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Original Research Article

Efficacy of H1 receptor antagonist plus pregabalin capsules in skin pruritus: A controlled study

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Abstract

Purpose: *To determine the effectiveness of histamine H1 receptor antagonist combined with pregabalin capsules in the treatment of skin pruritus.*
Methods: *From June 2018 to June 2019, 90 patients who presented pruritus in the Second Hospital of Shandong University were recruited and randomized into control and study groups. The control group was treated topically with conventional drug (umiconazole ointment), while the study group was treated with the combination of histamine and H1 receptor antagonist and pregabalin capsules. Clinical efficacy for the two groups was assessed.*
Results: *The study group obtained clinical efficiency than the control group ($p < 0.05$); No significant difference was found in the degree of pruritus between the two groups before treatment and 12 h after treatment ($p > 0.05$). At 48 and 72 h after treatment, the two groups showed significant differences in the degree of pruritus ($p < 0.05$). The study group had a significantly lower Pittsburgh Sleep Quality Index (PSQI) score after treatment when compared to the control group ($p < 0.001$). A lower incidence of adverse reactions was observed in the study group in contrast to the control group ($p < 0.05$). The level of parathyroid hormone (PTH) of the study group was significantly lower than that of the control group ($p < 0.001$).*
Conclusion: *The combined use of Histamine H1 receptor antagonist with pregabalin capsule effectively alleviates the degree of pruritus, ensures good sleep quality, and lowers the incidence of adverse reactions.*

Keywords: *Histamine H1 receptor antagonist, Pregabalin capsule, Skin pruritus, Parathyroid hormone, Sleep quality*

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INTRODUCTION

Pruritus is a common skin disease with complicated etiology. The disease is reported to be associated with drug stimulation, living habits, environmental factors, systemic diseases, and neuropsychological factors [1-3]. The clinical manifestations are generalized itching and localized itching. Delayed treatment may result in blood scabs, pigmentation, and in severe cases, pyoderma, lichenoid degeneration, eczema-like

degeneration, and lymphadenitis, which compromises the quality of life of patients [4,5].

External application of ointment is the primary option for the clinical treatment, which, however, fails to achieve a radical cure, with a predisposition to relapse. Accordingly, this study is conducted to assess the treatment efficiency of the combined use of histamine H1 receptor antagonist with pregabalin capsules in the treatment of patients with pruritus.

METHODS

Patients

Ninety patients with pruritus presenting to the Dermatology Department in the Second Hospital of Shandong University from June 2018 to June 2019 were recruited after obtaining written informed consent, and equally randomized to control group and study group, with 45 cases in each group. This study was ethically approved by the Ethics Committee of Shandong University (approval no. 2017KY-2945). The protocol followed the Declaration of Helsinki for human studies [6].

Inclusion criteria

Pruritus occurred at least 3 days in an average of 2 weeks, and several times on the day of onset, lasting more than several minutes each time. Patients aged from 18 to 80 years with no gender limitation. Patients participate voluntarily and signed an informed consent form.

Exclusion criteria

Patients had systemic coagulation abnormalities. Patients had Mental disorders and cognitive impairment and were unable to cooperate with the study. Patients had allergies to the drugs that used in this study. Patients experienced skin itching due to other skin diseases.

Treatments

The control group was treated with conventional drugs. Urea miconazole ointment was applied topically to the itching area of the patients in the control group (Guizhou Jinqiao Pharmaceutical Co., Ltd.; SFDA approval no. H52020589; specification: 30 ml + 5 g * 2 pieces/box), once to twice daily for 3 weeks.

On the other hand, the study group was treated with histamine H1 receptor antagonist combined with pregabalin capsules. Histamine H1 receptor antagonist drug was administered. The epinastine hydrochloride capsules (manufacturer: Chongqing Yaoyou Pharmaceutical Co. Ltd; SFDA approval number H20130054; specification: 10 mg * 10 capsules) was orally administered once daily. Additionally, the study group was given 75 - 150 mg pregabalin capsules (Pfizer Pharmaceutical Co. Ltd; SFDA approval no. J20160022; specification: 150 mg * 8 capsules/box), twice daily, for 3 weeks.

Evaluation of clinical indices

Incidence of adverse events

The incidence of adverse events in the two groups of patients, including drowsiness, dizziness, nausea, and constipation were assessed.

Treatment efficacy

Treatment efficacy in the two groups was divided into three categories, namely, markedly effective, effective, and ineffective. If the clinical symptoms disappeared and no recurrence was observed in a short period of time, it was considered markedly effective. If the clinical symptoms improved, with occasional recurrence in a short time, it was considered effective. If the clinical symptoms showed no improvement or were aggravated, it was considered ineffective.

Degree of pruritus

The visual analogue scale (VAS) [7] was used to evaluate the degree of pruritus after treatment, with a total score of 10 points. The lower the score, the lower the milder the pruritus. T0, T1, T2, and T3 indicated before treatment, 12 h after treatment, 24 h after treatment, and 72 h after treatment, respectively. The degree of pruritus of the two groups at different time points were compared.

Sleep quality

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) [8] before and after treatment, with a total score of 15 points. The score is inversely proportional to the sleep quality.

Endocrine hormone

The serum level of Parathyroid hormone (PTH) of the two groups was compared. 3 mL of fasting venous blood was collected before and after the treatment and centrifuged to obtained the supernatant and stored in a refrigerator for the determination of PTH level using an Enzyme-

linked immunosorbent assay (ELISA). The PTH ELISA kit was purchased from Merck Chemical Technology (Shanghai) Co., Ltd., and the operation was strictly in accordance with the kit instructions.

Statistical analysis

Statistical analysis was done using the statistical package, SPSS 20.0, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to map the graphics. Measurement data were expressed as mean ± standard error and analyzed using normality test and t - test, and the count data were expressed as frequency with percentage and analyzed using the chi-square test. $p < 0.05$ indicates a significant difference.

RESULTS

Patient profile

The two groups showed no significant differences in terms of general data including gender, age, BMI, pathological type, smoking, drinking, and place of residence between the two groups did not reach statistical significance ($p > 0.05$)., as outlined in Table 1.

Adverse reactions

More cases with adverse reactions were observed in the control group than in the study group ($p < 0.05$), as shown in Table 2.

Treatment efficacy

The markedly effective rate of the study group was 60.00 % (27/45), the effective rate was 35.56 % (16/45), the ineffective rate was 4.44 % (2/45), and the total effective rate was 95.56 % (43/45). In the control group, the markedly effective rate was 44.44 % (20/45), the effective rate was 28.89 % (13/45), the ineffective rate was 26.67 % (12/45), and the total effective rate was 73.33 % (33/45). There was a significant difference in the treatment efficiency between the two groups of patients after treatment ($\chi 2 = 8.458$, $p = 0.004$),as presented in Table 3.

Table 1: Comparison of general information between the two groups of patients [n (%)]

Variable	Control group(n=45)	Study group(n=45)	χ^2/t	*P*-value
Gender			0.045	0.832
Male	26 (57.78)	25 (55.56)		
Female	19 (42.22)	20 (44.44)		
Age (years)	55.12±3.7	54.28±3.1	1.167	0.246
BMI (kg/m^2)	24.88±1.65	25.07±1.59	0.556	0.579
Pathological type			0.189	0.664
Pruritus universalis	16(35.56)	18(40.00)		
Pruritus localis	29(64.44)	27(60.00)		
Smoking			0.194	0.660
Yes	30(66.67)	28(62.22)		
No	15(33.33)	17(37.78)		
Drinking			0.420	0.517
Yes	29(64.44)	26(57.78)		
No	16(35.56)	19(42.22)		
Residence			0.050	0.822
Urban area	31(68.89)	30(66.67)		
Rural area	14(31.11)	15(33.33)		

Table 2: Comparison of adverse reaction rates (%, n)

Group	n	Drowsiness	Dizziness	Nausea	Constipation	Total incidence
Study group	45	1	0	1	0	2 (4.44%)
Control group	45	2	3	2	2	9 (20.00%)
χ^2						5.074
P-value						< 0.05

Table 3: Comparison of treatment efficacy

Group	n	Markedly effective	Effective	Ineffective	Total efficiency
Study group	45	27	16	2	43 (95.56%)
Control group	45	20	13	12	33 (73.33%)
χ^2					8.458
P -value					0.004

Degree of pruritus

The degree of pruritus at T0, T1, T2, and T3 in the study group was (8.89 ± 1.09), (7.83 ± 0.18), (5.21 ± 0.13), and (2.1 ± 0.6) points, respectively. The pruritus degree of the control group at T0, T1, T2, and T3 were (8.79 ± 1.11), (8.02 ± 0.56), (7.55 ± 0.31), (4.3 ± 0.6) points, respectively. No significant difference was observed in the pruritus degree before treatment and 12 h after treatment between the two groups ($p > 0.05$). A significant reduction in the degree of skin pruritus in the study group was observed in contrast to that in the control group at 48 and 72 h after treatment ($p < 0.05$), as shown in Figure 1.

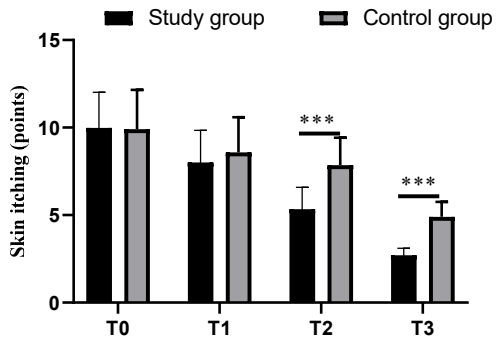

Figure 1: Comparison of pruritus scores between the two groups (***p < 0.001)

PSQI scores

Figure 2 displays the data comparing PSQI scores for the two groups before and after treatment. The PSQI scores of the study group before treatment and after intervention were (14.22 ± 0.67) points and (4.23 ± 0.88) points, respectively. The PSQI scores of the control group before treatment and after intervention were (14.17 ± 0.75) points and (5.27 ± 1.05) points, respectively. Results showed a significant reduction of the PSQI score in both groups after treatment, with lower results obtained in the study group than the control group ($p < 0.05$).

Serum level of PTH

The serum levels of PTH of the study group before treatment and after intervention were (349.55 ± 52.83) ng / L and (110.28 ± 7.08) ng / L, respectively. The serum levels of PTH of the control group before treatment and after intervention were (351.22 ± 52.33) ng / L and (215.64 ± 16.93) ng / L, respectively. Figure 3 presents the PTH scores, revealing a significant decrease in the PTH score in the two groups after treatment, with a lower outcome observed in the study group than the control group *(p* < 0.05).

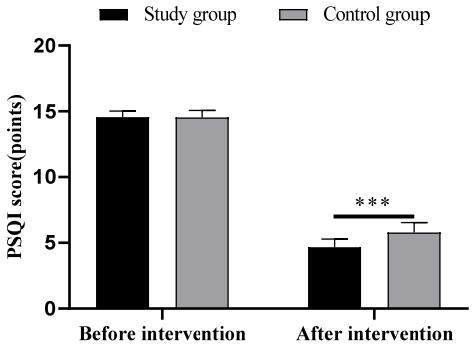

Figure 2: Comparison of PSQI scores between the two groups (***P < 0.001)

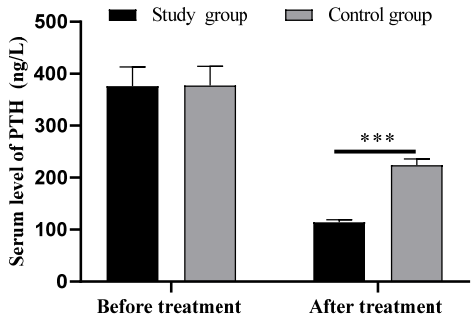

Figure 3: Comparison of the serum level of PTH. (***P<0.001)

DISCUSSION

Pruritus is a common skin disease, and its pathogenesis still remains elusive [9,10]. Its occurrence is mainly related to environmental factors such as temperature changes and irritants, and diseases such as dry skin, neurological dysfunction, endocrine disorders, drugs, allergies, and parasitic infections. Drugs are the mainstay for the treatment of pruritus and

are divided into two types, namely, external use and oral administration, according to different medication methods [11].

Pregabalin is a commonly used for the treatment of pruritus, which can effectively relieve symptoms of patients. Nevertheless, it may give rise to adverse reactions such as rashes and blisters, which prolongs the treatment cycle and compromises the quality of life of patients [12]. H1 histamine receptor antagonists play an anti-allergic role in preventing histamine from acting on target cells and preventing and antagonizing H1 receptors through reversible competition with histamine receptor sites on cells [13,14].

The present study has demonstrated that the clinical symptoms of patients after using Epinastine hydrochloride capsules have been significantly alleviated, with a high safety profile. In addition, pregabalin capsules effectively alleviated the symptoms of pruritus in patients by regulating the neuronal signal transmission [15]. It was also found that histamine H1 receptor antagonist combined with pregabalin capsules has a positive therapeutic effect on patients with itchy skin, and reduces the occurrence of adverse reactions [16]. Herein, the combined use of H1 receptor antagonist with pregabalin capsules yielded a better treatment efficiency than conventional treatment.

Moreover, the combination treatment protocol in this study had a lower incidence of adverse reaction when compared with the conventional treatment method, which was similar to the research results of Mansikka *et al* [17]. In their study, compared with the control group, the study group gained a better outcome in terms of total clinical efficiency (97.52 % vs 71.11 %) and the incidence of adverse reaction rate (7.73 % vs. 15.33 %), which indicated the promising treatment efficiency of the combined use of histamine H1 receptor antagonist combined with pregabalin capsule therapy.

CONCLUSION

The application of histamine H1 receptor antagonist combined with pregabalin capsules in the treatment of patients with pruritus improves the clinical status of patients, alleviates the degree of pruritus, and improves sleep quality. Thus, histamine H1 receptor antagonist combined with pregabalin capsules is a suitable treatment strategy for the management of skin pruritus.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We 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 the authors. Lingxi Li conceptualized and designed the experiments. Lingxi Li conducted the literature search and experiments and wrote the first draft of the manuscript. Lingxi Li performed the statistical analysis and edited the manuscript.

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