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Original Article

Narrow-band UVB combined with compound clobetasol propionate can improve the therapeutic effect in hand eczema patients

Ning Yuan[1], Zeyu Chen[2], Linfeng Li[1]

[1]*Department of Dermatology, Beijing Friendship Hospital Affiliated to Capital Medical University, Beijing 100050, China;* [2]*Department of Dermatology, Beijing Changping District Hospital, Beijing 102200, China*

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Abstract: Objective: To explore the therapeutic effect of narrow-band UVB combined with compound clobetasol propionate on hand eczema patients. Methods: From June 2017 to June 2020, 102 patients with hand eczema in our hospital were recruited for this study and divided into group A (GA) and group B (GB). The 50 patients in GA were treated with narrow-band UVB irradiation only, and the 52 patients in GB were treated with compound clobetasol propionate in addition to the treatment administered to GA. The patients' general data and therapeutic effects were observed in both groups. The adverse reactions were also observed during the treatment. The severity index scores (EASI) of the pruritus and eczema areas of the skin lesions were observed before and after the therapy. The IFN-γ and IL-4 levels in the serum were tested using ELISA. After the therapy, the quality of life and any recurrences within 3 months were observed in both groups. Results: There were no differences in the baseline data between the two groups ($P>0.05$). The curative effect in GB was better than it was in GA ($P<0.05$). The incidence of adverse reactions in GB was significantly lower than the incidence in GA ($P<0.05$). After the therapy, the EASI scores of the pruritus and eczema areas of the skin lesions in GB were significantly lower than they were in GA ($P<0.05$). After the therapy, the patients' serum IFN-γ and IL-4 levels in GB were significantly better than they were in GA. After the therapy, the quality of life of the patients in GB was significantly higher than it was in in GA ($P<0.05$). After 3 months of therapy, the recurrence rate in GB was significantly lower than it was in GA ($P<0.05$). Conclusion: Narrow-band UVB combined with compound clobetasol propionate is effective at treating patients with hand eczema, as it can effectively improve their clinical symptoms and is very safe.

Keywords: Hand eczema, narrow-band UVB, compound clobetasol propionate, recurrence rate

Introduction

Eczema is a common clinical skin disease. It often develops on the head, face, limbs, and scrotum, and its incidence is often urgent. Patients experience skin flushing, pruritus, and scorching hot sensations, and even papules, erosions, desquamation, and other changes, so it has a great impact on patients' quality of life [1, 2]. Hand eczema is a stubborn type of eczema with more incidences at present, and its incidence has been constantly rising in recent years [3]. Hand eczema is very difficult to treat, and its course of disease is long. It can easily relapse and may trigger a series of inflammatory reactions, so it has a great impact on the appearance of the hands and the patients' quality of life [4]. Therefore, it is of great clinical significance to find a quick and effective treatment plan for hand eczema patients.

In recent years, narrow-band ultraviolet B (NB-UVB) at a wavelength of 311-312 nm has been widely used in dermatology, as it mainly inhibits the degranulation of dermal mast cells to release histamine by enhancing the barrier function of the skin and affecting the body's immune function, thus alleviating the eczema symptoms [5, 6]. However, some clinical studies have revealed that NB-UVB has certain limitations, such as its slow onset and its poor antipruritic effect. Therefore, it is necessary to combine other therapeutic schemes to enhance the

curative effect [7]. Compound clobetasol propionate is a yellow oil- and fat-based ointment, and it was mainly used to treat psoriasis in the past. In recent years, it has been found that it can also play a role in treating hand eczema [8]. Also, in recent years, studies have revealed that it has anti-inflammatory, anti-proliferative, and anti-immune effects, and it can effectively alleviate hand eczema [9]. For now, there are few studies on the efficacy of NB-UVB combined with compound clobetasol propionate in the treatment of hand eczema.

In our research, we analyzed the efficacy of NB-UVB combined with compound clobetasol propionate in the treatment of hand eczema and its influence on patients' recurrence rates, aiming to provide a more effective treatment scheme for hand eczema patients.

Materials and methods

Clinical data

From June 2017 to June 2020, 102 patients with hand eczema in the Beijing Changping District Hospital were recruited as the study cohort. The cohort included 53 male patients and 49 female patients. According to the treatment scheme each patient underwent, they were divided into GA (50 cases) or GB (52 cases). In GA, they were treated with narrowband UVB irradiation only. In GB, they were treated with compound clobetasol propionate in addition to the treatment administered in GA.

Inclusion criteria: (1) Patients who met the diagnostic criteria for hand eczema [10]. (2) Patients who had not undergone systematic treatment in the past one month.

Exclusion criteria: (1) Patients comorbid with other serious diseases that might affect the treatment effect. (2) Patients comorbid with abnormal heart, liver, or kidney function. (3) Patients with severe immune dysfunction. (4) Pregnant or lactating women. (5) Patients allergic to the therapeutic drugs.

All the patients agreed to participate in the trial and signed the informed consent forms. This research was approved by our hospital's ethics committee, and it conformed with the *Declaration of Helsinki*.

Therapeutic schemes

In both groups, the patients were treated with NB-UVB irradiation first, and they were instructed to wear special protective glasses to protect against the ultraviolet rays. A UV SS-04C NB-UVB phototherapy instrument (produced by Shanghai Sigma Technology Co., Ltd., wavelength 311 nm) was used to irradiate the local skin lesions. The affected part of the patient was placed flat on the glass panel, and the affected part of the hand was irradiated at 400 m J/cm^2, and the first irradiation time was 90 s. If there was no asymptomatic erythema reaction with a clear boundary after the previous irradiation, the radiation dose was gradually increased by 20% until the single maximum dose was 1110 m J/cm^2. In the case of severe erythema (painful, with or without edema or bullae), the irradiation was conducted until the skin lesion subsided completely. The dose was reduced by 20% when the irradiation was restored, and the dose was fixed for the irradiation, three times a week. In addition to the light therapy, the patients in GB were treated with compound clobetasol propionate ointment (produced by Jiangsu Zhiyuan Pharmaceutical Co., LTD., SFDA Approval No. H20040122) for external use, twice/d, once in the morning and once before going to bed in the evening. The ointment was evenly smeared on the affected part. Then, the affected part was gently rubbed to effectively promote the absorption of the drug. Significantly, after applying the medicine in the evening, it was necessary to use cling film to wrap it locally and remove it after getting up in the morning. The curative effect was assessed after 6 weeks of treatment.

Outcome measures

(1) The patients' therapeutic effects were assessed and compared in the two groups, and they were classified into four outcomes: Cured: the total number of skin lesions was reduced by >90%. Markedly effective: the total number of skin lesions declined by 60%-90%. Effective: the total number of skin lesions was reduced by 20%-60%. Ineffective: the total number of skin lesions was reduced by <20%. Effective rate (%) = (cured number + markedly effective number)/total number of cases × 100%. (2) The severity index scoring method (EASI) [11] was used to score the pruritus and eczema areas of

Table 1. Baseline data

Factors	GA (n=50)	GB (n=52)	t/χ^2	P
Gender			0.001	0.994
Male	26 (52.00)	27 (51.92)		
Female	24 (48.00)	25 (48.08)		
Age/years old			0.002	0.962
≥39	31 (62.00)	32 (61.54)		
<39	19 (38.00)	20 (38.46)		
BMI (kg/m^2)	21.89±1.03	22.01±1.06	0.580	0.564
Course of disease (years)	4.21±1.34	4.14±1.41	0.257	0.798
Smoking history			0.025	0.874
Yes	20 (40.00)	20 (57.14)		
No	30 (60.00)	32 (42.86)		
Alcoholism history			0.002	0.963
Yes	16 (30.77)	15 (38.46)		
No	34 (69.23)	37 (61.54)		
Occupation distribution			0.151	0.927
Mental labor	15 (30.00)	14(26.92)		
Manual labor	30 (60.00)	32 (61.54)		
Inoccupation	5 (10.00)	6 (11.54)		

Table 2. Evaluation of the clinical efficacy in both groups [n, (%)]

Efficacy	GA (n=50)	GB (n=52)	χ^2	P
Cured	17 (34.00)	25 (48.08)	-	-
Markedly effective	20 (40.00)	14 (26.92)	-	-
Effective	11 (22.00)	2 (3.85)	-	-
Ineffective	2 (4.00)	1 (1.92)	-	-
Total effective rate	37 (74.00)	49 (94.23)	7.888	0.005

the skin lesions in both groups before and after the therapy. (3) The IFN-γ and IL-4 inflammation-related factor levels in the patients' peripheral blood were tested in both groups before and after the therapy. Elbow venous blood (3.0 ml) was drawn on an empty stomach in the morning, and the serum IFN-γ and IL-4 levels were tested using ELISA after centrifugation. (4) The adverse reactions were recorded and compared in both groups during the therapy, including erythema, rhagades, keratosis, and pruritus. (5) The recurrence rate was recorded and compared between the two groups within three months after the therapy. (6) The simplified quality of life scale (SF-36) [12] was used to investigate the quality of life, including four dimensions: physiological function, social function, emotional function and physical function. The higher the score, the higher the quality of life.

Statistical methods

In this research, SPSS 20.0 (Boyi Zhixun (Beijing) Information Technology Co., Ltd.) was used to statistically analyze the data. GraphPad Prism 6 was used to draw all the figures in this study. Chi-square tests were used for the comparisons of the count data. The measurement data were represented as the mean ± standard deviation. T tests were applied for the comparisons between the two groups. There was a significant difference when $P<0.05$.

Results

Comparison of the baseline data

There were no significant differences in terms of gender, age, BMI, course of the disease, smoking history, alcoholism history, or occupation distribution between the two groups, so they were comparable ($P>0.05$) (**Table 1**).

Comparison of the therapeutic effects

The numbers of the cured, markedly effective, effective, and ineffective patients in GA were 17, 20, 11, and 2, and the numbers in GB were 25, 14, 2, and 1. The total effective rate in GB was 94.23%, which was significantly higher than the effective rate in GA (74.00%). The difference was statistically significant ($P<0.05$) (**Table 2**).

The pruritus and eczema skin lesion area EASI scores before and after the therapy in both groups

Before the therapy, there was no statistically significant difference between the two groups in terms of their pruritus and skin lesion EASI scores ($P>0.05$). After the therapy, the pruritus and skin lesion EASI scores in GB were significantly lower than they were in GA, and the difference was statistically significant ($P<0.05$, **Figure 1**).

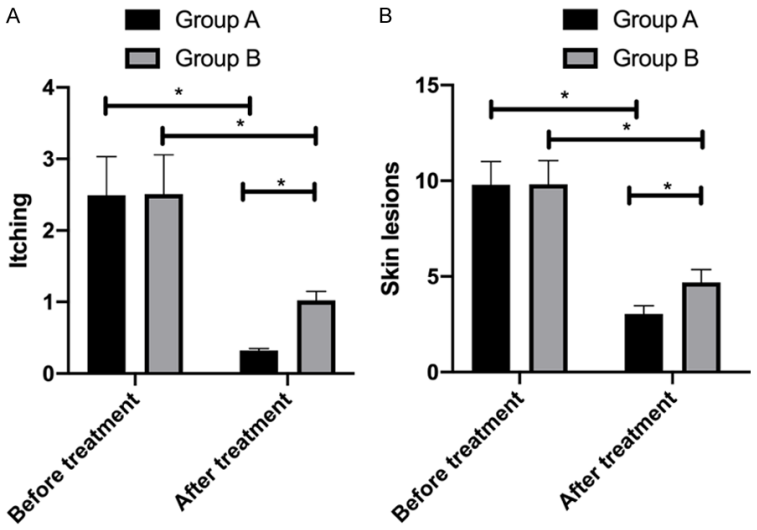

Figure 1. The pruritus and eczema skin lesion area EASI scores before and after the therapy in both groups; A: The pruritus scores, B: The skin lesion area scores. *P<0.05.

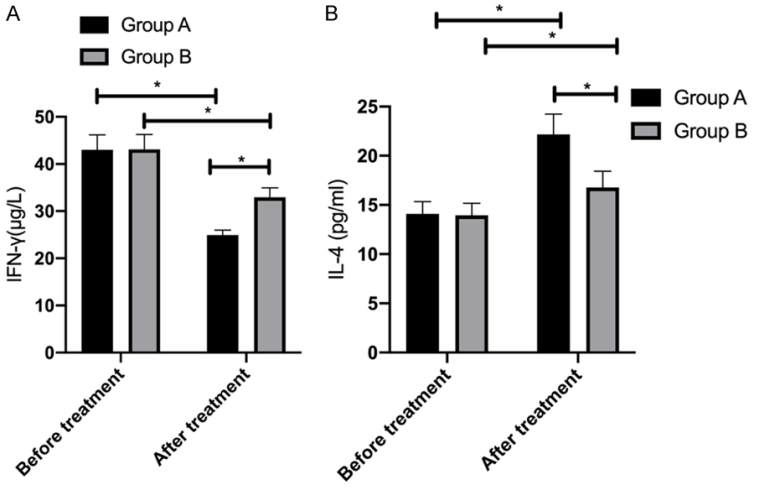

Figure 2. The serum IFN-γ and IL-4 levels before and after the therapy in both groups. A: The IFN-γ expression. B: The IL-4 expression. *P<0.05.

The serum IFN-γ and IL-4 levels before and after the therapy in both groups

There were no statistically significant differences in the serum IFN-γ and IL-4 levels between the two groups before the therapy (P>0.05). After the therapy, the serum IFN-γ levels were lower, and the IL-4 levels were enhanced in both groups. The difference was statistically significant compared with the pre-therapy levels (P<0.05). However, the serum IFN-γ in GA was lower than it was in GB, and the IL-4 level was higher than it was in GB. The difference was statistically significant (P<0.05) (**Figure 2**).

The adverse reactions

After the therapy, the numbers of patients with erythema, rhagades, keratosis, and pruritus in GA were 2, 1, 1, and 1, and the incidence of adverse reactions was 10.00%. The numbers of patients with erythema, rhagades, keratosis, and pruritus in GB were 1, 2, 2, and 1, and the incidence of adverse reactions was 11.54%. There was no significant difference in the incidences of adverse reactions between the two groups (P<0.05) (**Table 3**).

Comparison of recurrence rates between the two groups within 3 months after the therapy

At the 3 month follow up, there were 9 patients with recurrences in GA, for a recurrence rate of 18.00%. In GB, there was 1 patient with a recurrence, for a recurrence rate of 1.92%. The recurrence rate of the patients in GB was significantly lower than the recurrence rate in GA, and the difference was statistically significant (P<0.05) (**Table 4**).

Evaluation of the quality of life in both groups after the therapy

The physiological function, social function, emotional function, and physical function scores in GB were significantly higher than they were in GA, so the quality of life of the patients in GB was higher than it was in GA. The difference was statistically significant (P<0.05) (**Table 5**).

Discussion

With the development of society and the extensive use of toiletries in various groups, the incidence of hand eczema is gradually increasing at present [13]. For now, studies have found

Table 3. Comparison of the incidences of adverse reactions between the two groups [n, (%)]

Adverse reaction	GA (n=50)	GB (n=52)	χ^2	P
Erythema	2 (4.00)	1 (1.92)	-	-
Rhagades	1 (2.00)	2 (3.85)	-	-
Keratosis	1 (2.00)	2 (3.85)	-	-
Pruritus	1 (2.00)	1 (1.92)	-	-
Incidences of adverse reactions	5 (10.00)	6 (11.54)	0.063	0.802

Table 4. Comparison of the recurrence rates between the two groups at one year after the therapy

Items	GA (n=50)	GB (n=52)	χ^2	P
Number of relapses	8	1	-	-
Recurrence rate	18.00%	1.92%	2.506	0.012

Table 5. Comparison of the quality of life between the two groups

Items	GA (n=50)	GB (n=52)	t	P
Physiological function	15.23±1.21	10.38±1.21	20.24	<0.001
Social function	14.96±1.28	11.22±1.18	15.35	<0.001
Emotional function	15.06±2.14	11.27±1.24	11.00	<0.001
Physical function	14.85±1.22	10.23±1.19	19.36	<0.001

that the incidence of hand eczema is closely tied to allergic reactions and immune dysfunction caused by microbial infections such as bacteria and fungi [14]. In recent years, NB-UVB irradiation, the main method for treating hand pruritus, can strengthen the skin's barrier function, induce skin keratin to produce interleukin, suppress its cellular immune response, regulate the inflammatory response, and repair skin lesions [15]. However, the treatment still has some limitations, and its targeting, accuracy, and onset speed are insufficient. Therefore, its combined medication scheme has been investigated in this study [16].

In our research, the curative effects of NB-UVB alone and in its combination with compound clobetasol propionate ointment in hand eczema patients were compared. The results revealed that NB-UVB combined with compound clobetasol propionate ointment had a higher curative effect than NB-UVB alone, and the pruritus and eczema skin lesion area EASI scores after the treatment were improved more significantly than the scores of the patients treated with NB-UVB alone. Compound clobetasol propionate ointment contains 0.05% clobetasol propionate and 0.025% all-trans retinoic acid, and it has anti-inflammatory, anti-allergic, vasoconstrictive, and antiproliferative effects [17]. In the past, some studies [18] have pointed out that even if compound clobetasol propionate ointment is used alone in the treatment of eczema, it can also have a better curative effect. Current studies on dermatopathology and immunology [19, 20] have shown that eczematous skin lesion tissues are often accompanied by an infiltration of cytokines, eosinophils, and mast cells. Therefore, the lesions may be mainly type IV delayed allergic reactions, in which cell immunity mediated by T lymphocytes plays a vital role. Resting CD4+ T cells in the human body can differentiate into Th1 and Th2 subtypes under the stimulation of some antigens, and IFN-γ and IL-4 are important components of the Th1 and Th2 subtypes respectively [21]. Earlier studies [22, 23] have shown that the imbalance of Th1/Th2 cytokine interactions are bound up with the severity and duration of eczema. IFN-γ in the peripheral blood of eczema patients is significantly higher than it is in normal subjects, but the Th2 subtype cytokines, such as IL-4, are lower than they are in normal subjects, indicating that the function of the Th1 cell subsets in eczema patients is hyperfunction, but the function of the Th2 subsets is decreased. Therefore, serum IFN-γ and IL-4 were selected as indexes to evaluate the Th1 and Th2 subtypes respectively in this research. The results revealed that the serum IFN-γ levels were lower and the IL-4 levels were increased in both groups after the treatment, but the patients in GB were more significantly improved than the patients in GA. Some studies [24] have found that NB-UVB can reduce the number of infiltrating CD4+ cells in skin lesions and inhibit the activity of Th1 subtype cytokines. At the same time, the antigen presentation of Langerhans cells and the function of activating T cells are suppressed, thus inhibiting Th1-mediated delayed hypersensitivity and contact hypersensitivity.

Our research revealed that compound clobetasol propionate ointment combined with NB-UVB can play a synergistic role, speed up the onset of action, and enhance the therapeutic effect.

Then, the adverse reactions, the recurrence rates at three months, and the quality of life improvements were also compared between the two groups to analyze the safety of the combined treatment scheme and its influence on patient prognosis. The results indicated that there were few adverse reactions between the two groups, and there was no significant difference suggesting that the combined treatment scheme was safer, and it would not increase the risk of side effects while improving the treatment efficacy. In the past, some studies [25] discovered that compound clobetasol propionate is not only effective at treating hand eczema, but it is also safe and reliable, which is consistent with our observation results. Next, the prognosis was analyzed, and it was found that the recurrence rate of the patients in GB was significantly lower than it was in GA at three months, and the improvement in the quality of life was significantly better than it was in GA, indicating that the combined treatment of NB-UVB and compound clobetasol propionate ointment can not only effectively improve the curative effect, but it can also significantly ameliorate patient prognosis and reduce the recurrence rate.

To sum up, NB-UVB combined with compound clobetasol propionate ointment has a high clinical total effectiveness rate and significantly improves the skin lesions of hand eczema. It can effectively reduce patients' recurrence rates, improve their quality of life, and is very safe, it has a certain guiding significance for the clinical treatment of hand eczema, so it is worthy of clinical application. However, there are also shortcomings in this study. First of all, due to the small size of the study cohort, the conclusions of this study need to be further validated in the future. Second, the precise mechanism that narrow-band UVB combined with clobetasol propionate uses to treat hand eczema has not been elaborated in detail, but we will further explore and elaborate the deficiencies in our follow-up studies.

Disclosure of conflict of interest

None.

Address correspondence to: Linfeng Li, Department of Dermatology, Beijing Friendship Hospital Affiliated to Capital Medical University, No. 95, Yong'an Road, Xicheng District, Beijing 100050, China. Tel: +86-010-63016616; E-mail: lilinfeng_yy@126.com

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