# The choice of modern antihistamines for the treatment of allergodermathosis of food and drug etiology with regard to possible damage of the hepatobiliary system.

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**Abstract**
The prevalence of major allergic diseases ranges from 6% to 16% of the total population. Second and third generation non-sedative antihistamines have already proven their safety and efficacy and are included in all international recommendations. Nevertheless, the matter of choosing the best medicine always remains open.
A particular problem in the administration of this product groups is the problem of their biotransformation in hepatocytes with the release of several active and inactive metabolites, either of which has its features in the routes and rates of clearance. This is especially important in abnormalities of the liver and biliary tract that often associated with allergic diseases. In this paper, we highlighted the results of an open, non-randomized observational trial of the efficacy and safety of desloratadine (deslor), a domestic drug of the so-called third generation, in the treatment of the typical symptoms of food allergy with manifestations of allergic urticaria.
**Key words:** Allergy; Allergic urticaria; Desloratadine.
The prevalence of allergic diseases in the world is constantly growing [1]. Trial conducted by World Allergy Organization in 2007 showed that the prevalence of allergic rhinitis exceeded 16% in most of the 37 countries involved in the project, and reached 40% in Ukraine. Degree of bronchial asthma incidence for 35 studied countries ranged from 6% to 15% which corresponded to the prevalence of atopic dermatitis studied in 30 countries [2].
Allergy symptoms are nasal congestion; itchy nose; rhinorrhea; burning and eye redness, tearing; pruritus and rash may be extremely consumptive and often cause sleep disturbances, performance degradation and learning, significantly reducing the quality of life [3-7]. An allergic inflammatory response involves a cascade of cellular reactions in which histamine plays a key role. Many of the inflammatory and immunomodulatory effects of histamines are mediated through the H1 receptors [8,9]. Thus, H1 receptor antagonists are often first-line agents for conditions that include allergic inflammation [10,11,12,13].
Second-generation antihistamines for oral administration such as loratadine and cetirizine are prodrugs that converted into a number of active metabolites after hepatic biotransformation processes. In some cases, this may be an obstacle to their safe and effective use especially in food allergies with concomitant damages of the hepatobiliary system.
In recent years, the so-called 3rd generation drugs, which are the selected most active metabolites of loratadine and cetirizine, have become more prevalent. This group includes desloratadine and levocetirizine which can effectively relieve a number of symptoms of allergic rhinitis (rhinorrhea, sneezing/itching), eye symptoms (tearing, itching and redness), as well as manifestations of allergic urticaria (rash, pruritus) with minor hypnotic effect or without it [12]. In addition, these drugs can inhibit the activity of other mediators secreted by mast cells and basophils, thereby reducing nasal congestion and swelling of its mucous membrane [14].
In recent times, the market of Kazakhstan acquired a number of auto-generic drugs (yesterday's brands) and generic drugs from different producing countries. A separate achievement can be considered the deployment of production of domestic antihistamines of the latest generations, for example, Deslor (desloratadine), the effectiveness and safety of which will be discussed in this paper.
Desloratadine is a potent H1 receptors antagonist with no sedation effect with antiallergic and anti-inflammatory properties. *In vitro* studies have shown that desloratadine inhibits chemical mediators involved in both the early and late phases of the allergic response [12]. In addition, desloratadine has been proven to improve nasal breathing in patients with allergic rhinitis [15]. The proven ability of desloratadine to prevent the release of cytokines, chemokines, and adhesins associated with the late phase of the immune response may explain its properties of decongestant [12,16,17,18,19].

The **purpose** of this trial was to assess the safety and efficacy of desloratadine (deslor) in relation to skin allergy symptoms, assess the profile of drug undesirable effects, determine the degree of patient satisfaction in treatment with desloratadine in real conditions.

**Methods**

This observational trial was carried out by the allergologists of the Republican Allergy Center of the Scientific and Research Institute in 2013-2014. Written informed consent was obtained from all subjects. Neither the researchers nor the patients received payment for participation in the trial. The drug was delivered free of charge. Exclusion criteria were: children's age up to 6 years, pregnancy, breast-feeding, or continued administration of other systemic antihistamines or oral corticosteroids.

Deslor was approved in Kazakhstan in 2013, was prescribed exclusively in accordance with the instructions for use.

All patients received deslor in a standard dose of 5 mg 1 time a day for 10-30 days, depending on the symptoms severity and response rate. Patients could also receive concomitant therapy, for example, topical corticosteroids, enterosorbents, anti-leukotriene agents, beta-2-agonists if the specialist considered this to be justified. The need for additional prescriptions was taken into account in the findings of the trial.

Allergy symptoms were assessed before and immediately after desloratadine therapy. Patients categorized their skin (itching, rashes, dryness) symptoms according to severity evaluating them on a four-point scale of severity: 0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe/significant.

The difference in percent between the initial and ending points was analyzed for patients of each symptom category using the McNemar test and Wilcoxon Matched-Pairs Signed-Ranks test. Percentages were calculated without taking into account missing values. Moreover, the overall efficacy of desloratadine therapy was evaluated by patients at the end of the trial as excellent, good, satisfactory, or inadequate. Subsequently, the specialists prescribing desloratadine and the patients taking it indicated whether desloratadine was "better than previous therapy."

The tolerability of desloratadine therapy was evaluated by researchers and patients at the end of the trial using the same four characteristics as in efficacy assessment. Patients should have indicated all possible adverse effects, including dry mouth, drowsiness, headache, or dyspepsia events. In addition, the subjects described all newly emerging diseases and complications of existing pathologies after initiating desloratadine therapy.

**Findings**

41 people with allergic urticaria, with or without other concomitant allergopathologies, participated in this observational open case-control trial. In the absence of entire therapy effect, topical steroids were prescribed to the patients.

The age of patients ranged from 7 to 86 years, the average age was 37.1±6.1 years, 85.4% were women.

Immediately, we note that all patients showed a positive effect from the use of deslor, while 78.0% assessed the effect as “full”, and 22.0% as “moderate”. The average duration of treatment was 11.7±1.2 days.

The proportion of patients who combined desloratadine with other groups of drugs was 78.0 (including glucocorticoids - less than 50%) (Table 1).

Table 1. Concomitant medication

| Drug | Patients,% of total (n) |
|---|---|
| Any other medicines, including: | 78.0 (32) |
| Antibiotics | 0 (0) |
| Topical antihistamines | 12.2 (5) |
| Beta sympathomimetics | 19.5 (8) |
| Glucocorticosteroids | 43.9 (18) |
| Skin creams/ointments | 39.0 (16) |
| Bronchial | 14.6 (6) |
| Combined | 12.2 (5) |
| Intranasal sprays | 34.1 (14) |
| Systemic infusion, short duration | 4.9 (2) |
| Systemic oral | 0 (0) |
| Hyposensitizing | 17.1 (7) |
| Leukotriene inhibitors | 29.9 (9) |
| Local vasoconstrictors | 19.5 (8) |
| Enterosorbents | 73.2 (30) |

| | |
|---|---|
| Other | 46.3 (19) |

It should be noted that, 43.9% of patients had to use topical glucocorticosteroids in short periods of 5-14 days to achieve the full effect.

Many of the patients previously taken drugs from other manufacturers. For ethical reasons, questions of the comparative effectiveness of drugs from different companies are beyond the scope of this publication.

The proportion of patients with no or slightly apparent skin symptoms increased from 73.2% at the baseline, to 95.1% after deslor treatment for rashes; from 82.9% to 92.7% for dry skin; and from 61.0% to 87.8% in relation to pruritus (Pic. 1). The proportion of patients with moderate to severe symptoms decreased from 26.8% at the baseline to 4.9% at the trial end in relation to rashes; from 17.1% to 7.3% for dry skin; and from 39.0% to 12.2% for pruritus.

**Patient evaluation**

The efficacy of deslor was considered excellent or good in 82.9% of patients at the end of therapy (Pic. 2). Moreover, approximately 73% of respondents rated the tolerability of this drug with these two characteristics. Almost 83% of patients described deslor treatment as superior to previous antiallergic therapy and expressed a desire to continue deslor therapy in case of similar manifestations in the future.

**Safety**

Adverse effects were observed in 10 patients (24.4%). Drowsiness was observed in 9 patients (22.0%), while in 7 of them there was mild drowsiness and only 2 subjects had moderate (4.88%) At the same time, it is necessary to take into account the fact that these patients had previously suffered from a decrease in the quality and duration of sleep due to disease symptoms, therefore, drowsiness may be to some extent regarded as an indicator of the drug effectiveness. Drowsiness peak was noted in 2-3 hours after taking the drug. 3-4 days after initiation of treatment, a decrease in the intensity of drowsiness was noted in all patients. At the same time, most patients, on the contrary, noted positive changes in their psychoemotional state – improvement in the quality of sleep, reduction of irritability, and general mood improvement! In patients with moderate drowsiness, the drug administration was switched to the late evening.

One patient had dry mouth and headache (2.4%). No cardiac rhythm disorder, intestinal dyspeptic and toxic effects have been identified. None of the subjects discontinued treatment due to side effects. Compliance in the trial group was 100%.

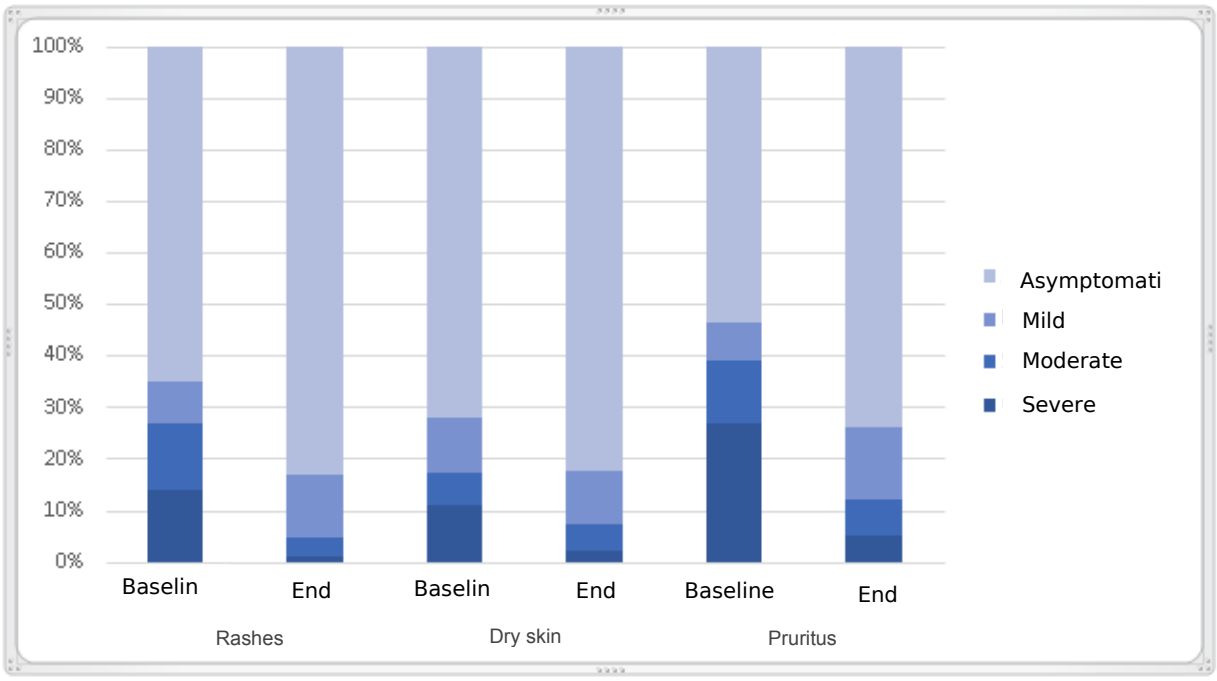
**Results and discussion**

Thus, from the presented data it is apparent that Deslor, the domestic analogue of desloratadine, has a sufficient safety level for patients, side effects are mild and correctable, which, together with a good efficacy profile and price characteristics contribute to high compliance.

The identified improvement in the course of allergic diseases confirms the results of previous trials proving that desloratadine is an effective and well-tolerated agent for the treatment of typical symptoms of the main skin allergic diseases [21, 22, 23].

The lack of hepatic biotransformation, a twice lower dose while persisting (or even enhancing) the therapeutic effect, the practical absence of gastrointestinal adverse events and excellent compatibility with other groups of drugs used in allergology and gastroenterology allows consider desloratadine as the agent of choice in the presence of liver damage and other digestive organs.

**Picture 1.** Dynamics of the severity of skin symptoms at the baseline and end of the trial concerning rashes (A), dry skin (B) and pruritus (C) after 3 weeks of therapy with desloratadine. The severity was assessed as asymptomatic, mild, moderate, severe.

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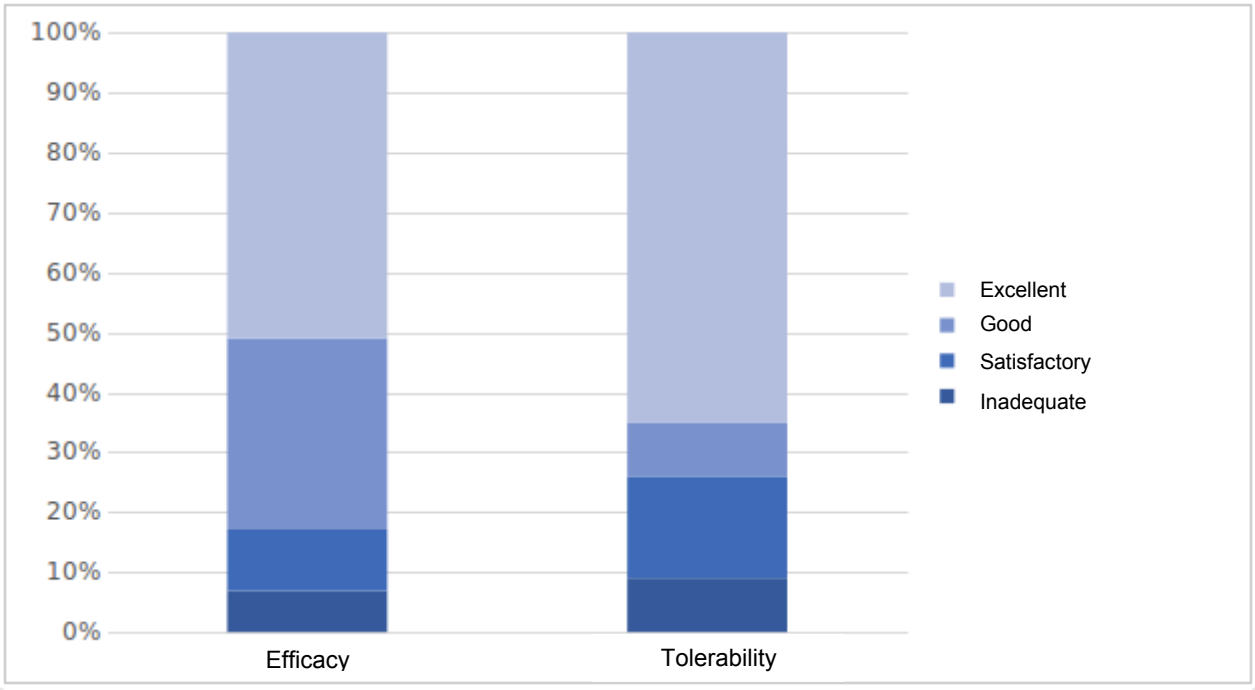


**Picture 2.** Efficacy (A) and tolerability (B) of desloratadine as assessed by patients at the end of the trial. Efficacy and tolerability were assessed as excellent, good, satisfactory and inadequate.

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