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Original Research Article

Therapeutic effect of the combination of fractional laser and recombinant bovine basic fibroblast growth factor in acne scar patients

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Abstract

Purpose: *To assess the feasibility and safety of a combination therapy involving fractional laser treatment and recombinant bovine basic fibroblast growth factor (rb-bFGF) in acne scar patients.*
Methods: *90 patients with acne scar admitted at Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology from September 2020 to December 2022 were enrolled in retrospective study. Patients were divided into control group (n = 41), treated with rb-bFGF alone and study group (n = 49), which underwent fractional laser treatment using Lutronic fractional laser device involving 40 days per session for three sessions, with additional application of rb-bFGF in the affected area at a dose of 300 IU/cm^2, three times daily, for seven consecutive days following the completion of each laser treatment session. Treatment effect, skin physiological indices, lactic acid stinging test (LAST) scores, stratum corneum integrity, and incidence of adverse reactions were determined.*
Results: *Study group demonstrated superior efficacy with a total effectiveness of 97.96 %, significantly outperforming control group at 85.3 % ($p < 0.05$). Pre-treatment, both groups exhibited comparable values in trans-epidermal water loss (TEWL), pH, stratum corneum hydration, and erythema (a-value) ($p > 0.05$). Post-treatment, both groups exhibited significant improvements, with reduced TEWL, pH, and a-value, along with increased stratum corneum hydration ($p < 0.05$). Compared to control group, study group showed significantly lower TEWL, pH, and a-value, coupled with higher stratum corneum hydration ($p < 0.05$). Post-treatment, study group demonstrated lower total LAST scores, improved stratum corneum integrity, and a significantly lower incidence of adverse reactions.*
Conclusion: *The combination of fractional laser and rb-bFGF in patients with acne scar improves skin barrier function, reduces lactic acid-induced stinging, and enhances stratum corneum integrity. Further research and clinical trials are needed to optimize the treatment protocols.*

Keywords: *Acne scars, Fractional laser, Recombinant bovine basic fibroblast growth factor, Combined effect, Skin barrier, Treatment safety*

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INTRODUCTION

Acne is a skin condition characterized by inflammation that develops within the pilosebaceous unit, mostly triggered by Cutibacterium acnes infection, follicular hyperkeratinization in the sebaceous gland, excessive sebaceous gland and androgen secretion, and adolescents are the most prevalent population for acne [1,2]. Acne commonly occurs on adolescents' faces, neck, forehead, and back. Severe acne may lead to scarring, with an incidence of nearly 20 % in adolescents, greatly impacting patients, physically and psychologically [3]. A questionnaire survey [4,5] revealed that 33 % of 4,618 acne patients had facial scars, and follow-up interviews showed that these patients were perceived as being less attractive and less confident, and more introverted, shy, and insecure than those with normal skin.

Currently, a variety of treatments are available for acne scars, including laser treatment, autologous fat or collagen injectable fillers, α-hydroxy acid or β-hydroxy acid chemical peels, corticosteroids, and adipose tissue transplantation. However, there is still a lack of definitive treatment guidelines [6]. Laser treatment mainly relies on photothermal effects to stimulate the patient's dermal collagen and accelerate the remodeling of tissue structure at the scar site, and although it has been proven to be effective, laser treatment equipment is more expensive and more difficult to promote in primary care institutions compared to the various treatment modalities currently being used. Recombinant human epidermal growth factor (rb-bFGF) is a biological product that is highly effective in repairing skin tissue and lightening skin discoloration with few toxic side effects [7]. There are few clinical studies on the combined use of fractional laser and rb-bFGF in patients with acne scars, hence this study.

METHODS

Patient selection

Ninety patients with acne scars treated in The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology between September 2020 and December 2022 were included in this retrospective study. They were divided into a study group (n = 49, treated with fractional laser and recombinant human epidermal growth factor (rb-bFGF)) and a control group (n = 41, treated with rb-bFGF alone). The work was approved by the Ethics Committee of Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology (approval no. EC-103), and complied with international guidelines for human studies [8]. The patients signed informed consent forms.

Inclusion criteria

Patients who were diagnosed with acne scars according to the diagnostic criteria [9]; patients with lesions located on their faces, with stable skin damage of six months or more; patients whose clinical data were complete and available; and patients who were ≥ 18 years old were included in the study.

Exclusion criteria

Patients with a recent history of photosensitizing drug usage or sun exposure; who were pregnant or lactating; with co-morbid psychiatric disorders; patients with poor compliance, scarring tendency, coagulation disorders, laser peels, filler treatments, or facial chemical therapy received within six months prior to this study.

Intervention

Control group received fractional laser treatment using the "Lutronic fractional laser device (South Korea). The power was set to 1 - 25 W, wavelength to 10 - 600 nm, microwave impulse energy to 10 - 100 mJ, and pulse width < 1 ms. The treatment area was square or round. Manual intermittent fine treatment was performed at the scar depression, followed by peripheral grinding in the fractional mode to a depth of just visible punctate bleeding. The treatment cycle was 40 days per session, with three sessions in a course of treatment.

Study group received rb-bFGF in addition to control group's treatment. rb-bFGF gel was used (manufacturer: Zhuhai Yisheng Biopharmaceutical Co., Ltd., specification 200,000 IU (5 g)/tube, approval no. S20040001). The appropriate amount of gel (recommended dose 300 IU/cm^2) was applied topically to the affected area three times daily for seven consecutive days after the completion of each session of laser treatment [10].

Evaluation of parameters/indices

Therapeutic effect

Photographs were taken before the treatment and two months following the third treatment (laser treatments induced damage to the skin of

patients, and the immediate assessment following the completion of the treatment may not accurately reflect the recovery progress of the skin. Therefore, it was imperative to allow a minimum of 2 months for skin recovery before conducting any assessment), and two dermatologists evaluated the results before and after treatment. Scars with new skin flatness and more than 80 % repair with normal skin tone were considered cured. Scars with relatively flat new skin and 60 - 80 % repair with only mild pigmentation were considered effective while scars with 40 - 60 % repair were considered ineffective [10].

Skin physiological indices

Before the treatment and two months following the third treatment, patients were made to sit for 30 min under a constant temperature and humidity environment, and thereafter their faces were cleaned, and transepidermal water loss (TEWL), pH, stratum corneum hydration, and erythema (a-value) were determined using Tewameter TM300 probe, Skin-pH-Meter pH900, and Corneometer CM825 (Courage & Khazaka GmbH, Cologne, Germany), and Minolta Chroma Meter CR200 (Minolta, Osaka, Japan), respectively [11].

Lactic acid stinging test (LAST) and Stratum Corneum Integrity

These parameters were assessed before treatment and two months following the third treatment. The LAST was conducted in the following manner: 10 % lactic acid was applied to the nasolabial folds and on either cheek at room temperature. The intensity of stinging was judged using a 4-point scale at 5 min. No stinging was scored 0 points, mild stinging was scored 1 point, moderate stinging was scored 2 points, and severe stinging was scored 3 points. Stratum corneum integrity was evaluated using D-aquame tape applied to patients' skin 20 times consecutively. Total protein amounts were also evaluated using a bicinchoninic acid (BCA) protein analyzer.

Incidence of adverse reactions

A comparison was made in terms of the occurrence of adverse reactions including hyperpigmentation, keloid hyperplasia, and persistent flushing during treatment (the collection of adverse reactions following the first treatment was conducted at the second treatment, and a follow-up approach, whether through telephone or WeChat, was used to record the adverse reactions following the second treatment) between the two groups.

Statistical analysis

The statistical analyses were made employing SPSS 24.0 software. The t-test was employed for the comparison of normally distributed measures with homogeneous variance, described by mean ± standard deviation (SD). The Mann-Whitney test (U test) in non-parametric analysis was utilized for the comparison of measures with skewed data or heterogeneous variance, described as median (upper and lower quartiles). The chi-square test was utilized for categorical data comparisons, described by cases (%). A *p*-value < 0.05 was deemed to have statistical significance.

RESULTS

General information

The demographic characteristics of the patients in both groups, such as gender, age, mean disease duration, skin typing, and acne scar weighting score, were compared. Both groups showed no statistically significant differences with regard to these variables ($p > 0.05$: Table 1).

Table 1: Comparison of intergroup differences in general clinical information between the two groups of patients

Parameter		Study group	Control group	$t/^2\chi$	*P*-value
Gender	*Male*	12	10	0.000	0.991
	Female	37	31		
Mean age (years)		26.06±3.05	26.11±2.98	0.114	0.909
Mean disease duration (years)		5.06±0.65	4.98±0.87	0.499	0.619
Acne scar weighting score (points)		43.56±5.11	43.98±5.18	0.386	0.700
Fitzpatric skin typing	*Type III*	26	27	1.509	0.219
	Type IV	23	14		

***Note*:** Values are mean ± SD; n = 49 for study group and 41 for control group

Therapeutic effect

Study group exhibited significantly higher total effectiveness (97.96 %, 48/49) compared to control group (85.37 %, 35/41; $p < 0.05$), as shown in Figure 1.

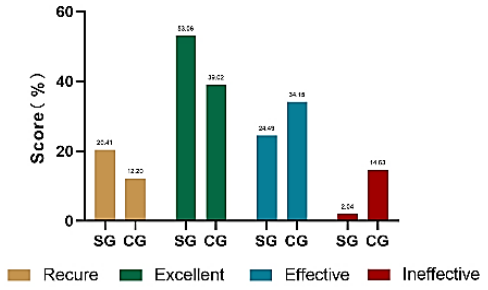

Figure 1: Comparison of treatment effect between the two groups. ***Key:*** SG: Study group; CG: Control group

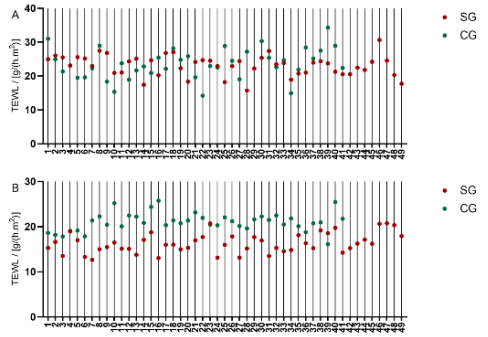

Figure 2: Comparison of TEWL levels, (A) Before treatment $P > 0.05$ vs. control (B) After treatment, TEWL levels in study group (SG). $P < 0.05$ vs. control.

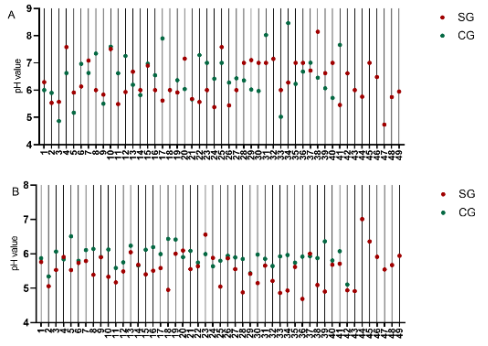

Figure 3: Comparison of pH levels. (A) Before treatment ($p > 0.05$ vs. control). (B) After treatment ($p < 0.05$ vs. control).

Skin physiological indices

Before treatment, no statistically significant differences were observed in TEWL, pH, stratum corneum hydration, and a-value between the two groups ($p > 0.05$). However, after treatment, both groups showed markedly lower TEWL, pH, and a-value, while exhibited notably higher stratum corneum hydration compared to their pre-treatment values ($p < 0.05$). Study group exhibited lower TEWL, pH, and a-value and higher stratum corneum hydration in contrast to control group ($p < 0.05$) (Figures 2 - 5).

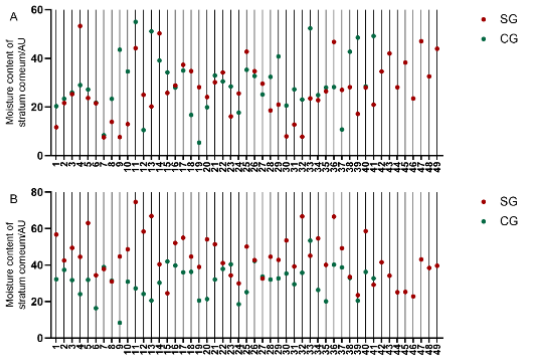

Figure 4: Comparison of stratum corneum hydration. (A) Before treatment ($p > 0.05$ vs. control). (B) After treatment ($p < 0.05$ vs. control).

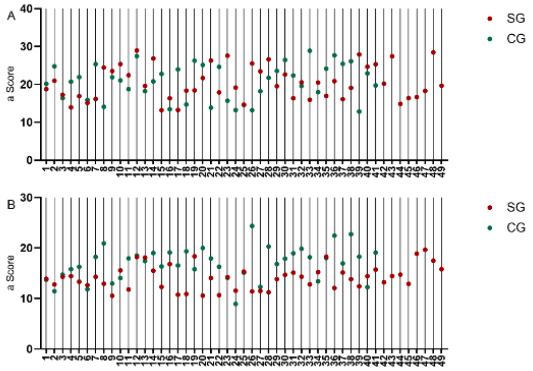

Figure 5: Comparison of a-values between the two groups before and after treatment. (A) Before treatment ($p > 0.05$ vs. control). (B) After treatment ($p < 0.05$ vs. control)

Lactic acid irritation and stratum corneum integrity

Before treatment, both groups exhibited no statistically significant differences in terms of lactic acid irritation and stratum corneum integrity ($p > 0.05$). However, after treatment, both groups exhibited notably reduced total scores of the lactic acid irritation test and stratum corneum integrity compared to before treatment ($p < 0.05$). Moreover, the total scores of the lactic acid irritation test and stratum corneum integrity in study group after treatment were markedly lower than those in control group ($p < 0.05$) (Figure 6 and Figure 7).

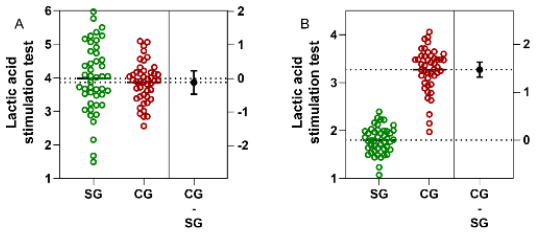

Figure 6: Differences in total lactic acid irritation test scores between the two groups. (A): Before treatment, (B): After treatment. ***Key*:** SG: Study group, CG: Control group.

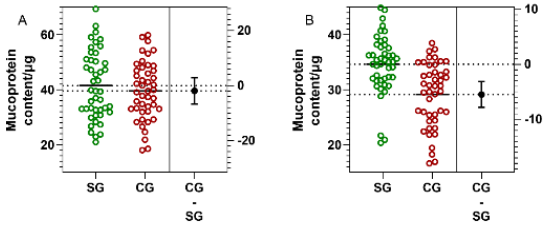

Figure 7: Differences in stratum corneum integrity scores between the two groups before and after treatment. (A): Before treatment (B): After treatment. ***Key*:** SG: Study group, CG: Control group

Incidence of adverse reactions

Study group exhibited a notably lower total incidence of adverse reactions (6.12 %, 3/49) in contrast to control group patients (26.83 %, 11/41) ($p < 0.05$, Figure 8).

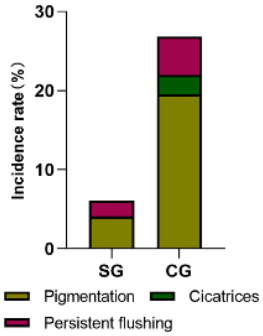

Figure 8: Comparison of the incidence of adverse reactions. ***Key*:** SG: Study group, CG: Control group

DISCUSSION

Acne scars typically result from collagen loss during the healing process of acne, which is mainly associated with the severity of inflammation in acne lesions and the lack of timely medical intervention. Initially, most acne scars are erythematous, followed by fibrosis and pigmentation. While erythema and pigmentation are temporary, scars caused by collagen destruction are permanent, necessitating aggressive treatment measures to improve patient outcomes [11,12].

Currently, various clinical treatments are available for acne scarring, including fractional laser therapy. Fractional laser primarily forms minimally invasive pores through thermal coagulation and thermal exfoliation, creating thermal bridges between these pores and normal tissues. This stimulates the skin's repair process, producing a substantial amount of collagen for reconstructing the dermal framework structure, ultimately achieving scar remediation [13,14]. Some studies have suggested that fractional laser stimulates skin renewal by creating small, uniform holes in the patient's skin, resulting in skin resurfacing. This technique is widely recognized for effectively preserving the patient's normal skin and enabling rapid postoperative recovery [15]. However, other studies have indicated that despite the effectiveness of fractional laser, there are limitations in its application, and combining it with other treatments could improve patient experiences [16].

In the present research, the clinical value of combining fractional laser and rb-bFGF in treating acne scars was analyzed by comparing with a control group. The results showed that study group, treated with a combination of fractional laser and rb-bFGF, had significantly higher treatment outcomes compared to control group, treated with fractional laser alone (97.96 vs. 85.37 %). A controlled study of 100 patients with acne scarring [17] found that the addition of rb-bFGF to fractional laser increased the total treatment effectiveness from 76.00 to 96.00 %, consistent with the results of this study. However, fractional laser has limited coverage and is less effective in treating the superficial epidermal layer of the scar. The addition of rb-bFGF significantly increases DNA, RNA, and hydroxyproline production, accelerating wound epithelial cell proliferation and granulation tissue formation, ultimately improving the quality of repair [18,19].

The effectiveness of combined treatment in improving the physiological indices of patients' skin was also compared in this research. We hypothesize that the mechanism may be related to the ability of rb-bFGF to promote the synthesis and secretion of extracellular macromolecules such as hyaluronic acid and glycoproteins, which help maintain a moist environment on the skin surface and provide optimal conditions for cell growth [20]. It has been suggested that acne

patients, due to increased facial oil secretion, experience disruption of their intercellular lipid bilayer structure and a reduction in skin barrier function, potentially increasing the risk of local infection [21]. In a study of 89 patients with acne scarring [22], rb-bFGF was found to form a thin film on skin lesions, acting as an effective barrier and preventing bacterial infection to some extent. The combination of fractional laser and rb-bFGF enhances patients' skin resistance to external microorganisms, reduces skin sensitivity, and ultimately achieves better therapeutic effects. Additionally, the incidence of adverse reactions was compared between the two groups, revealing that the combined treatment had a significantly lower incidence of adverse reactions. This is attributed to the combined treatment's effectiveness in improving clinical symptoms of pain and erythema, facilitating the patients' postoperative recovery process.

Limitations of this study

While this study demonstrated the efficacy and safety of the combined fractional laser and rb-bFGF treatment for acne scars, certain limitations should be acknowledged. The study's retrospective nature introduces inherent biases, and the relatively short follow-up period may not capture long-term outcomes or potential delayed adverse effects. Additionally, the study did not explore individual variations in treatment responses, such as differences in scar types or patient characteristics. Further investigations with larger sample sizes, longer follow-up durations, and a more comprehensive exploration of patient heterogeneity are warranted to validate and extend the findings of this study.

CONCLUSION

The combination of fractional laser and rb-bFGF in treating acne scars is more beneficial than using rb-bFGF alone. Patients' skin barrier function significantly improves after treatment, and skin lactic acid irritation and stratum corneum integrity are effectively regulated. Safety of the combined treatment is also considerably good, making it a valuable option for clinical application in the management of acne scars. Further research and clinical trials are needed to optimize the treatment protocols and assess long-term outcomes for patients undergoing this treatment approach.

DECLARATIONS

Acknowledgements

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None provided.

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Bingwei Wu and Mingju Gao contributed equally to this work.

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