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Skin barrier function and changes of serum inflammatory factor level in hyperpigmentation disorders treated with Nd:YAG laser

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ABSTRACT

It was to compare the differences in efficacy and safety for the treatment of hyperpigmentation disorders by Q-switched alexandrite (Q-SA) laser and Neodymium-doped Yttrium Aluminium Garnet (Nd:YAG) laser. The clinical data of 86 patients with hyperpigmentation disorders were collected and grouped: in the Q-SA laser and Nd:YAG laser groups according to the treatment methods, with 43 cases in each group. The clinical efficacy, skin barrier function (transdermal water loss (TEWL), stratum corneum water content, pH value, proteoglycan content), degree of pigmentation, serum inflammatory factors (high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)), and adverse reaction rate were compared after treatment. Compared with the Q-SA laser group, Nd:YAG laser group had decreased scab formation, healing, and scab shedding time, TEWL, pH value, and proteoglycan content, the increased water content of stratum corneum, decreased pigmentation score and area, and decreased serum levels of hs-CRP, TNF-α, and IL-6 ($P<0.05$). The total effective rates were 76.74% and 95.35%, and the adverse reaction rates were 30.23% and 6.98%, respectively in the Q-SA laser and Nd:YAG laser groups. Compared with the Q-SA laser group, Nd:YAG laser group had a higher total effective rate and lower incidence rate of adverse reactions ($P<0.05$). Nd:YAG laser plus rhEGF gel in the treatment of hyperpigmentation disorders can effectively protect the skin barrier function, reduce skin pigmentation, reduce the inflammatory response, and improve the therapeutic effect, with high safety.

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Introduction

hyperpigmentation disorders are common skin diseases, which are mainly caused by abnormal melanocytes and melanogenesis. Common hyperpigmentation disorders, such as senile spots, fades, Ota nevus and other seborrheic coke disease or exogenous pigmentary diseases, affect the aesthetic degree of patients' faces (1). In clinical practice, traditional surgical methods such as freezing, skin grafting, dermabrasion, and carbon dioxide laser are adopted for the treatment of hyperpigmentation disorders. Such methods mainly achieve the purpose of treatment by destroying the epidermis and dermis (2). Studies have shown that traditional surgical methods have excellent effects in the treatment of hyperpigmentation disorders, but adverse reactions such as pigmentation, loss or scarring occur, so the prognosis of patients is poor (3,4). Q-SA laser is a kind of laser that penetrates the skin with specific energy and wavelength and selectively affects melanocytes or particles, without causing damage to normal tissues and cells, and removes the debris of melanocytes or particles destroyed by laser through the epidermis and lymphatic system (5). Huang et al. (2022) (6) showed that Q-SA laser has a high therapeutic outcome on hyperpigmentation disorders, but has a poor therapeutic effect on post-inflammatory hyperpigmentation and melasma. Nd:YAG laser is a therapeutic method that causes the rupture of melanocytes or granules through pressure effect and instantaneous thermal effect, followed by the removal of debris through tissue absorption and metabolism (7). Nd:YAG laser can limit thermal energy to melanocytes through re-amplification of high-energy pulses, without affecting other normal tissues or causing large area damage to facial skin, so as to avoid scar formation during treatment (8,9).

It aimed to compare the clinical efficacy of Q-SA laser and Nd:YAG laser in the treatment of hyperpigmentation disorders, observe the effects of different treatment methods on skin barrier function, pigmentation, and inflammatory response, and evaluate their safety. It was to find the effective and safe treatment of hyperpigmentation disorders, to improve the clinical treatment outcome.

Materials and Methods

General information

86 patients with hyperpigmentation disorders treated in Sichuan Huamei Zixin Medical Beauty Hospital from June 2021 to June 2022 were enrolled. According to the treatment methods, they have grouped: Q-SA laser and Nd:YAG laser groups, with 43 cases in each group. There were 17 men and 26 women in the Q-SA laser group, with a mean age of (36.2 ± 1.0) years (range, 22-58). The disease duration was 2-5 years, with an average of (3.4 ± 0.5) years. There were senile spots in 8 cases, freckles in 14, lentigo nevus in 3, nevus of Ota in 6, nevus fuscocaeruleus in 10, and tattoos in 2. Nd:YAG laser group had 15

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men and 28 women, aged from 24 to 57 years (mean age: 35.5 ± 1.4). The disease duration was 2-6 years, with an average of (3.2 ± 0.8). There were 7 cases of senile spots, 11 cases of freckles, 5 cases of lentigo nevus, 7 cases of Ota nevus, 11 cases of nevus fuscocaeruleus, and 2 cases of tattoo. There was no marked difference in general data between the two groups (P>0.05). Inclusion criteria: hyperpigmentation disorders; The clinical data were complete. Exclusion criteria: pregnant or lactating women; The constitution of the scar; Severe organ diseases; Coagulopathy or blood system disorders; Use of basic fibroblast growth factor and other drugs within the past 3 months; Patients allergic to therapeutic drugs.

Treatment methods

Preoperative anesthesia was determined according to the type, location, range, and pain degree of the patient. If anesthesia was required, compound lidocaine ointment (Beijing Tongfang Pharmaceutical Group Co., LTD., 10 g, H20063466) was adopted for local anesthesia, and the skin of the operation area was routinely sterilized. The treatment methods of patients in different groups were as follows: patients in the Q-SA laser group were treated with Q-SA laser, and the parameters were set as wavelength =755 nm, pulse width =60 ms, energy density = 3.0-9.0 J/cm^2, spot diameter =3 mm, frequency = 1-4 Hz. Until the local skin turned white, the treatment was finished, and the surgical site was treated with a cold compress for 15 min. Nd:YAG laser group received Nd:YAG laser treatment, the parameters were set as wavelength =1,064 nm, pulse width ≤10 ns, output energy =800 mJ, energy =350 mJ, spot diameter =3 mm (for light or brown skin lesions, the wavelength can be adjusted to 532 nm, and energy adjusted to 150 mJ). Following the operation, the surgical site was cooled with an ice pack for 15 min. Treatment intervals were 3 to 6 months, and patients required three to four sessions. The Nd:YAG laser group required external application of recombinant human epidermal growth factor gel post-treatment (Guilin Pavay Gene Pharmaceutical Co., LTD., 20 g, S20020112). In order to avoid infection within a week, chlortetracycline hydrochloride eye cream (Xinxiang Huaqing Pharmaceutical Co., LTD., 2 g, H19983006) can be given to prevent infection.

Observation indicators

Evaluation of curative effect: following 1 to 6 months of treatment, the skin lesions were observed. It was considered that the pigment in the skin lesions basically disappeared as cured, the pigment in the skin lesions was obviously diluted and the skin lesion area was reduced by more than 70% as markedly effective, the pigment in the skin lesions was diluted and the skin lesion area was reduced by 30 to 70% as effective, and the pigment in the skin lesions was not changed as ineffective. Effective rate = (number of cured cases + number of markedly effective cases + number of effective cases)/total number of cases ×100%. The time of skin scab formation, healing time, and scab shedding time at the treatment site were recorded. Skin barrier function evaluation: Skin barrier function was evaluated pre-treatment and 3 months post-treatment. Patients were instructed to stay in a constant temperature and humidity environment for 30 min after cleansing, and then TEWL, pH value, and water content of stratum corneum were measured by TM300, pH900, and CM825. The skin at the treated site was debonding (20 times) adopting D-Squame, and the cuticle was immersed in 1% trichloroacetic acid filling solution and placed at 4℃ for 12h. Then, the protein content was detected by BCA method protein quantitative detection kit (ThermoFisher Scientific Company, USA). Pigmentation evaluation: the degree and area of skin pigmentation were evaluated pre-treatment and 3 months post-treatment. A score of 9: was reddish-brown or dark red, 6: yellow brown, 3: light brown, and 0: loss of pigmentation (10). Detection of serum inflammatory factors: the levels of serum inflammatory factors were detected pre-treatment and 3 months post-treatment. Fasting venous blood (3 ml) was collected from the patients, allowed to stand at room temperature for 30 min, and centrifuged at 3,000 r/min for 10 min. The supernatant was collected and the serum levels of hs-CRP, TNF-α, and IL-6 were tested by an enzyme-linked immunosorbent assay kit (Shanghai Mlbio Co., LTD.). The occurrence of adverse reactions such as dry skin, muscle pain, facial desquamation, infection, and the scar was recorded during the treatment.

Statistical analysis

SPSS 19.0 statistical software was adopted for analyzing and processing data. The count data were presented as frequency (rate) and χ^2 test was adopted. Measurement data were presented by $(\bar{x} \pm s)$ and t-test was adopted. P <0.05 was considered statistically meaningful.

Results

Comparison of clinical effect

Clinical effects of the Q-SA laser and Nd:YAG laser groups were compared (Table 1). Through 3 months of Q-SA laser treatment, 14 cases were cured, 11 were markedly effective, 8 were effective, and 10 were ineffective. The total effective rate was 76.74% (33/43); In Nd:YAG laser group, 20 cases were cured, 14 were markedly effective, 7 were effective, and 2 were ineffective, with a total effective rate of 95.35% (41/43). The total effective rate of Nd:YAG laser group was higher (P<0.05).

Comparison of symptom improvement

The time to symptom improvement at 3 months post-treatment in both groups is illustrated in Figure 1. In the Q-SA laser group, the scab formation time was (4.6±0.3) d, the healing time was (12.6±1.2) d and the scab shedding time was (9.8±0.7) d. In Nd:YAG laser group, scab formation time was (2.5±0.7) d, the healing time was (6.3±0.6) d, and scab shedding time was (6.2±0.8) d. The time in Nd:YAG laser group was shorter (P<0.05).

Table 1. The contrast of treatment effect.

Group	Cured	Markedly effective	Effective	Ineffective	Effective rate %
Q-SA laser (n=43)	14	11	8	10	76.74
Nd:YAG laser (n=43)	20	14	7	2	95.35

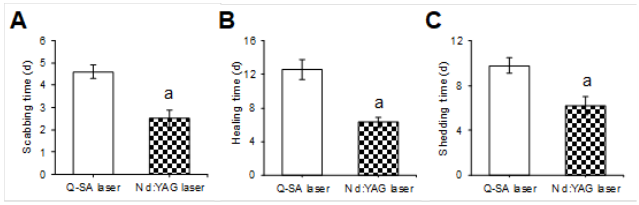

Figure 1. The contrast of symptom improvement time in patients. Note: A is scab formation time; B is healing time; C is scab shedding time; Compared with the Q-SA laser group, $^{a}P<0.05$.

Comparison of skin barrier function

The skin barrier function indexes of the two groups are illustrated in Figure 2. Through treatment, the TEWL of the Q-SA laser group was (18.6 ± 1.2) g/h·m^2, the pH value was (5.7 ± 0.4), the water content of stratum corneum was (34.1 ± 3.5) AU, and the proteoglycan content was (36.3 ± 3.7) μg. In Nd:YAG laser group, the TEWL was (15.4 ± 1.4) g/h·m^2, the pH value was (5.0 ± 0.3), the water content of stratum corneum was (45.6 ± 4.1) AU, and the proteoglycan content was (30.7 ± 3.2) μg. After treatment, as against before treatment, TEWL, pH value, and proteoglycan content in both groups were lower, and the water content of stratum corneum was higher; relative to the Q-SA laser group, Nd:YAG laser group had lower TEWL, pH value, and proteoglycan content, and higher water content of stratum corneum ($P<0.05$).

Comparison of pigmentation

The pigmentation of both groups is illustrated in Figure 3. Through treatment, the pigmentation score was 2.6 ± 0.4, and the pigmentation area was (3.1 ± 0.6) cm^2 in the Q-SA laser group. The pigmentation score was 0.8 ± 0.2, and the pigmentation area was (1.5 ± 0.7) cm^2 in Nd:YAG laser group. The pigmentation score and pigmentation area of the two groups post-treatment were lower than before treatment, and those in Nd:YAG laser group were smaller following treatment ($P<0.05$).

Comparison of peripheral blood inflammatory factor levels

Figure 4 suggests that after treatment, in Q-SA laser group, the serum hs-CRP was (3.3 ± 0.3) μg/l, the TNF-α was (25.7 ± 4.0) μg/l, and the IL-6 was (19.5 ± 3.8) μg/l; Nd:YAG laser group was (2.4 ± 0.4) μg/l, (19.8 ± 2.2) μg/l, (11.7 ± 1.8) μg/l. The serum levels of hs-CRP, TNF-α, and IL-6 in two groups post-treatment were lower as against before treatment, and through treatment, the serum levels of hs-CRP, TNF-α, and IL-6 in Nd:YAG laser group were lower ($P<0.05$).

Comparison of adverse reaction rate

Table 2 suggests that there were 5 cases of dry skin, 2 cases of muscle pain, 4 cases of facial desquamation, 1 case of infection, and 1 case of scar in the Q-SA laser group during 3 months of treatment, with a total adverse reaction rate of 30.23% (13/43). In Nd:YAG laser group, there were 2 cases of dry skin, 0 cases of muscle pain, 1 case of facial desquamation, 0 case of infection, and 0 cases of scar during 3 months of treatment, and the total adverse reaction rate was 6.98% (3/43). The total incidence of adverse reactions in Nd:YAG laser group was lower ($P<0.05$).

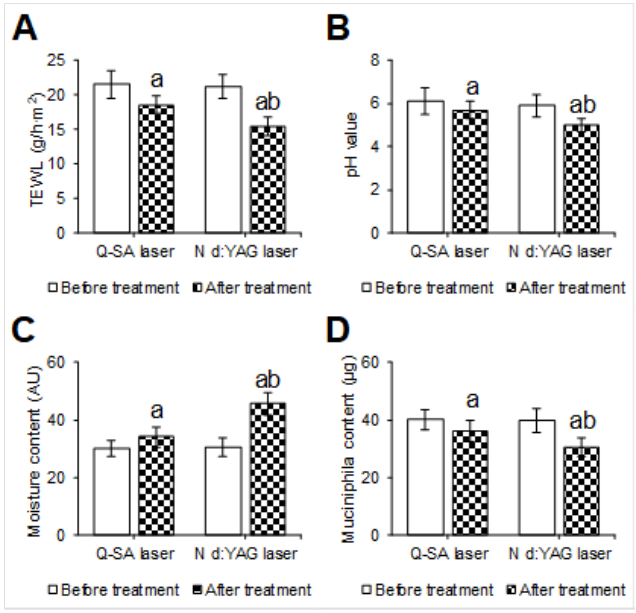

Figure 2. The contrast of skin barrier function indexes in patients. Note: A is TEWL; B is pH value; C is the water content of stratum corneum; D is proteoglycan content; Compared with the same group pre-treatment, $^{a}P<0.05$; relative to Q-SA laser group, $^{b}P<0.05$.

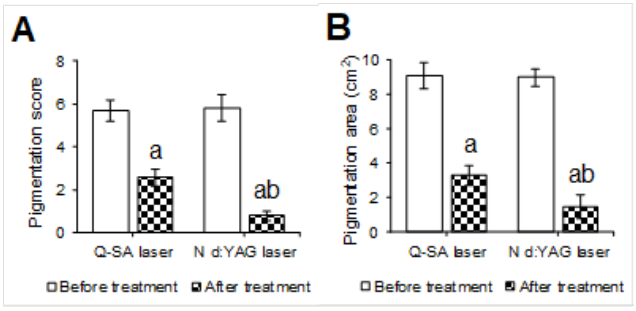

Figure 3. The contrast of pigmentation in patients. Note: A is the pigmentation score; B is the pigmentation area.

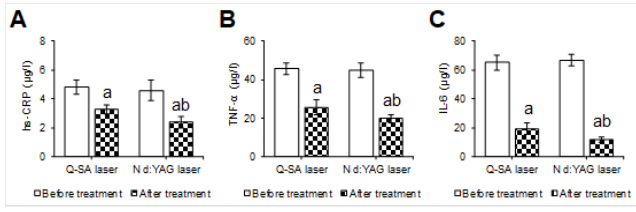

Figure 4. The contrast of inflammatory factor levels in peripheral blood of patients. Note: A is hs-CRP; B is TNF-α; C is IL-6.

Table 2. The contrast of adverse reactions.

Group	Dry skin	Muscle pain	Facial desquamation	Infection	Scar	Incidence %
Q-SA laser (n=43)	5	2	4	1	1	30.23
Nd:YAG laser (n=43)	2	0	1	0	0	6.98

Discussion

Hyperpigmentation disorders are common in clinical practice, mainly including freckles, Ota nevus, senile spots, seborrheic coiling, and so on (11). Hyperpigmentation disorders affect the facial aesthetics of patients and then affect their level of mental health. In clinical practice, traditional methods such as freezing, chemical exfoliation, dermabrasion, and plastic surgery have certain therapeutic effects, but they can't eliminate pigmentation in the dermis tissue, which is prone to complications such as pigmentation and scarring after treatment (12,13). With the rapid development of medical and biological science and technology, laser surgery has been gradually applied to the treatment of many diseases, and has achieved excellent results. The clinical efficacy of Q-SA laser and Nd:YAG laser in the treatment of hyperpigmentation disorders was compared. Q-SA laser can emit very high-power laser in a short time, and the heat energy converted by high power can quickly break melanin in skin tissue. The thermal relaxation time of pigment particles is greater than the pulse width of the laser, so the laser will not cause damage to other normal skin (14). The results revealed that compared with Q-SA laser treatment, Nd:YAG laser treatment clearly shortened the scab formation time, healing time, and scab shedding time in patients with hyperpigmentation disorders. It is because rhEGF gel is applied following Nd:YAG laser treatment and rhEGF can promote cell proliferation, and differentiation and accelerate wound vascular activity, thereby promoting wound re-growth and granulation tissue regeneration, and accelerating skin healing (15).

Studies have confirmed that Q-SA laser can effectively eliminate pigmentation in the skin and reduce scar formation (16,17). The principle of Nd:YAG laser treatment is to use the laser to pass through the epidermis to reach the dermis and act on the pigment cells. When the target color absorption wavelength is consistent with the laser reflection wavelength, it can absorb light waves and produce photothermal and photochemical effects. At this time, pressure and instant thermal effects can cause the destruction of pigment cells. Some ragged pigment cells or particles can be removed by transferring from the epidermis to the skin surface, while the other part can be engulfed by phagocytic cells or removed by capillary lymphatic vessels (18). It was found that relative to Q-SA laser treatment, Nd:YAG laser treatment clearly reduced TEWL, pH value, and proteoglycan content, while increased cuticle water content in patients with hyperpigmentation disorders. Nd:YAG laser treatment of hyperpigmentation disorders can effectively enhance the protective effect of skin barrier function in patients. As against Q-SA laser, Nd:YAG laser treatment markedly reduced skin pigmentation score and hyperpigmentation area in patients with hyperpigmentation disorders. Only a small part of pigment groups can be removed after being transferred to the skin surface, and most of them are swallowed by macrophages, so the process of pigment group removal is very long (19). Application of rhEGF gel following Nd:YAG laser treatment can increase the water content of the stratum corneum, increase the resistance of the skin to external microorganisms, and thus reduce pigmentation.

Laser beam therapy can cause skin damage to a certain extent and increase the degree of the inflammatory response (20). hs-CRP is an acute protein synthesized and secreted by hepatocytes when the body is subjected to inflammatory stimuli such as microbial invasion or tissue damage (21). When inflammation occurs, the level of hs-CRP in the body increases and reaches its peak at 48h. It will decrease to a normal level with the regression of the disease and the recovery of tissue, structure, and function. TNF-α is a kind of pro-inflammatory cytokine, which is mainly produced by activated monocytes and macrophages and participates in the normal inflammatory response and immune response (22). After TNF-α binds to its corresponding receptors, it can cause cell apoptosis, inflammation, and tumorigenesis, etc. Its dysfunction is also related to cardiovascular disease, rheumatoid arthritis, and inflammatory bowel disease (23-25). IL-6 is a cytokine in the chemokine family, which has a major factor in information transmission, activation, and regulation of immune cells, and mediating the biological functions of T or B cells and inflammatory response (26). It was found that the levels of hs-CRP, TNF-α, and IL-6 in the peripheral blood of patients with hyperpigmentation disorders were clearly decreased through Q-SA laser and Nd:YAG laser treatment and the incidence of adverse reactions was also clearly reduced. The parameters of Nd:YAG laser treatment for patients with different degrees and types of hyperpigmentation disorders were adjusted, so as to reduce the degree of skin tissue damage. Topical rhEGF gel can accelerate the healing of skin lesions in patients with hyperpigmentation disorders following laser treatment, with high safety.

Nd:YAG laser has a good therapeutic outcome in the treatment of hyperpigmentation disorders. It can effectively promote the healing of skin lesions, protect the skin barrier function, reduce pigmentation in the skin, reduce the inflammatory response, and has high safety. It only compared the clinical effect of Q-SA laser and Nd:YAG laser in the treatment of hyperpigmentation disorders, and the sample size was small. In the future, more sample data are needed to explore the efficacy and safety of Nd:YAG laser in the treatment of different types of hyperpigmentation disorders, and to evaluate the long-term efficacy. It can provide help with the choice of clinical treatment for hyperpigmentation disorders.

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