monotherapy, respectively. Evaluation at baseline and every visit was carried out and compared at the end of 12 weeks. **Results:** Of the 33 patients, 25 completed the study. The mean change in score was higher in subjects of Group A. The mean scar score significantly reduced in both groups. The mean visual analog scale was higher in Group A. The reduction in scar score was significantly higher in patients with rolling scars and boxcar scars and least in ice pick scars. Erythema, edema, pain, and hyperpigmentation were higher in Group B. **Conclusion:** Combination therapy with PRP is more efficacious in reducing post-acne atrophic scars and reducing adverse effects of laser therapy as compared to fractional CO_2 laser monotherapy.

Keywords: Fractional carbon dioxide laser, platelet-rich plasma, post-acne atrophic scars

Introduction

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit. In a world where both women and men are conscious about their appearance, acne poses as a psychological and social burden of high gravity.[1]

Inflammatory acne can produce permanent facial scarring by the healing of all forms of active acne,[2] which is an element of peril for low academic performance, unemployment, depression, and dysmorphophobia, leading to suicide. Broadly, acne scars are classified into atrophic and hypertrophic scars. Atrophic acne scars have been additionally categorized as ice pick, rolling, and shallow or deep boxcar scars.[2]

Although challenging to treat, various non-energy-based techniques and energy-based modalities can be used for improvement of acne scars.[3] However, the introduction of fractional carbon dioxide (CO_2) laser and platelet-rich plasma (PRP) therapy for atrophic scars has opened up new avenues for management of acne scars.

Access this article online

Quick Response Code:

Website: www.jcasonline.com

DOI: 10.4103/JCAS.JCAS_142_19

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How to cite this article: Arsiwala NZ, Inamadar AC, Adya KA. A comparative study to assess the efficacy of fractional carbon dioxide laser and combination of fractional carbon dioxide laser with topical autologous platelet-rich plasma in post-acne atrophic scars. J Cutan Aesthet Surg 2020;13:11-7.

The fractional CO_2 laser thermally modifies a portion of the skin, leaving intervening zones of normal skin intact, which rapidly regenerates the ablated columns of tissue.[4] In spite of being unparalleled in results, fractional CO_2 laser is followed by side effects such as erythema, edema, infections, and risk of developing hyper- or hypopigmentation making it unappealing for patients.[5] Autologous PRP provides with a full array of potential bioactive growth factors and chemokines released on platelet activation, which aid in quick wound healing and actively reduce atrophic acne scarring making these two modalities synergistic in nature.[6]

This study aimed to gauge and compare the effectiveness and safety of fractional CO_2 laser resurfacing and combination of fractional CO_2 laser resurfacing and topical PRP to provide the best possible treatment and relief to patients anguished by post-acne atrophic scars.

Subjects and Methods

A total of 33 patients with post-acne atrophic scars of moderate to severe grade were included for a hospital-based prospective study from November 2017 to June 2019. Exclusion criteria comprised patients with active acne, patients with macular or mild atrophic acne scars, predisposition to keloidal or hypertrophic scarring tendency, and patients with active bacterial or viral infections. Detailed history with respect to the onset and duration of acne and scarring, any treatment for acne or acne scars received within past 6 months, and preexisting medical conditions were recorded.

Initial clinical examination of the patient was carried out to determine the grade and score of acne scars using Goodman and Baron qualitative grading and quantitative scoring chart[2,7] and was recorded. Informed consent for the study was obtained from all the patients. Patients were randomly allotted into Group A and Group B, and were treated for three monthly sessions of fractional CO_2 laser followed by topical PRP and fractional CO_2 laser monotherapy, respectively. Baseline investigations and clinical photographs were taken. The end point of the study was three laser ablation sessions.

Equipments

1. eCO_2 laser: The fractional CO_2 laser (Lutronic, Goyang, Korea) system with a wavelength of 10,600 nm was used with treatment settings of a pulse energy of 50–100 mJ, and a spot density of 50–100 spots cm^2 in the static mode; 1–2 passes were delivered using a 120-density tip with beam size of 120 μm and peak power of 30 W. The laser was irradiated to the entire area containing acne scars.
2. Method of PRP preparation: Two-stage centrifugation process (double-spin method) was used in the preparation of PRP. Whole blood samples (10 mL) was drawn from the patient and transferred into a tube prefilled with citrate anticoagulant solution. The mixture was centrifuged at 1600 rpm for 7 min (first spin). After the first spin, the lower red blood cell portion was discarded and supernatant containing platelet-poor plasma and buffy coat was centrifuged again at 4000 rpm for 5 min (second spin). The lower one-third of this solution provided approximately 2 mL of autologous PRP for topical application.

Treatment procedure

The face was cleaned with mild cleanser before the procedure. Topical anesthetic containing lidocaine 2.5% + prilocaine 2.5% was applied under occlusion and left for 1 h. The topical anesthetic was completely removed and affected areas were irradiated with fractional CO_2 laser using the same standard parameters in patients of both groups.

After the laser, patients in Group A received topical autologous PRP plasma application. All patients were instructed to apply topical mupirocin for 5 days, and regular use of sunscreen was advocated. They were instructed to avoid washing their face for 6 h after the procedure, direct sunlight, heat, or friction on the treated areas. Two more sessions were performed 4 weeks apart following similar protocol.

Follow-up

The patients in both groups were asked to follow-up for next laser session every 4 weeks up to 12 weeks. During each visit, the investigator recorded the findings related to treatment response such as reduction or improvement in acne scars (acne scar score), patient satisfaction, and general perception regarding the treatment. Clinical photographs were taken with identical settings and lighting at every follow-up before successive laser session. Any adverse effects related to therapy were recorded in the pro forma immediately after laser ablation (short term) and at each follow-up before successive session (long term). At the end of 12 weeks, the final response was evaluated according to the aforementioned procedure.

Efficacy evaluation

The following two primary efficacy parameters were assessed: (1) Objective assessment—Change from baseline acne scar score using Goodman and Baron quantitative scoring system at the end of 12 weeks. (2) Subjective assessment—Patient assessment of improvement of acne scars after the end of 12 weeks; patients in both the groups were asked to mark their improvement on a 10-inch long "visual analog scale (VAS)."

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 17,

Chicago, Illinois. Results were compared using independent *t* test or Mann–Whitney *U* test, paired *t* test, repeated measures of analysis of variance (ANOVA), and one-way ANOVA. Categorical data were compared using chi-square test. For all tests, significant was achieved at $P < 0.05$.

Results

Of the 33 patients enrolled in the study, 25 patients completed the study and 8 patients were lost to follow-up due to unknown reasons. Summary of patients characteristics are given in Table 1. The mean scar scores of patients in both groups are summarized in Table 2.

The mean change in score at the end of the study was higher in subjects of Group A (4.17) when compared to those in Group B (3.15), which was statistically insignificant [Table 3]. The mean scar score in Group A reduced significantly from 11.5 to 4, and in Group B, it reduced significantly from 12 to 3 ($P < 0.0001$) [Table 4]. The mean VAS for patient's assessment of improvement was higher in subjects in Group A (4.08) when compared to those in Group B (3.46). However, this was not significant.

Clinical photographs taken at baseline and at the end of the study in patients of Group A are as seen in Figures 1 and 2.

Clinical photographs taken at baseline and at the end of the study in patients of Group B are as seen in Figures 3 and 4.

Immediate adverse effects were observed in 21 patients. Twenty patients developed erythema, eight patients developed edema, and one patient had pain after the procedure. Erythema, erythema with edema, and pain was more in the subjects of Group B even though there was no significant difference between two groups.

Long-term adverse effects were observed in 10 patients. Hyperpigmentation [Figure 5] was observed in three patients; pain, erythema, and acne [Figure 6] was observed in two patients each; and secondary infection was observed in one patient. Pain and hyperpigmentation was more in subjects in Group B even though no significant difference was observed between two groups.

The change in scar score irrespective of treatment was the highest in patients with rolling scars with a mean of 4.2, followed by boxcar scars with a mean of 3.89 and the lowest in ice pick scars with a mean of 2.33, which was highly statistically significant.

Table 1: Patient characteristics (original)

Age	24.36 ± 4.37 years
Gender	
Males	21 (63.6%)
Females	12 (36.4%)
Mean duration of scars	2.74 ± 1.57 years
Fitzpatrick skin type	
III	3 (9.1%)
IV	20 (60.6%)
V	10 (30.3%)
Type of scars	
Rolling	14 (42.4%)
Ice pick	6 (18.2%)
Boxcar	13 (39.4%)

Discussion

Our study enrolled 33 patients of post-acne atrophic scars, of which 25 patients completed the study. In our study,

Table 2: Mean scar score at baseline (original)

	Group	*N*	Mean ± SD	*P* value
Scar score baseline	A	17	12.41 ± 3.792	0.635
	B	16	11.75 ± 4.139	

SD = standard deviation

Independent *t* test was used for analysis. $P < 0.05$ is considered significant

Table 3: Mean change in scar scores at the end of the study

	Type of treatment	*N*	Mean ± SD	*P* value
Change in score at the end of study	Group A	12	4.17 ± 1.528	0.129
	Group B	13	3.15 ± 1.676	

SD = standard deviation

Independent *t* test was used for analysis. $P < 0.05$ is considered significant

Table 4: Baseline scar scores and change in the scar scores study

Groups	Baseline scar score		Scar scores at the end		*P* value
	Mean	SD	Mean	SD	
A	11.08 (11.5)	3.45	4.17 (4.0)	1.53	$P < 0.0001$ HS
B	12.08 (12)	4.48	3.15 (3.0)	1.68	$P < 0.0001$ HS

HS = highly significant, SD = standard deviation

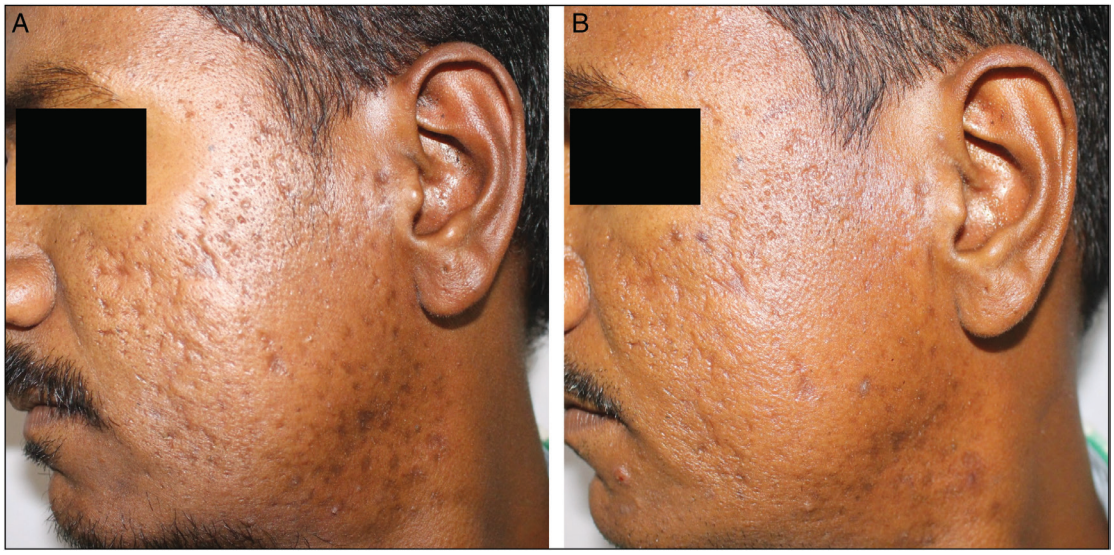

Figure 1: (A) Clinical photograph of a male patient at baseline (Group A). (B) Clinical photograph of a male patient at the end of the study (Group A)

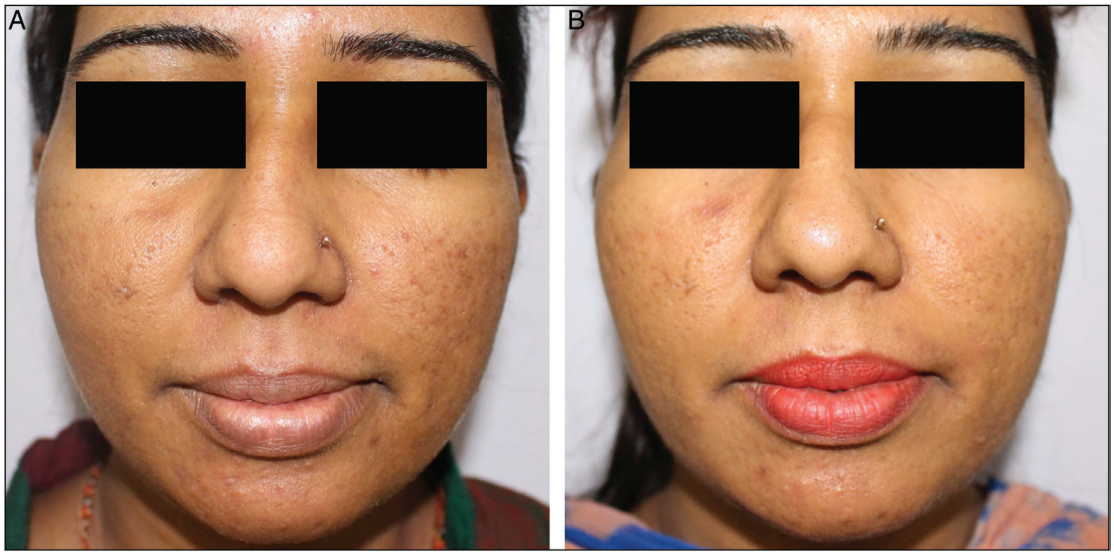

Figure 2: (A) Clinical photograph of a female patient at baseline (Group A). (B) Clinical photograph of a female patient at the end of the study (Group A)

males were predominant. As acne is more severe in boys than that in girls, it may have probably resulted in severe acne scarring in males.[1]

Where type of acne scars of the patients was simplified as mixed type in a study conducted by Layton *et al.*,[8] the majority of our patients presented with rolling type of scars (n = 14) followed by boxcar (n = 13) and ice pick type (n = 6). The skin type distribution showed that the majority were type IV (n = 20), followed by type V (n = 10), and least were type III (n = 03), which form the predominant skin types found in south India.

In this study, a statistically significant improvement was observed in scar score in the patients treated with fractional CO_2 laser ablation followed by topical PRP, after each sitting, as well as in the patients treated with the fractional CO_2 laser alone. From this observation, we inferred that fractional CO_2 laser with or without PRP is an effective treatment modality for post-acne atrophic scars as confirmed by similar studies.[9-11]

On comparison of the mean scar scores improvement at each visit between the two groups, the mean change in scar scores was higher in the fractional CO_2 with PRP group patients compared to fractional CO_2 laser alone, showing an added reduction in the scar score by addition of topical PRP. In addition, there was a better mean VAS improvement of the patient after fractional CO_2 laser ablation followed by topical PRP (4.08 ± 1.44) than that after CO_2 laser ablation alone (3.46 ± 1.05). Subjective improvement in the post-acne atrophic scars was better where fractional CO_2 laser treatment was followed by topical PRP as corroborated by various studies.[12-14]

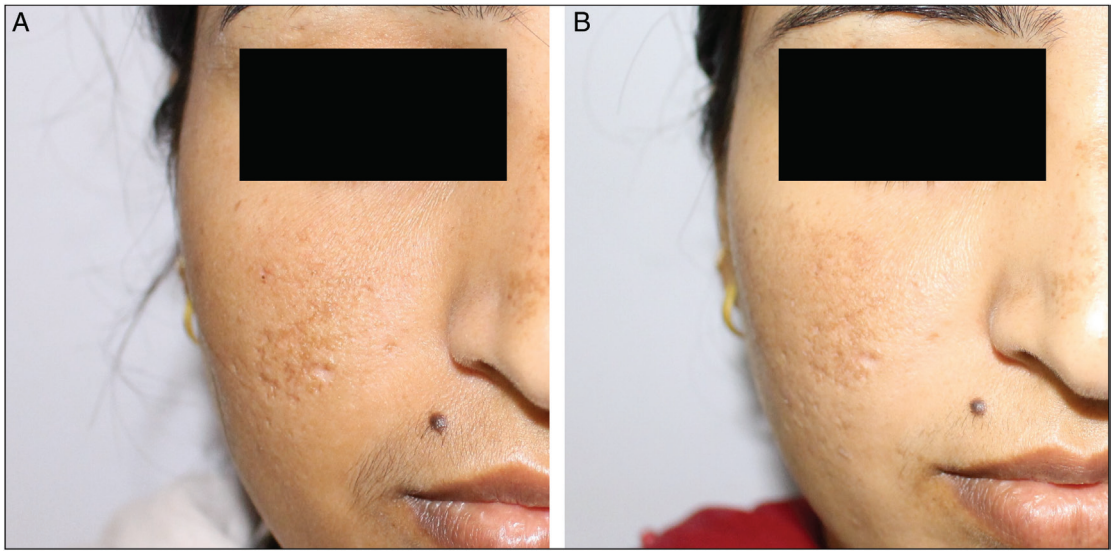

Figure 3: (A) Clinical photograph of a female patient at baseline (Group B). (B) Clinical photograph of a female patient at the end of the study (Group B)

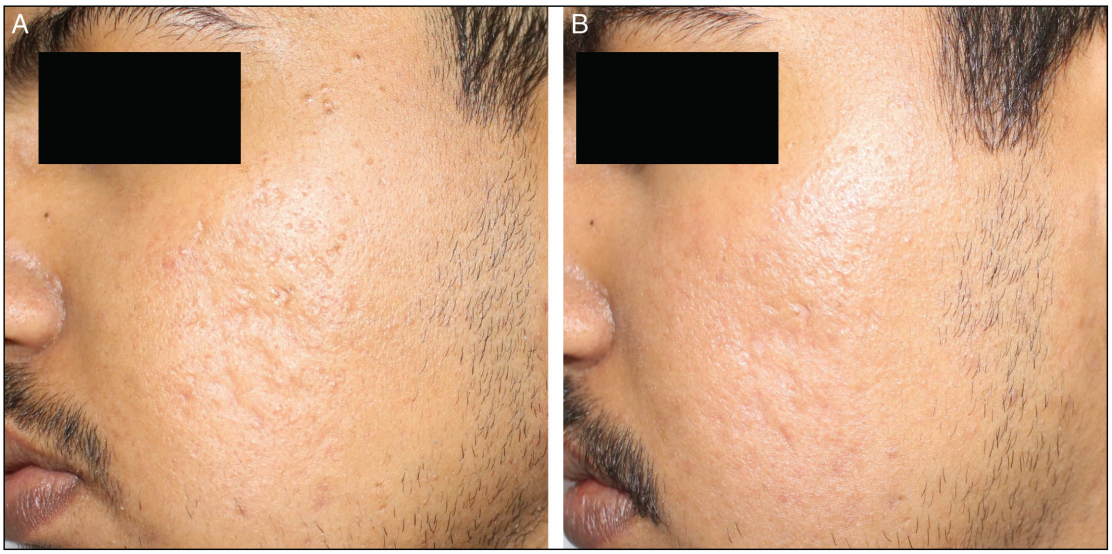

Figure 4: (A) Clinical photograph of a male patient at baseline (Group B). (B) Clinical photograph of a male patient at the end of the study (Group B)

The immediate adverse effects reported in the patients were erythema (39.4%) followed by erythema and edema (21.2%) as well as pain as documented by similar studies.[13-15] Erythema, erythema with edema, and pain were more in subjects treated with fractional CO_2 laser only, which denotes that immediate side effects (such as erythema, edema, and pain) reduce when fractional CO_2 laser treatment is followed by topical application of autologous PRP probably due to the regenerative properties of PRP.[16]

Hyperpigmentation was observed in three patients, pain, erythema, and acne was observed in two patients each, and secondary infection was observed in one patient. Treatment with fractional CO_2 laser had to be discontinued for one patient as she developed acne after each laser sitting as observed at follow-up. This decision was taken in view of exacerbation of acne, which was observed as an adverse effect of fractional CO_2 laser.[17] Pain and hyperpigmentation were observed lesser in patients treated with fractional CO_2 laser followed by topical PRP. As validated by numerous studies over the last 10 years,[5,11-13,18] PRP following fractional CO_2 laser therapy leads to a considerable reduction in long-term adverse effects such as pain and post-laser hyperpigmentation, which are commonly observed in Fitzpatrick skin type III to V owing to its richness of growth factors responsible for reducing inflammation and hastening the wound-healing process.

Moreover, we used topical PRP instead of injecting PRP intradermally, which probably prevented additional inflammation due to injection, in turn reducing pain and post-laser hyperpigmentation.[19]

Poorer response of ice pick scars as compared to rolling and boxcar scars was observed in our study, which was

Figure 5: Post-laser hyperpigmentation (post-inflammatory hyperpigmentation) over treated areas (forehead and cheeks)

similar to a study by Imran Majid.[20] This is probably attributed to the depth of ice pick scars and the inability of thermal effect to reach their base for dermal stimulation.

Synergizing fractional laser therapy with PRP is recognized to dynamically reduce atrophic acne scarring as documented by many authors.[21,22] Combination of fractional CO_2 laser with topical PRP had synergistic positive effects on the clinical outcome for acne scars and accelerated recovery. Faster reduction of routinely encountered adverse effects such as post-laser edema, erythema, and hyperpigmentation is observed with the use of both topical and intradermal PRP. Fractional CO_2 laser gives better response for rolling and boxcar scars as compared to ice pick scars.

Therefore, our study concludes that although fractional CO_2 is an effective modality for treating post-acne atrophic scars, combination therapy with PRP is more efficacious in reducing the appearance of scars, reducing adverse effects of laser therapy, and providing better patient satisfaction by the means of subjective improvement.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Figure 6: Exacerbation of acne post laser

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Fabbrocini G, Annunziata MC, D'Arco V, De Vita V, Lodi G, Mauriello MC, *et al*. Acne scars: pathogenesis, classification and treatment. Dermatol Res Pract 2010;2010:893080.
2. Clark AK, Saric S, Sivamani RK. Acne scars: how do we grade them? Am J Clin Dermatol 2018;19:139-44.
3. Kravvas G, Al-Niaimi F. A systematic review of treatments for acne scarring. Part 1: non-energy-based techniques. Scars Burn Heal 2017;3:1-17.
4. Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol 2008;58:719-37.
5. Gawdat HI, Hegazy RA, Fawzy MM, Fathy M. Autologous platelet rich plasma: topical versus intradermal after fractional ablative carbon dioxide laser treatment of atrophic acne scars. Dermatol Surg 2014;40:152-61.
6. Alsousou J, Ali A, Willett K, Harrison P. The role of platelet-rich plasma in tissue regeneration. Platelets 2013;24:173-82.

7. Goodman GJ, Baron JA. Postacne scarring: a qualitative global scarring grading system. Dermatol Surg 2006;32:1458-66.
8. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. Clin Exp Dermatol 1994;19:303-8.
9. Omi T, Numano K. The role of the CO_2 laser and fractional CO_2 laser in dermatology. Laser Ther 2014;23:49-60.
10. Alster TS, West TB. Resurfacing of atrophic facial acne scars with a high-energy, pulsed carbon dioxide laser. Dermatol Surg 1996;22:151-4.
11. Min S, Yoon JY, Park SY, Moon J, Kwon HH, Suh DH. Combination of platelet rich plasma in fractional carbon dioxide laser treatment increased clinical efficacy of for acne scar by enhancement of collagen production and modulation of laser-induced inflammation. Laser Surg Med 2018;50:302-10.
12. Faghihi G, Keyvan S, Asilian A, Nouraei S, Behfar S, Nilforoushzadeh MA. Efficacy of autologous platelet-rich plasma combined with fractional ablative carbon dioxide resurfacing laser in treatment of facial atrophic acne scars: a split-face randomized clinical trial. Indian J Dermatol Venereol Leprol 2016;82:162-8.
13. Kar BR, Raj C. Fractional CO_2 laser vs. fractional CO_2 with topical platelet-rich plasma in the treatment of acne scars: a split-face comparison trial. J Cutan Aesthet Surg 2017;10:136-44.
14. Shah SD, Mehta BD, Borkar MA, Aswani RC. Study of safety and efficacy of autologous platelet rich plasma combined with fractional CO_2 laser in the treatment of post acne scars: a comparative simultaneous split-face study. Int J Res Med Sci 2017;5:1344-51.
15. Alser OH, Goutos I. The evidence behind the use of platelet-rich plasma (PRP) in scar management: a literature review. Scars Burn Heal 2018;4:1-8.
16. Mahajan PV, Abbasi J, Subramanian S, Parab SC, Danke A. Regenerative medicine using platelet rich plasma and stem cells in atrophic acne scars: a case report. J Cosmo Trichol 2017;3:120.
17. Maria-Angeliki G, Alexandros-Efstratios K, Dimitris R, Konstantinos K. Platelet-rich plasma as a potential treatment for noncicatricial alopecias. Int J Trichology 2015;7:54-63.
18. Kim SA, Ryu HW, Lee KS, Cho JW. Application of platelet-rich plasma accelerates the wound healing process in acute and chronic ulcers through rapid migration and upregulation of cyclin A and CDK4 in HaCaT cells. Mol Med Rep 2013;7:476-80.
19. Na JI, Choi JW, Choi HR, Jeong JB, Park KC, Youn SW, *et al*. Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. Dermatol Surg 2011;37:463-8.
20. Majid I, Imran S. Fractional CO_2 laser resurfacing as monotherapy in the treatment of atrophic facial acne scars. J Cutan Aesthet Surg 2014;7:87-92.
21. Ortiz AE, Tremaine AM, Zachary CB. Long-term efficacy of a fractional resurfacing device. Lasers Surg Med 2010;42:168-70.
22. Arsiwala SZ, Desai SR. Fractional carbon dioxide laser: optimizing treatment outcomes for pigmented atrophic acne scars in skin of color. J Cutan Aesthet Surg 2019;12:85-94.