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Effect of compound glycyrrhizin combined with fractional CO_2 laser on the improvement of skin lesions and skin barrier function in rosacea

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Abstract: Rosacea is a chronic facial inflammatory disease affecting quality of life, with complex causes including psychological, lifestyle and immune factors. This study examines the use of compound glycyrrhizin with fractional CO2 laser treatment for rosacea patients. From January 2018 to January 2022, 108 patients with rosacea lesions were randomly assigned to a control group (conventional treatment) and an observation group (glycyrrhizin plus laser treatment). Both groups received 12 weeks of therapy. Analysis using SPSS26.0 and GraphPad Prism 8.0 showed improvement in skin lesions and barrier function post-treatment. The observation group had fewer lesions and better skin hydration compared to the control group ($P<0.05$). Adverse reactions were higher in the observation group but not significantly different ($P>0.05$). The combination treatment enhances therapeutic effects, improves skin lesions, and strengthens the skin barrier, warranting promotion.

Keywords: Rosacea; Compound glycyrrhizin; fractional CO_2 laser; skin barrier function

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INTRODUCTION

Rosacea is a chronic inflammatory skin disease that is prone to occur in the middle of the face and is mainly characterized by persistent erythema, telangiectasia and empyema, with red papules scattered on the face being the most common (Sharma A *et al*., 2022). These symptoms not only affect the patient's appearance but also impose a heavy burden on their psychology and quality of life. Currently, there are no clear conclusions regarding the etiology and pathogenesis of rosacea in clinical practice. However, most scholars believe that (Thiboutot D *et al*., 2020; Paiva-Santos AC *et al*., 2023) the occurrence of this disease is related to factors such as the mental state of the patient and the imbalance of the facial vasomotor nerves. In addition, poor lifestyle choices such as drinking, smoking and other factors, as well as immune abnormalities, may play a role in the occurrence of rosacea. The complex combination of these factors makes the treatment of rosacea difficult and requires careful consideration of the patient's overall condition.

Rosacea is prevalent among the fair-skinned population between the ages of 30 and 60 years when the population is in the prime of life because the importance of appearance is self-evident. A healthy and beautiful face can often bring confidence and advantages to people in many aspects, such as social interaction, work and marriage. With the continuous development of medical technology, the number of treatments for rosacea has been increasing. In addition to traditional drug therapy, physical therapy and surgical treatment, there are some emerging treatments, such as laser therapy and photodynamic therapy. However, the choice of treatment also varies from person to person in different patient and physical conditions (Doan NQH *et al*., 2021). Hydroxychloroquine sulfate tablets are usually used for clinical therapy because they can inhibit inflammatory cells and reduce the continuous growth of inflammatory cells (Zhang L *et al*., 2021). The clinical mechanism of action for this disorder is unclear and may include interaction with thiols, DNA synthesis, interference with monocyte interleukin -1 formation, and inhibition of neutrophil superoxide release, which has a definite effect on rosacea; however, the potential side effects of this drug exacerbated skin lesions in our patient, resulting in low safety. Glycyrrhizin, a well-proportioned compound, is derived from active substances extracted from glycyrrhiza. It has been proven to have a significant protective effect on the liver. It is, therefore, commonly used clinically for the treatment of chronic hepatitis with the aim of improving liver function. Recent studies have further expanded its scope of application and attempted to apply it to the treatment of rosacea. The results showed that glycyrrhizin has definite efficacy in the treatment of rosacea. However, its efficacy is limited when used alone.

Laser therapy has been gradually applied in the field of skin diseases, especially in carbon dioxide fractional laser technology. Its unique selective photothermal effect is excellent in alleviating tissue damage. At the same time, this technology can finely regulate the laser energy density (Sun HY *et al*., 2022). Laser therapy can achieve even greater efficacy by combining these functions.

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Hydroxychloroquine demonstrates significant effects on erythema, yet prolonged use can lead to adverse outcomes such as gastrointestinal disturbances and macular lesions, making the search for a treatment with pronounced efficacy and fewer side effects particularly crucial. Laser therapy, which can be tailored to the severity of the patient's condition, offers the advantages of high safety and efficacy. Compound glycyrrhizinic acid is effective in treating eczema and dermatitis, but is typically used as an adjuvant therapy due to its limited efficacy when used alone. This study explores the efficacy of glycyrrhizin in combination with fractional CO2 laser therapy for patients with rosacea skin lesions.

MATERIALS AND METHODS

General data

A total of 108 patients with rosacea skin lesions were selected and treated at Suzhou Kowloon Hospital. Diagnostic criteria: It met the diagnostic criteria of rosacea (Clanner-Engelshofen BM *et al*., 2022). The inclusion criteria were as follows: (1) The patient had erythema in the middle of the face with periodic or hypertrophic proliferative changes; (2) complications such as papules, pustules, local flushing, and other symptoms; and (3) informed consent obtained from the patients and their families. The exclusion criteria were as follows: (1) pregnancy or lactation, (2) photosensitive disease, (3) combined with other facial diseases, (4) scar constitution, (5) non-resident patients or patients who could not be followed up after discharge, and (6) patients who had undergone other treatments. The general data of the two groups were balanced and comparable (P>0.05)(table 1).

When selecting patients, strict adherence to inclusion and exclusion criteria is imperative, with eligible participants randomly assigned to either the control or observation group. Furthermore, all potential confounding variables should be identified prior to the commencement of the trial and meticulously documented throughout the study.

Control group: Conventional treatment: The patient was administered hydroxychloroquine sulfate tablets (Shanghai Shangyao Zhongxi Pharmaceutical, H19990263), 0.2g/times, oral administration, 2 times/d; Mei Lu Xiao Cuo Ointment (Guizhou Liangji Pharmaceutical Co., Ltd., Z20027273) was applied evenly to the skin lesion and massaged for 5 min, 3 times/d. Continuous use for 12 weeks.

Observation group: Glycyrrhizin combined with fractional CO_2 laser was added to the control group. Compound glycyrrhizin tablets (Kaiyin Science and Technology, Beijing, H20083001), 1 tablet/time, were administered orally 3 times/day after meals. Fractional CO_2 laser therapy was performed using a CO_2 therapeutic apparatus (Puate Instruments, Model: JC25). Compound lidocaine cream (Beijing Ziguang Pharmaceutical Co., Ltd., H20063466) was applied externally before treatment and wrapped with plastic wrap for 1h. The treatment parameters were as follows: Wavelength, 10600nm; energy density, 40-80 MJ/cm^2; space, 2-4mm and external application of Sibaoli ointment immediately after surgery. Those who received laser treatment 24h after the operation could not contact water and insisted on external application of Sibaoli Ointment thrice daily, with four weeks as a course of treatment, and received continuous treatment for three courses.

Outcome indicators

1. Improvement in skin lesions: The number of papules, pustules, acne and nodular cysts in the two groups before and after treatment were recorded.
2. Skin barrier function: Before and after treatment, percutaneous water loss, oil secretion, epidermal water content, and number of erythema lesions in the two groups were measured using a skin image analyzer (Thermo-Med Biotech, S7) and the average value of the three measurements was taken as the final result.
3. Incidence of adverse reactions: The incidence of adverse reactions (pigmentation, edema and local bleeding) was recorded for both groups.

Ethical approval

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STATISTICAL ANALYSIS

All data collected in this study were processed using SPSS26.0 statistical software. The measurement data conformed to a normal distribution and the difference was considered significant at P<0.05. Measurement data: x±s, Between groups: independent samples *t-test, Within group: paired samples t-test*; Chi-square test (count data: n,%) was mainly used.

RESULTS

Improvement of skin lesions

After treatment, skin lesions in both groups improved. The numbers of papules, pustules, acne and nodular cysts were significantly lower in the observation group than in the control group (P<0.05)(table 2).

Skin barrier function

After treatment, the skin barrier function of the two groups improved and the percutaneous water loss and number of erythematous lesions in the observation group decreased. Oil secretion and epidermal water content were higher in the observation group than in the control group (P<0.05)(table 3).

Incidence of adverse reactions

The incidence of adverse reactions was higher in the observation group than in the control group, but there was no significant difference between the groups (P>0.05)(table 4).

Table 1: General data ($x\pm s$)/(n (%))

General data	Observation group (n=54)	Control group (n=54)	$Z/t/c^2$	P
Mean age (years)	38.42±8.44	38.39±7.78	0.02	0.985
Gender				
Male	24	22	0.15	0.697
Female	30	32		
Mean course of disease (d)	18.89±2.11	18.92±2.02	0.08	0.940
Mean number of skin lesions	88.46±3.41	88.37±3.52	0.14	0.893
Pillsbury classification				
Class I	9	10	0.01	0.990
Class II	20	19		
Class III	18	17		
Class IV	7	8		

Table 2: Improvement of skin lesions ($x\pm s$)

Group	Papule		t	P	Pustule		t	P
	Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Observation group (n=54)	33.48±10.11	8.44±2.85	17.52	<0.001	23.44±7.46	11.44±3.11	10.91	<0.001
Control group (n=54)	33.28±10.28	11.34±2.44	15.53	<0.001	23.67±6.89	14.36±3.28	8.97	<0.001
t	0.102	5.68			0.17	4.75		
P	0.919	<0.001			0.87	<0.001		
Group	Acne				Nodular cyst			
	Pre-treatment	Post-treatment	T	P	Pre-treatment	Post-treatment	t	P
Observation group (n=54)	20.64±7.11	10.24±3.24	9.78	<0.001	15.46±3.24	8.46±2.11	13.30	<0.001
Control group (n=54)	20.77±6.87	14.22±2.66	6.53	<0.001	14.39±4.11	12.34±3.44	2.81	0.01
t	0.097	6.977			1.502	7.065	t	P
P	0.923	<0.001			0.136	<0.001	13.30	<0.001

Table 3: Skin barrier function ($x\pm s$)

Group	Percutaneous water loss (g/(h·m^2))		t	P	Oil secretion (%)		t	P
	Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Observation group (n=54)	31.02±6.24	17.44±4.11	13.36	<0.001	68.22±3.87	78.44±3.66	14.099	<0.001
Control group (n=54)	31.12±5.87	21.33±3.87	10.23	<0.001	68.34±3.44	72.66±4.02	6.00	<0.001
t	0.07	5.06			0.17	7.81		
P	0.93	<0.001			0.87	<0.001		
Group	Epidermal water content (%)		t	P	Number of erythema (g/(h·m^2))		t	P
	Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Observation group (n=54)	54.88±3.77	70.88±4.11	21.08	<0.001	451.36±18.66	322.46±10.22	44.52	<0.001
Control group (n=54)	54.36±3.67	67.44±4.08	17.52	<0.001	452.12±17.46	384.12±12.44	23.31	<0.001
t	0.73	4.37			0.22	28.14		
P	0.47	<0.001			0.83	<0.001		

Table 4: Incidence of adverse reactions (n(%))

Group	Pigmentation	Oedema	Local bleeding	Incidence of adverse reactions
Observation group (n=54)	1(1.85)	3(5.56)	1(1.85)	5(9.26)
Control group (n=54)	2(3.70)	1(1.85)	1(1.85)	4(7.41)
c^2				0.12
P				0.728

DISCUSSION

Hydroxychloroquine, a commonly used antimalarial in clinical practice, effectively ameliorates inflammatory facial erythema in patients with systemic lupus erythematosus (SLE). The anti-inflammatory and immunosuppressive effects of hydroxychloroquine may also exert a suppressive effect on the localized inflammatory facial flushing and persistent erythema in patients with rosacea. It has been reported (Li C *et al*., 2022) that a variety of lasers, such as strong pulsed light, dye lasers, and photodynamic therapy, are effective for the treatment of rosacea in photoelectric therapy. The results of this study showed that the skin lesions of patients in both groups improved after treatment. The numbers of papules, pustules, acne, and nodular cysts were significantly lower in the observation group than in the control group (P<0.05). Fractional CO_2 laser treatment has been shown to effectively initiate the wound healing process of the body and stimulate the skin self-repair mechanism. The treatment promoted the regeneration and remodeling of various structures of the whole layer of skin, including the epidermis and dermis, and provided positive support for skin recovery. In addition, fractional CO_2 laser treatment had a significant bactericidal effect, providing a new means for the treatment of rosacea. By applying this treatment method, symptoms such as acne, nodular cysts, and empyema caused by microbial infections can be effectively reduced or eliminated, thereby remarkably enhancing the treatment effect (Dong JN *et al*., 2021). At the same time, the use of glycyrrhizin tablets could improve the anti-stress response of hormones, resist granulation and thymus atrophy, and have a positive effect on recovery from skin lesions.

After treatment, the skin barrier function of the two groups improved, and the percutaneous water loss and number of erythematous lesions in the observation group decreased. Oil secretion and epidermal water content were higher in the observation group than in the control group (P<0.05). It has been shown that the penetrating power of the CO_2 laser can effectively inhibit the proliferation of fibrous tissues and thus induce the apoptosis of fibroblasts in the middle and deep layers of chronic skin lesions. In addition, its unique mechanism of action can damage blood vessels in skin lesions and inhibit excessive proliferation of vascular endothelial cells, thereby eliminating dilated facial capillaries to a certain extent and effectively reducing inflammatory exudation. To further improve the therapeutic effect, percutaneous absorption of CO_2 fractional laser combined with adjuvant treatment with compound glycyrrhizin tablets and postoperative skin repair drugs promoted the recovery of skin barrier function. It significantly improved the skin state (Huang, F *et al*., 2023).

The incidence rate of adverse reactions was higher in the observation group than in the control group; however, there was no significant difference between the groups (P>0.05). Analysis showed that glycyrrhiza was a traditional Chinese medicine with relatively few chemical additives in the preparation process. Western medicines such as hydroxychloroquine sulfate tablets would use multiple buffers in the preparation process, especially in the techniques of expression and purification of recombinant protein. Buffers with multiple components could protect the protein from denaturation in the purification process. Hence, the toxic and side effects of Western medicine on the human body were more significant. At the same time, treatment with Chinese medicine does not target a specific physiological index of patients but helps patients correct an extensive range of physiological dysfunctions, while under normal circumstances, the physiological activities of the human body are bidirectionally regulated, so the interaction of Chinese medicine with multiple components on the human body is milder than that of western medicine (Chen, F *et al*., 2022). Therefore, after rosacea was treated with compound glycyrrhizin tablets combined with a fractional CO_2 laser, adverse reactions were not significantly increased, confirming the safety of this protocol.

CONCLUSION

The synergistic application of glycyrrhizin and fractional CO2 laser therapy in patients with rosacea enhances therapeutic outcomes, improves dermatological manifestations and bolsters skin barrier function, offering novel perspectives for clinical management and warranting dissemination.

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