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Original Article

Effect of minocycline hydrochloride combined with photodynamic therapy on skin barrier function of patients with acne

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Abstract: Objective: The aim of this study is to evaluate the effects of minocycline hydrochloride combined with photodynamic therapy on skin barrier function of patients with acne. Methods: Eighty-eight acne patients admitted to our hospital were randomized into research group (n=44, photodynamic therapy on the basis of minocycline hydrochloride) and control group (n=44, minocycline hydrochloride). The clinical efficacy, skin barrier function indexes (transdermal water loss (TEWL), stratum corneum water content, pH value), scores of GAGS and Acne-QOL, cosmetic satisfaction and adverse reaction rates of the two groups were compared. Results: The total effective rate of research group was higher than that of control group (P<0.05). After treatment, TEWL, cuticle water content and pH value were improved compared with those before treatment, and the research group was superior to the control group (all P<0.05). After treatment, the GAGS scores of both groups were lower than those before treatment, and the research group was lower than that of the control group (all P<0.05). The cosmetic satisfaction in the research group was higher than that in the control group (P<0.05). There was no marked difference in the incidence of adverse reactions between the two groups (P>0.05). After treatment, the quality of life scores of patients were higher than before treatment, and the research group was higher than that of the control group (all P<0.05). Conclusion: Minocycline hydrochloride combined with photodynamic therapy can effectively improve the skin barrier function of patients, relieve clinical symptoms, and enhance the overall efficacy and quality of life. It is also safe and patients are highly satisfied with the cosmetic effect.

Keywords: Minocycline hydrochloride, photodynamic therapy, acne, skin barrier function

Introduction

Acne is a chronic inflammatory skin disease of pilosebaceous unit, mainly occurs in teenagers, which threatens beautiful appearance and quality of life of patients [1]. At present, the general treatment scheme for acne is daily nursing combined with medication. Minocycline hydrochloride is a highly effective and spectrum antibacterial drug for acne, which mainly reduces cortical secretion and skin free fatty acid content, resists inflammation, promotes oil balance and relieves skin lesions [2, 3]. However, there is room for improvement in the overall effect of minocycline hydrochloride alone on acne. Photodynamic therapy is also an important treatment, which can resist the pathogenic organisms by ray radiation, induce the occurrence of oxidation reaction by photosensitizers, promote the recovery of skin lesions and improve the aggravation of acne symptoms [4, 5]. Based on this, this research plans to select 88 acne patients in our hospital and assess the application value of minocycline hydrochloride combined with photodynamic therapy.

Materials and methods

General data

Eighty-eight patients with acne admitted into our hospital from March 2019 to October 2020 were prospectively selected and divided into research group (n=44, photodynamic therapy based on minocycline hydrochloride) and con-

Table 1. Comparison of two general data ($\bar{x} \pm sd$, n, %)

Group	Research group	Control group	t/χ^2	P
Number of cases	44	44		
Gender			0.503	0.478
Male	11	14		
Female	33	30		
Age (years)	26.65±3.11	27.32±2.98	1.032	0.305
Course of disease (years)	1.98±0.59	2.10±0.63	0.922	0.359
Acne area (n (%))				
Forehead	5 (11.36)	8 (18.18)	0.812	0.367
Cheek	11 (25.00)	14 (31.82)	0.503	0.478
Nose	13 (29.55)	10 (22.73)	0.530	0.467
Tip of the nose	15 (34.09)	12 (27.27)	0.481	0.488

trol group (n=44, minocycline hydrochloride) according to random number table method. Inclusion criteria are as follows: (1) Those meet the diagnostic criteria of acne [6]. (2) Age >18 years old; (3) No skin surface inflammation or secondary infection; (4) No hyperplastic old scar. Exclusion criteria are as follows: (1) Lactating and pregnant women; (2) Sensitive skin; (3) Those who take hormone drugs before being included in the research; (4) There are wounds in acne that are healing; (5) Those participate in other researchers at the same time; (6) Those with mental illness and other diseases can not cooperate with researchers.

All patients and their families have known the contents of the research and signed an informed consent form. The research has been approved by the hospital Ethics Committee.

Treatment methods

In the control group, minocycline hydrochloride (Hisun Pfizer Pharmaceutical Co., Ltd., China, 100 mg) was taken orally, 50 mg/twice a day, for 4 weeks. On the basis of the control group, the research group used LED-IA dynamic therapeutic apparatus (Wuhan Yage Optic And Electronic Technique Co., Ltd., China) for photodynamic therapy. The specific method was as follows: before treatment, 5% 5-aminolevulinic acid gel (Shanghai Fudan Zhangjiang Biomedical Co., Ltd., H20070027) was evenly applied to acne area, wrapped with plastic wrap, and the patient was put on eye mask after 1.5 h; 5-aminolevulinic acid red light was applied at a distance of about 10 cm from the light source. The irradiation wavelength was 628-633 nm, the power was 103 mW/cm^2, the irradiation dose was 90-100 J per square centimeter, and the treatment was 20 min each time, once every 7 days, for 4 times. The medical workers should pay attention to skin protection and avoid exposure during treatment.

Outcome measures

Main outcome measures are as follows: (1) The therapeutic effects of both groups are counted. After treatment, it is cured when the skin lesions subside ≥90%, markedly effective when 75%≤ skin lesions subside <90%, effective when 25%≤ skin lesions subside <75%, and ineffective when the skin lesions subside less than 25%. The total effective rate = (cured + markedly effective + effective)/total cases ×100% [7]. (2) The skin barrier function indexes (transcutaneous water loss (TEWL), stratum corneum water content, pH value) before and after treatment were counted. The stratum corneum water content was measured by CM825 skin moisture tester made by CK, Germany. TEWL was measured by TM300 skin moisture loss tester of CK. The pH value of normal skin ranges from 5 to 7; The higher the pH value, the lower the water permeability barrier function is. Secondary outcome measures are as follows: (3) The improvement of acne and the score of quality of life before and after treatment were counted. The improvement of acne was evaluated by the Global Acne Grading System (GAGS): ≥39 points belonged to extremely severe, 31-38 to severe, 19-30 to moderate, and 1-18 to mild. The quality of life was evaluated according to the Acne-Specific Quality of Life Questionnaire (Acne-QOL), including emotional function (30 points), social function (24 points), self-perception (30 points) and acne symptoms (30 points). The higher the score, the better the quality of life is [8]. (4) The cosmetic satisfaction was counted and evaluated by self-designed satisfaction questionnaire, 100 points in total: 95-100 being very satisfied, 80-94 being satisfied, 60-79 being average, 50-59 being dissatisfied, and less than 50 being very dissatisfied. The cosmetic satisfaction = (very satisfied + satisfied)/total number of cases ×100%. (5) The incidence of adverse reactions was counted, and the adverse reaction rate = the number of adverse reactions/the total number of cases ×100%.

Table 2. Comparison of treatment effects between both groups (n, %)

Group	Number of cases	Cure	Markedly effective	Effective	Invalid	Total effective rate
Research group	44	26 (59.09)	11 (25.00)	4 (9.09)	3 (6.82)	41 (93.18)
Control group	44	19 (43.18)	10 (22.73)	5 (11.36)	10 (22.73)	34 (77.27)
χ^2						4.423
P						0.035

Table 3. Comparison of skin barrier function between both groups ($\bar{x} \pm sd$)

Group	Number of cases	TEWL (g/(h·m^2))	Cuticle water content (AU)	pH
Before therapy				
Research group	44	23.38±4.11	31.40±4.14	6.19±0.22
Control group	44	24.10±4.25	32.30±3.98	6.21±0.20
t		0.808	1.040	0.446
P		0.421	0.302	0.657
After treatment				
Research group	44	13.32±2.64[a]	47.70±5.08[a]	5.61±0.11[a]
Control group	44	16.11±3.05[a]	41.63±4.91[a]	5.80±0.14[a]
t		4.588	5.699	7.079
P		0.000	0.000	0.000

Note: Compared with this group Before therapy, [a]P<0.001; TEWL: Trans Epidermal Water Loss.

Statistical methods

The data were processed by SPSS 22.0. The measurement data were analyzed by Bartlett variance homogeneity and Kolmogorov-Smirnov normality tests, both of which were confirmed to have homoscedasticity and approximately obeyed the normal distribution, expressed as ($\bar{x} \pm sd$). The comparison between groups was conducted by independent-samples t-test, and that within groups was conducted by paired t-test. The counting data were expressed by (case (%)); those were compared by the exact probability method when the number of cases was less than 40 or the theoretical frequency T≤1, and assessed by the χ^2 test when the number was ≥40 and the frequency T>5 or 1<T<5. P<0.05 is statistically remarkable.

Results

General data

There was no marked difference in gender, age, course of disease and acne location between the research group and the control group (all P>0.05; **Table 1**).

Efficacy evaluation

The total effective rate of the research group was higher than that of the control group (P<0.05; **Table 2**).

Skin barrier function

Before treatment, there was no obvious difference in TEWL, cuticle water content and pH value between the two groups (all P>0.05). After treatment, those were improved, and the research group was superior to the control group (all P<0.001; **Table 3**; **Figure 1**).

GAGS scores

There was no marked difference in GAGS scores between the two groups before treatment (P>0.05). After treatment, the scores were lower, and the research group was lower than the control group (P<0.001; **Table 4**).

Acne-QOL scores

There was no obvious difference in emotional function, social function, self-perception and acne symptom scores between the two groups before treatment (P>0.05). After treatment, the scores were higher, and the research group was higher than that in the control group (P<0.05; **Table 5**).

Cosmetic satisfaction

The cosmetic satisfaction in the research group was higher than that in the control group (P<0.05; **Table 6**).

Adverse reactions

There was no obvious difference in the incidence of adverse reactions between the

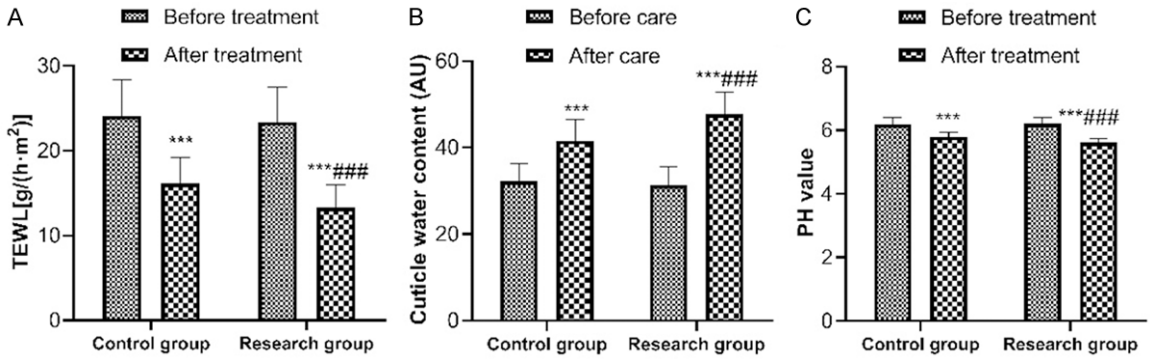

Figure 1. Comparison of skin barrier function between both groups. A: TEWL (g/(h·m^2)); B: Cuticle water content (AU); C: pH. Compared with this group Before therapy, ***P<0.001; Compared with Control group, ###P<0.001.

Table 4. Comparison of GAGS scores between both groups ($\bar{x}$ ± sd)

Group	Number of cases	Before therapy	After treatment	t	P
Research group	44	25.10±5.93	10.13±2.19	15.708	0.000
Control group	44	23.98±6.11	13.69±2.66	10.243	0.000
t		0.873	6.854		
P		0.385	0.000		

Note: GAGS: Global Acne Grading System.

research group and the control group (P>0.05; **Table 7**).

Discussion

Minocycline hydrochloride, due to its good lipophilicity, can quickly enter the lesion site and exert its inhibitory effect on Propionibacterium acnes [9]. At the same time, the drug can also activate the complement C3 system, inhibit the inflammation under the chemotaxis of neutrophils, and rejuvenate the damaged skin. Zhuo et al. found that the total effective rate of minocycline hydrochloride alone in treating moderate and severe acne was only 70.0%, and the GAGS score was not improved obviously [10]. To further improve the efficacy of acne, photodynamic therapy is gradually introduced into the treatment. It mainly mediates oxidation reaction through photosensitizer and light radiation, thereby damaging sebaceous glands, causing atrophy of sebaceous glands, inhibiting secretion of sebaceous glands, stimulating synthesis of macrophages, generating cytokines, and accelerating repair of damaged skin and proliferation of fibroblasts [11, 12]. Chen et al. confirmed that after the intervention of photodynamic therapy on rose acne patients based on conventional drugs, the total effective rate was as high as 100.0%, and the symptoms such as telangiectasia, papules, erythema and pustules were obviously alleviated [13]. This research shows that the total effective rate, GAGS and Acne-QOL scores of the research group are higher than those of the control group, and the cosmetic satisfaction of the research group is higher; But adverse reactions showed no obvious difference. It is suggested that minocycline hydrochloride combined with photodynamic therapy has marked advantages in relieving patients' clinical symptoms, improving efficacy, enhancing quality of life and facial beauty, which is quite safe.

In addition, skin lesions and impaired skin barrier function will aggravate the inflammation of acne patients and reduce skin tolerance, thus reducing treatment compliance [14, 15]. Therefore, effectively reducing skin lesions and restoring skin barrier function will help alleviate inflammation and improve patients' treatment compliance. In this research, the TEWL, stratum corneum water content and pH value of the research group were better than those of the control group after treatment, which indicated that minocycline hydrochloride combined with photodynamic therapy was also beneficial to improve the skin barrier function of acne patients. The main reasons are as follows: photodynamic therapy can use 5-aminolevulinic acid as photosensitizer and red and

Table 5. Comparison of two groups of Acne-QOL score ($\bar{x} \pm sd$)

Group	Affective function	Social function	Self perception	Acne symptoms
Before therapy				
Research group (n=44)	10.69±2.38	11.59±2.29	12.55±2.53	13.13±2.45
Control group (n=44)	11.04±2.51	12.10±2.46	13.28±2.91	12.79±2.60
t	0.671	1.007	1.256	0.631
P	0.504	0.317	0.213	0.530
After treatment				
Research group	23.88±3.25[a]	19.56±3.45[a]	25.05±2.89[a]	25.51±2.62[a]
Control group	19.91±3.03[a]	16.23±3.19[a]	21.29±2.66[a]	22.01±2.18[a]
t	5.927	4.701	6.350	6.812
P	0.000	0.000	0.000	0.000

Note: Compared with this group Before therapy, [a]P<0.05.

Table 6. Comparison of satisfaction between two groups of cosmetic effects (n, %)

Group	Very satisfied	Satisfaction	General	Not satisfied	Very dissatisfied	Total satisfaction
Research group (n=44)	25 (56.82)	16 (36.36)	1 (2.27)	1 (2.27)	1 (2.27)	41 (93.18)
Control group (n=44)	15 (34.09)	18 (40.91)	6 (13.64)	3 (6.82)	2 (4.55)	33 (75.00)
χ^2						5.436
P						0.020

Table 7. Comparison of adverse reactions between both groups (n, %)

Group	Pigmentation	Redness	Itching	Local pain	Total incidence
Research group (n=44)	1 (2.27)	0 (0.00)	2 (4.55)	2 (4.55)	5 (11.36)
Control group (n=44)	1 (2.27)	1 (2.27)	0 (0.00)	1 (2.27)	3 (6.82)
χ^2					0.550
P					0.458

blue light as light source, and transform propionibacterium acnes into porphyrin. Macrophages proliferate actively and promote the synthesis of related cytokines, improve the generation of fibroblasts, and make the skin return to normal [2, 16, 17]. Nevertheless, there is synergism combined with minocycline hydrochloride. It can enhance the anti-inflammatory and bactericidal effects, reduce skin lesions, and then improve the skin barrier function to achieve the therapeutic purpose [8, 18-20].

This research also has some shortcomings. First of all, the sample size is small, and it is a single center study. In addition, the follow-up time is short. Large sample, multi-center and long-term follow-up experiments are still needed to confirm the results of this research.

In general, minocycline hydrochloride combined with photodynamic therapy can effectively improve the skin barrier function of patients, relieve clinical symptoms, improve the overall efficacy and quality of life. It is quite safe, so patients are highly satisfied with the cosmetic effect.

Disclosure of conflict of interest

None.

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