

# Comparative study of the effectiveness of antihistamine preparations in the treatment of patients with atopic dermatitis

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## Key words:

antihistamines, atopic dermatitis, treatment.

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**The objective** of the study – to determine the comparative effectiveness of I-generation antihistamines and active metabolites of II-generation in treatment of patients with atopic dermatitis.

**Materials and methods.** The study included 40 patients with atopic dermatitis. SCORAD scale was used for the assessment of the disease severity and Ukrainian translation of the Dermatology Life Quality Index – for the quality of life assessment. Patients were randomized into two groups that received I generation antihistamines and active metabolites of the II generation. Student's criterion or Wilcoxon criterion was used for statistical analyses. Normality of data distribution was verified using Shapiro–Wilk criterion.

**Results.** A high  $\Delta$ SCORAD (%) was observed in patients, who used I generation antihistamines. The significantly higher DLQI was in the group which used active metabolites of the II generation.  $\Delta$ DLQI (%) was significantly lower in patients from the comparison group compared with individuals from the main group. Significant differences in neuroticism and state anxiety were obtained in patients from main and comparative groups with lower values in patients taking I generation antihistamines. In the group of patients before the start of treatment, the state of subdepression was noted, and in those of the main group there were no depressive symptoms at the end of the course of therapy.

**Conclusions.** First-generation antihistamines are more effective in the treatment of atopic dermatitis compared to the active metabolites of second-generation, as evidenced by significant differences in SCORAD,  $\Delta$ SCORAD (%), the severity of pruritus between groups of patients after completion of treatment. I-generation antihistamines indirectly have a positive effect on the quality of life, anxiety, depression and neuroticism, which explains the need for their priority choice in the treatment of atopic dermatitis.

## Ключові слова:

антигістаміни, atopічний дерматит, лікування.

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## Порівняльне дослідження ефективності антигістамінних препаратів у лікуванні хворих на atopічний дерматит

Н. Ю. Резніченко

**Мета роботи** – визначення порівняльної ефективності антигістамінних препаратів I покоління та активних метаболітів препаратів II покоління в лікуванні хворих на atopічний дерматит.

**Матеріали та методи.** У дослідження включили 40 осіб, які хворі на atopічний дерматит. Шкалу SCORAD використовували для оцінювання тяжкості захворювання. Якість життя оцінювали відповідно до українського перекладу Dermatology Life Quality Index. Хворі на atopічний дерматит рандомізовані у 2 терапевтичні групи, які отримували антигістамінні препарати I покоління або активні метаболіти препаратів II покоління. Критерій Стьюдента або критерій Вілкокса використовували для статистичного аналізу залежно від нормальності розподілу. Нормальність розподілу даних визначали за критерієм Шапіро–Уїлка.

**Результати.** Високий показник  $\Delta$  SCORAD (%) визначили у хворих, які отримували антигістамінні препарати I покоління. Вірогідно вищим індекс DLQI був у групі осіб після застосування активних метаболітів антигістамінних препаратів II покоління. Встановили, що показник  $\Delta$ DLQI (%) був вірогідно нижчим у пацієнтів із групи порівняння щодо осіб з основної групи. Між основною та порівняльною групами пацієнтів встановили вірогідну різницю за рівнями невротизації та ситуативної тривожності з меншими значеннями в осіб, які отримували антигістамінні препарати I покоління. У групі пацієнтів до початку лікування відзначали стан субдепресії згідно з інтегральним показником за шкалою Бека, а в осіб основної групи після завершення курсу терапії не спостерігали депресивні симптоми.

**Висновки.** Антигістамінні препарати I покоління є ефективнішими в лікуванні atopічного дерматиту порівняно з активними метаболітами препаратів II покоління, що підтверджується статистично вірогідною різницею в бальній оцінці за шкалою SCORAD,  $\Delta$ SCORAD (%), у вираженості свербіжів та його об'єктивної ознаки – екскоріацій – між групами пацієнтів після завершення курсу лікування. Антигістамінні препарати I покоління опосередковано чинять позитивний ефект щодо якості життя, рівнів тривожності, депресії та невротизації пацієнтів, що пояснює необхідність їх пріоритетного вибору під час лікування atopічного дерматиту.

## Ключевые слова:

антигистамины, atopический дерматит, лечение.

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## Сравнительное исследование эффективности антигистаминных препаратов в лечении больных atopическим дерматитом

Н. Ю. Резніченко

**Цель работы** – определение сравнительной эффективности антигистаминных препаратов I поколения и активных метаболитов препаратов II поколения в лечении больных atopическим дерматитом.

**Материалы и методы.** В исследование включили 40 больных atopическим дерматитом. Шкалу SCORAD использовали для оценки тяжести заболевания. Качество жизни оценивали соответственно украинскому переводу Dermatology Life Quality Index. Больные atopическим дерматитом рандомизированы в 2 терапевтические группы, которые получали антигиста-

минные препараты I поколения либо активные метаболиты препаратов II поколения. Критерий Стьюдента или критерий Уилкоксона использовали для статистического анализа в зависимости от нормальности распределения. Нормальность распределения данных определяли по критерию Шапиро–Уилка.

**Результаты.** Высокий показатель  $\Delta$ SCORAD (%) отмечен у больных, принимавших антигистаминные препараты I поколения. Достоверно более высоким индекс DLQI был в группе лиц после применения активных метаболитов препаратов II поколения. Установлено, что показатель  $\Delta$ DLQI (%) достоверно ниже у пациентов из группы сравнения по сравнению с лицами из основной группы. Между основной и сравнительной группами пациентов получены достоверные различия по уровням невротизации и ситуативной тревожности с меньшими значениями у лиц, принимавших антигистаминные препараты I поколения. В группе пациентов до начала лечения отмечено состояние субдепрессии согласно интегрального показателя по шкале Бека, а у лиц основной группы по завершению курса терапии не установлены депрессивные симптомы.

**Выводы.** Антигистаминные препараты I поколения более эффективны в лечении atopического дерматита по сравнению с активными метаболитами препаратов II поколения, что подтверждается статистически достоверными различиями в балльной оценке по шкале SCORAD,  $\Delta$ SCORAD (%), выраженности зуда и его объективного признака – экскориаций – между группами пациентов после завершения курса лечения. Антигистаминные препараты I поколения опосредовано оказывают положительный эффект относительно качества жизни, уровней тревожности, депрессии и невротизации пациентов, что объясняет необходимость их приоритетного выбора в лечении atopического дерматита.

## Introduction

Atopic dermatitis is considered to be one of the main dermatoses, in the occurrence and development of which allergic component is the leading one [1–3]. The study of the etiology, pathogenesis and clinical features of atopic dermatitis, as well as the grounded choice of its optimal treatment, are extremely urgent problems of modern medicine [4–6]. The problem is associated with a high incidence of the disease, a constantly recurrent course, an increase in the number of trigger factors, an insufficient effectiveness of standard therapy, and the need for complex treatment with the recommendations of doctors of various specialties [1,5,7].

The main tasks of therapeutic and preventive measures for atopic dermatitis are: elimination or reduction of itching and inflammatory changes in the skin; prevention of the development of severe forms of the disease, which lead to a decrease in the quality of life [8,9].

Treatment for atopic dermatitis includes the mandatory use of antihistamines, which block the H1-histamine receptors, prevent the development of the main effects of histamine and thus eliminate the main clinical manifestations of atopic dermatitis. Modern medicine has a wide range of antihistamines, represented by three generations. Each of the generations of antihistamines has certain advantages and disadvantages. For example, first-generation antihistamines can penetrate the blood-brain barrier and bind to the brain's H1 receptors, have sedative and hypnotic effects. In addition, first-generation antihistamine drugs have an M-anticholinergic effect. Antihistamines of II generation practically do not possess anticholinergic properties and almost no adverse effects on the central nervous system. However, their use in medical practice is limited due to the possibility of extending the QT interval. Active metabolites of II-generation antihistamines have no cardiotoxic and sedative effect. In spite of the safety of their use in clinical efficacy, active metabolites of II-generation antihistamines are often inferior to the preceding ones. First of all it concerns antipruritic action.

Recently, there have been discussions in medicine about the most effective antihistamines for the treatment of atopic dermatitis. This is due to the fact that in adulthood, exacerbations of atopic dermatitis are potentiated by stress and constant emotional violations, which suggests the need for the introduction of a sedative effect into a therapeutic course [10–12]. The availability of debatable data in the literature on the effectiveness of certain antihistamines use

in the treatment of allergic diseases [12–14], indicates the need for additional clinical studies.

## Objective

The objective of the study was to determine the comparative efficacy of I-generation antihistamine preparations and active metabolites of II-generation antihistamines in the treatment of patients with atopic dermatitis.

## Materials and methods

The study was conducted at the clinical base of the Community Institution “Zaporizhzhia Regional Dermatovenerologic Clinical Dispensary” of Zaporizhzhia Regional Council. Under our supervision, there were 40 patients with atopic dermatitis aged 18 years and older, including 21 female patients and 19 male patients. All patients signed informed consent form for participation in clinical study.

The study did not include patients with the presence of other skin diseases, severe diseases of the cardiovascular system, gastrointestinal tract, diabetes mellitus, liver and kidney failure, mental disorders, as well as other serious diseases. In addition, the study did not include patients whose work required a quick physical or mental reaction (driving vehicles, etc.).

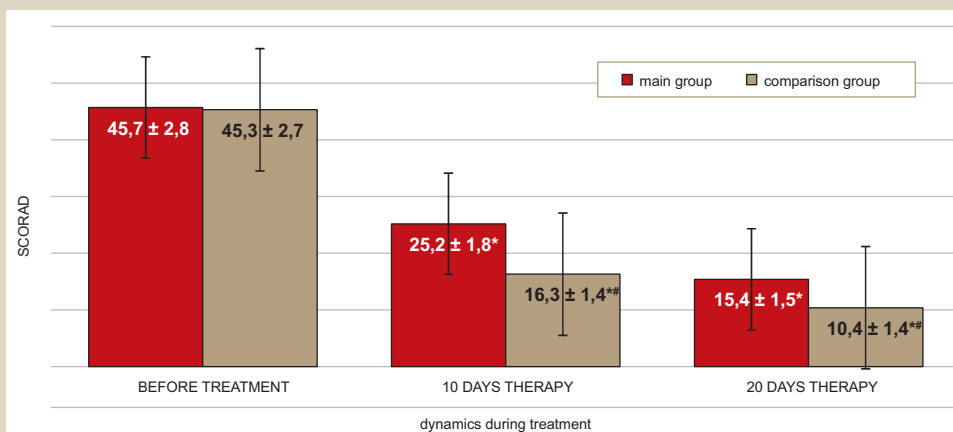
Patients were monitored for 20 days.

Patients with atopic dermatitis were randomized (1:1) into two therapeutic groups, identical in age, sex, stage and prevalence of the pathological process: 1) the main group (20 people), who received oral treatment with an antihistamine drug of I generation; 2) the comparison group (20 people), who received active metabolites of II-generation antihistamines.

As an accompanying treatment, only emollients were allowed if they were used in a stable dose for at least 1 month prior to the start of the study.

The effectiveness of the treatment of patients with atopic dermatitis was assessed according to the following criteria: the severity of atopic dermatitis, the severity of itching and the assessment of its objective signs, the assessment of the quality of life of patients and changes in their psychological state.

The severity of the disease was determined by the Scoring of Atopic Dermatitis (SCORAD). To determine the effec-



**Fig. 1.** The dynamics of the point score on the SCORAD scale in patients with atopic dermatitis during treatment

\*: significant differences ( $P < 0.05$ ) when compared with the corresponding indicators in the group of patients before treatment;  
#: significant differences ( $P < 0.05$ ) when compared with the corresponding indicators in the group of patients taking active metabolites of II-generation antihistamines.

tiveness in the treatment process, the percentage change in the SCORAD index ( $\Delta$ SCORAD, %) was calculated.

The severity of itching was studied separately on a ten-point numerical rating scale, in which 0 points was the complete absence of itching, and 10 points was its maximum intensity. The assessment of objective signs of itching, such as changes in the nail plates and excoriations, was carried out according to the method of I. A. Babiuk et al. (2009). Each of the objective signs of itching was assessed on a point scale, in which 0 points was the absence of a sign, 1 point was its weak degree, 2 points was moderate degree, 3 points was significant degree.

The quality of life of patients was assessed according to an authorized Ukrainian translation of the Dermatology Life Quality Index (DLQI) [15]. To assess the effectiveness of treatment, the percentage change in the DLQI index ( $\Delta$  DLQI, %) and the percentage of patients whose DLQI index at the end of the treatment was less than 5 points (DLQI <5,0 %) were determined.

Changes in the psychological state of patients were assessed using a card questionnaire: 1) the level of anxiety – according to the Spielberger–Hanin self-assessment scale; 2) the level of neuroticism – according to the methods of diagnostics by L. I. Wasserman; 3) the level of depression – according to the questionnaire “Beck scale for self-assessment of the severity of depression”.

Clinical assessment of the skin condition, evaluation using the SCORAD system, severity of pruritus on a 10-point scale, as well as physical examination of patients were performed prior to treatment, 10 and 20 days from the start of therapy. Objective signs of itching were evaluated before and after treatment. Questionnaires for quality of life, anxiety, neuroticism and depression were filled with patients before and after treatment.

Statistical processing of the results was carried out using the software package Statistica for Windows 13 (StatSoft Inc., № JPZ804I382130ARCN10-J). In order to compare the indicators in different groups, the double criterion of the Student with the calculation of the arithmetic mean (M) and the standard error of the arithmetic mean (m) or the Wilcoxon sign criterion, depending on the normality of distribution, was applied. Normality of data distribution was verified using the Shapiro–Wilk criterion at the significance level of 0.01. In applying all statistical methods, besides the criterion of Shapiro–Wilk, the significance level was

taken to be 0.05 – the difference between the data was considered reliable at  $P < 0.05$ . Determination of the required volume of the sample population (n) was carried out according to the formulas of P. F. Rokitsky (1973):  $n = t^2\sigma^2/\Delta^2$  – with quantitative variation;  $n = t^2 [P(1-P)/\Delta^2]$  – with an alternative variation, where  $\Delta$  – accuracy, P – the proportion of individuals with a certain quantitative sign.

## Results

In both therapeutic groups, an improvement in the clinical picture of the disease was observed in the treatment course, which was manifested by a significant decrease in the SCORAD score compared to the group of individuals before treatment (Fig. 1). On the 10th and 20th day of treatment, SCORAD scores were significantly lower in patients with atopic dermatitis who received I-generation antihistamines as compared to the group of people taking active metabolites of II-generation antihistamines.

Significant differences were obtained in  $\Delta$  SCORAD (%) on the 10th ( $46.1 \pm 3.2$  in the main group and  $66.1 \pm 4.1\%$  in the comparison group) and on the 20th day of treatment ( $63.2 \pm 2.6$  in the main group and  $76.8 \pm 3.7\%$  in the comparison group) between the main and comparative groups of patients. Significantly higher  $\Delta$  SCORAD (%) was established in patients from the main group, which indicated a higher efficiency of I-generation antihistamine drugs regarding the regression of the clinical manifestations of atopic dermatitis (erythema, edema, papules, weeping, crusts, excoriations, lichenification and dryness). In addition, a low score on the SCORAD scale in patients from the main group indicated a reduction in the area of lesions as a result of the use of I-generation antihistamine preparations, as well as their greater efficacy regarding pruritus and sleep disorders, compared to active metabolites of II-generation antihistamines. Regardless of the therapeutic group, in patients with atopic dermatitis, a decrease in pruritus and its objective signs (primarily excoriation) was observed in the dynamics of treatment (Table 1). Significant differences were obtained in the point assessment of itching and the severity of excoriation between the group of patients before the start of treatment and after its completion in both therapeutic groups. However, after 10 days of antihistamines use, the score for itching in patients from the main group was 1.6 times lower than in the comparison group.

**Table 1.** Itching of the skin and its objective signs severity during the treatment of patients with atopic dermatitis

Indicators, units	Groups of patients with atopic dermatitis:					
	Before treatment		10 days from the start of the therapy		20 days from the start of the therapy	
	Main group, n = 20	Comparison group, n = 20	Main group, n = 20	Comparison group, n = 20	Main group, n = 20	Comparison group, n = 20
Score itching on a 10-point scale, points (M ± m)	6.60 ± 0.52	6.40 ± 0.46	2.90 ± 0.31*	4.50 ± 0.41*#	1.30 ± 0.28*	2.20 ± 0.31*#
Evaluation of excoriation, scores (M ± m)	1.80 ± 0.11	1.70 ± 0.09	–	–	0.40 ± 0.06*	0.70 ± 0.07*#
Evaluation of the severity of changes in the nail plates, points (M ± m)	0.60 ± 0.08	0.60 ± 0.09	–	–	0.60 ± 0.07	0.50 ± 0.08

\*: significant differences (P < 0.05) when compared with the corresponding indicators in the group of patients before treatment; #: significant differences (P < 0.05) when compared with the corresponding indicators in the group of patients taking active metabolites of II-generation antihistamines.

**Table 2.** Dynamics of the DLQI index, levels of anxiety, neuroticism and depression in patients with atopic dermatitis during treatment

Indicators, units	Groups of patients with atopic dermatitis:			
	Before treatment		20 days from the start of the therapy, main group, n = 20	20 days from the start of the therapy, comparison group, n = 20
	Main group, n = 20	Comparison group, n = 20		
Index DLQI, points (M ± m)	14.20 ± 1.71	13.80 ± 1.68	4.00 ± 0.48*	6.50 ± 0.79*#
Δ DLQI, % (M ± m)			72.4 ± 5.5	51.5 ± 4.9#
DLQI <5, %			67.0	50.3
The level of state anxiety, points	47.60 ± 0.41	47.40 ± 0.38	43.40 ± 0.33*	45.10 ± 0.29*#
The level of neuroticism, points	13.60 ± 0.53	13.70 ± 0.44	9.80 ± 0.38*	11.50 ± 0.49*#
Depression scores, points	11.40 ± 0.65	11.30 ± 0.71	9.10 ± 0.61	10.10 ± 0.69*

\*: significant differences (P < 0.05) when compared with the corresponding indicators in the group of patients before treatment; #: significant differences (P < 0.05) when compared with the corresponding indicators in the group of patients taking active metabolites of II-generation antihistamines.

On the 20th day of treatment, the intensity of itching in the main group of patients was 1.9 times less than in patients from the comparison group. And although we did not receive statistically reliable data in assessing the severity of all objective signs of itching in patients before and after the treatment, there were significant differences in the point score of excoriation severity. Upon completion of the course of antihistamines, in patients from the main group, the score for the severity of excoriations was 1.8 times lower than in the comparison group.

In patients from both therapeutic groups, upon completion of the course of treatment, a significant decrease in the DLQI index was observed compared to its values before the start of the treatment, which indicated improvement in the quality of life of patients while reducing the clinical manifestations of dermatosis (Table 2). The significantly higher DLQI index was in the group of individuals after the use of active metabolites of II-generation antihistamines. It was also found that the ΔDLQI indicator (%) was significantly lower in patients from the comparison group compared with individuals from the main group. The percentage of patients whose DLQI index was below 5 points was higher in patients after taking I-generation antihistamine drugs, compared with the group of patients who were treated with an active metabolites of II-generation antihistamines. The findings suggest that I-generation antihistamines have higher clinical efficacy, quickly eliminate the symptoms of atopic dermatitis, lead to a significant improvement in the quality of life of patients, which is reflected in a statistically significant decrease in the DLQI index.

The use of I-generation antihistamine drugs eliminated the clinical manifestations of atopic dermatitis and led to a decrease in the levels of depression, neuroticism and state anxiety (Table 2). Between the main and comparative groups of patients, significant differences were obtained in the levels of neuroticism and state anxiety with lower values

in patients, who used I-generation antihistamines. It was indicative that in the group of patients before the start of the treatment, a state of subdepression was noted according to the integral indicator on the Beck's scale, and in those of the main group there were no depressive symptoms at the end of the therapy.

The results of the study show the benefits of I-generation antihistamine drugs in the treatment of patients with atopic dermatitis, which consist both in a rapid clinical effect (elimination of rashes and itching) and indirectly in improving the quality of life of patients, reducing their depression, anxiety and neuroticism.

## Discussion

The high rate of Δ SCORAD (%) in patients who took I-generation antihistamines for 10 days proved their rapid clinical effect, which was reliably inferior to active metabolites of II-generation antihistamines. The data obtained are evidence of a higher antipruritic effect of I-generation antihistamines. The same results were obtained by Y. F. Kutasevych [1] in the conducted clinical trial, which included patients with atopic dermatitis, allergic dermatitis and more rare allergic diseases. According to the study, I-generation antihistamines showed better clinical results in cases of chronic allergic skin diseases, which manifested in rapid rash regression. The antipruritic effect was also better in cases of I-generation antihistamines intake [1].

At the same time, clinical study which was performed by B. G. Kogan [10] showed clinical remission after the use of II-generation antihistamines. On the other hand, the psychological status of patients with allergic skin diseases was not examined in the study and the age group of patients was younger.

Our findings as well as findings of Y. F. Kutasevych [1] suggest that I-generation antihistamines have higher

clinical efficacy, quickly eliminate the symptoms of atopic dermatitis, lead to a significant improvement in the quality of life of patients, which is reflected in a statistically significant decrease in the DLQI index.

Between the main and comparative groups of patients, significant differences were obtained in the levels of neuroticism and state anxiety with lower values in patients, who used I-generation antihistamines. It was indicative that in the group of patients before the start of treatment, a state of subdepression was noted according to the integral indicator on the Becks' scale, and in those of the main group there were no depressive symptoms at the end of the therapy.

The results of the study show the benefits of I-generation antihistamine drugs in the treatment of patients with atopic dermatitis, which consist both in a rapid clinical effect (elimination of rashes and itching) and indirectly in improving the quality of life of patients, reducing their depression, anxiety and neuroticism. The same results according to the changes in the quality of life were obtained by Y. F. Kutasevych [1] in the conducted clinical trial.

According to the obtained data, the main criteria for prescription of I-generation antihistamines are atopic dermatitis combined with increased anxiety, increased neuroticism or depression as well as the presence of moderate-to-severe itching.

## Conclusions

1. I-generation antihistamines are more effective in the treatment of atopic dermatitis compared to III-generation preparations, which is confirmed by statistically significant differences in the SCORAD score and  $\Delta$ SCORAD (%), severity of pruritus and its objective symptom – excoriations between groups of patients after completion of the treatment course.

2. I-generation antihistamines indirectly have a positive effect on the quality of life, levels of anxiety, depression and neuroticism of patients, which explains the need for their priority choice in the treatment of atopic dermatitis.

3. Criteria for prescription of I-generation antihistamines are atopic dermatitis combined with increased anxiety, increased neuroticism or depression as well as the presence of moderate-to-severe itching.

**Prospects for further research.** The obtained results of the conducted study allow further research of different generation antihistamines effect on the course of other dermatological diseases.

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