

**CORRECTION OF DISORDERS OF A SPECTRUM OF DIGESTIVE
ENZYMES OF THE PANCREAS WITH ZADITEN IN SENSITIZATION
AND ANAPHYLACTIC SHOCK**

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Abstract: *in experiments on white rats, the effect of the antihistamine zaditen on the activity of digestive enzymes of the pancreas during sensitization and anaphylactic shock was studied. Sensitization and anaphylactic shock lead to significant shifts in the activity of digestive enzymes of the pancreas, which can lead to disruption of the breakdown and absorption of carbohydrates, proteins and fats. The usage of zaditen significantly smoothes the observed changes in the enzyme-synthesizing system of the pancreas in these pathologies.*

Keywords: *zaditen, sensitization, anaphylactic shock, digestive enzymes of the pancreas*

**КОРРЕКЦИЯ ЗАДИТЕНОМ НАРУШЕНИЙ СПЕКТРА
ПИЩЕВАРИТЕЛЬНЫХ ФЕРМЕНТОВ ПОДЖЕЛУДОЧНОЙ
ЖЕЛЕЗЫ ПРИ СЕНСИБИЛИЗАЦИИ И АНАФИЛАКТИЧЕСКОМ
ШОКЕ**

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***Аннотация:** в опытах на белых крысах изучено влияние антигистаминного препарата задитена на активность пищеварительных ферментов поджелудочной железы при сенсibilизации и анафилактическом шоке. Сенсibilизация и анафилактический шок приводят к существенным сдвигам в активности пищеварительных ферментов поджелудочной железы, что может привести к нарушению расщепления и усвоения углеводов, белков и жиров. Применение задитена заметно сглаживает наблюдаемые сдвиги в ферментсинтезирующей системе поджелудочной железы в данных патологиях.*

***Ключевые слова:** задитен, сенсibilизация, анафилактический шок, пищеварительные ферменты поджелудочной железы.*

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Currently, the problem of allergic conditions is given special attention. This is not accidental, in recent years almost all countries of the world have seen a continuous increase in the number of patients suffering from allergic diseases [4, 5]. Having the features of morphological and histological structure, as well as the functions performed, the mucous layer of the gastrointestinal tract prevents the penetration of the bulk of exogenous antigens into the internal environment of the body [6]. Unfortunately, in allergic reactions remains almost unexplored condition of digestive enzymes of the pancreas. Antihistamines are widely used in the complex therapy of allergic diseases [2, 3, 5], but their effect on the

hydrolytic function of the pancreas in healthy and allergized organisms is not studied yet.

Purpose of work. The aim of this work is to study the state of the hydrolytic function of the pancreas during sensitization and anaphylactic shock and correction of violations of this function with the help of antihistamine zaditen. According to the literature, zaditen, unlike other H1-receptor blockers, stabilizes the target cells of allergy, has an antagonistic effect in relation to the factor that activates platelets (FAT), which plays an important role in the pathogenesis of allergic reactions. Therefore, it has a more pronounced antihistamine effect [4]. Based on this, we chose zaditen in these series of experiments.

Method of research

The research was conducted on 210 white rats of both sexes weighing 120-200 g, divided into 5 groups: the first are subjected to the influence of sensitization, the second – subjected to the influence of sensitisation on the background of preventive repeated injection of zaditen, the third is subjected to the influence of anaphylactic shock, the fourth – subjected to the influence of anaphylactic shock on the background of preventive 26-day injection of zaditen, fifth– control animals.

Sensitization of rats was caused by triple subcutaneous injection (every other day) of 0.5–1 ml/kg of chicken egg protein solution (EPS) diluted with isotonic sodium chloride solution in a ratio of 1:5 with simultaneous injection of vaseline oil in a volume of 0.1 ml (A.D.Ado, 1978). The sensitized rats were decapitated (7 individuals from the experimental and control groups) on the 7th, 14th, 21st, 28th and 31st days after injection of the last sensitizing dose of antigen and the activity of pancreatic enzymes was determined at the same time. In a series of experiments with sensitization on the background of multiple daily injection of zaditen, the activity of the studied enzymes was determined at the same time as in sensitization.

Anaphylactic shock of rats was caused by the injection of 1-2 ml/kg of native EPS after 21 days of the final sensitizing injection of antigen (A.D.Ado, 1978).

For prophylactic purposes zaditen was injection daily, starting from the first day of administration of the solution of EP, i.e. within 26 days. Animals were decapitated by 7 individuals from each group immediately after the shock, as

well as 6, 24, 48 and 72 hours after it and determined their activity of the studied enzymes.

Zaditen was administered through the mouth in the morning before feeding animals at a dose of 1 mg/kg (this dose is the average therapeutic dose for rats). The animals of the control group received distilled water in an equivalent volume.

Alpha-amylase activity was determined (CF 3.2.1.1.) according to the method of Smyth and Roe (1949) in the modification of A. M. Ugolev. This method is based on photoelectrocolorimetry identifying loss of starch when using iodine reagent. The activity of the protease complex (CF 3.4.4.) was determined by the method of A. M. Ugolev and N. M. Timofeeva, based on photoelectrocolorimetry identifying growth free amino acid, which is formed by hydrolytic splitting of protein substrates and in reaction with ninhydrin gives a blue coloration. Lipase activity (CF 3.1.1.3.) was determined by the method of A. A. Lazdinis and M. R. Lasdyna based on photoelectrocolorimetry identifying loss of intralipid. The separated fatty acids are extracted before titration with acidified heptane and isopropanol. Titration was carried out with 0.01 N sodium hydroxide solution in methylbenzene [8]. The protein content in the pancreas was determined by the method of O. N. Lowry and co-authors. The method is based on color reaction of the phenol reagent Polina–Chocalteu with protein. To clarify some aspects of the mechanism of action of zaditen on the activity of the enzymes studied the activity of Mg²⁺-dependent ATPase (CF 3.6.1.3.) pancreas by the method of A. T. Ivashenko and co-authors [7]. The results were statistically processed by Student and Fisher method.

Research results and discussion

In the dynamics of the process of sensitization of chicken egg protein, starting from the 14th day and until the end of the experiment, the mass of the small intestine mucosa increased. Swelling and hyperemia of the mucous membrane were visually observed. The concentration and content of protein in the pancreatic tissue and in the mucous membrane of the small intestine increased, especially by the 21st day of sensitization.

During the experiment, significant deviations from the norm in the spectrum of the studied pancreatic enzymes were established. Thus, the specific activity of

alpha-amylase on the 7th day of sensitization was at the level of control. On the 14th day the enzyme activity increased by 15%. During the remaining periods of sensitization, this enzymatic activity remained reduced: 21st day – by 35%, 28th day – by 31%, 31st day – by 20% (table 1).

Table 1. Effect of zaditen on specific activity of alpha-amylase (g/min/g) of rat pancreas during sensitization ($M \pm m$, $n=7$)

Group of animals	Days of sensitization				
	7	14	21	28	31
Control	145,7 ±8,3	149,7±8,2	147,6±8,6	148,2±8,1	149,5±8,2
Sensitization	137,2 ±8,7	172,4±8,9	96,1 ±7,5	102,9±7,3	119,2±7,1
P ₁	> 0,25	< 0,05	< 0,001	< 0,002	< 0,02
Sensitisation on the background of zaditen	133,7 ±8,4	145,2±8,4	122,9±7,8	127,6±7,2	139,0±7,7
P ₁	> 0,25	> 0,5	< 0,05	> 0,5	> 0,5
P ₂	> 0,5	< 0,05	< 0,05	< 0,05	< 0,05

Note: P₁ - the reliability of the differences in the experimental groups compared with the control;

P₂ - reliability of differences between the experimental groups.

Specific proteolytic activity was also increased on the 7th and 14th days of the study by 25 and 22%, respectively. All other terms of sensitization activity of the protease complex also remained low: the 21st day was 34%, 28th day – 20% and a 31st day by 11%. Lipolytic activity was increased on the 7th, 14th and 21st days of sensitization by 20, 28 and 29%, respectively. In other terms, the enzyme activity was below the control values: 28th day – by 25% and 31st day – by 28%.

After anaphylactic shock caused by intraperitoneal injection 21 days after the last sensitizing injection of chicken egg protein, some individuals experienced instant death, and most rats had trembling of the whole body, and some – aggressiveness, which gradually passed by the end of the experiments. The concentration of protein in the pancreatic tissue during the first two days increased from the norm, normalization occurred to 72 hours after the introduction of a permissive dose of antigen. An increase in the total protein content was established immediately after the development of anaphylactic shock and after 48 hours no changes in the mass of the pancreas were detected.

There was hyperemia, swelling, violation of the integrity of the mucous membrane. So, 24 hours after the shock found erosion and ulceration in the stomach and duodenum. Visually, the restoration of the integrity of the mucous membrane in the oral departments was observed after 72h after the shock.

Against the background of anaphylactic shock, significant changes in the spectrum of the studied digestive enzymes were also observed. Thus, immediately after the shock, the specific activity of alpha-amylase decreased by 45%. After 6, 24, 48 and 72 hours after the shock enzymatic activity decreased by 48, 40, 32 and 25%, respectively (table 2). Proteolytic activity immediately after the shock decreased by 22%, after 6 and 24 hours after it increased by 23 and 16%, respectively, to 48 hours after the shock, enzymatic activity decreased by 23%, and by 72 hours it did not differ from the control. Specific lipolytic activity immediately after the shock remained within the normal range, 6 and 24 hours after it increased by 25 and 20%, respectively, and by the 48th and 72nd hours after the shock, its activity decreased by 18 and 12%, respectively.

Table 2. Effect of zaditen on specific activity of alpha-amylase (g/min/g) of rat pancreas in anaphylactic shock ($M \pm m$, $n=7$)

Group of animals	Time after anaphylactic shock, h				
	0	6	24	48	72
Control	147,7±9,1	146,3±10,2	144,7±10,7	151,8±10,6	148,4±10,1
Anaphylactic	81,2±6,8	76,2±7,6	86,8 ±8,2	103,3±8,4	111,3±8,7

shock					
P ₁	< 0,001	< 0,001	< 0,001	< 0,01	< 0,02
Anaphylactic shock on the background of zaditen	121,2±7,2	115,2±7,5	118,7±8,1	135,0±9,3	139,2±9,5
P ₁	< 0,05	< 0,02	< 0,05	< 0,05	> 0,5
P ₂	< 0,002	< 0,01	< 0,02	< 0,02	< 0,05

Note: P₁ - the reliability of the differences in the experimental groups compared with the control;

P₂ - reliability of differences between the experimental groups.

In sensitization, starting from the 21st day, and anaphylactic shock, there was an increase in Mg²⁺-dependent ATPase of the pancreas. As it is known from literature sources, the increase in Mg²⁺-ATPase in allergic reactions leads to a decrease in ATP content, which in turn leads to a decrease in ADP and camp content. By reducing the content of the latter, there is an increase in the release of biologically active mediators of allergy from mast cells.

So, in sensitization and anaphylactic shock, there are significant shifts in the activity of digestive enzymes of the pancreas. These changes should be considered as one of the links of a multi-stage response nonspecific reaction of the body to the release of histamine, serotonin and other mediators of allergy in sensitization and anaphylactic shock and their effect on sensitive receptors of the body. Undoubtedly, the above changes in the spectrum of the studied enzymes can lead to disruption of the breakdown and absorption of the main components of food – carbohydrates, proteins and fats.

Prophylactic repeated administration of zaditen in the process of causing sensitization and anaphylactic shock significantly leveled part of the violations caused by these pathologies, for example, there were no changes regarding the control of the total protein content in the pancreatic tissue. Also, the remedy is fully protected the mucous membrane of the stomach and duodenum from ulceration and erosive damage. In addition, there was no death of animals; there

was no shaking of the body and aggressiveness of rats.

The introduction of the remedy prophylactically, in the process of causing the studied allergic pathologies, significantly corrects shifts in the spectrum of digestive enzymes of the pancreas occurring in these conditions. Thus, in animals affected by sensitization on the background of zaditen, the specific activity of alpha-amylase decreased only on the 21st and 28th days of sensitization by 17 and 14%, respectively. In other terms of the study enzyme activity was at the level of control. Proteolytic activity in all terms of the study was within normal limits. Lipase activity on the 21st day of sensitization increased by 12%, and in other terms of research it was at the level of control.

In animals affected by anaphylactic shock against the background of prophylactic administration of zaditen, the specific activity of alpha-amylase immediately after the shock decreased by 18%, after 6, 24 and 48 hours after it, the inhibition of enzyme activity was 21, 18 and 11%, respectively. The rest of the study was within normal limits. Lipolytic activity in 6 hours after the shock increased by 13%, and in other terms it was at the level of control.

In sensitization and anaphylactic shock on the background of preventive repeated administration of zaditen in the functional state of Mg^{2+} -dependent ATPase, no violation occurred.

Based on this, it can be assumed that the prophylactic use of zaditen in the process of reproduction of sensitization and anaphylactic shock due to its protective action in the contents of ATP, ADP and cAMP changes are not observed. This, in turn, leads to a decrease in the release of mediators of allergic reactions from mast cells and basophils, a weakening of the course of sensitization and anaphylactic shock.

Thus, the antihistamine zaditen, introduced in the process of causing sensitization and anaphylactic shock, significantly corrects disorders in the activity of digestive enzymes of the pancreas, occurring in the conditions of these allergic reactions. Such a pronounced protective effect of zaditen is associated with its multifunctional action, which has a leveling effect on all three stages of an allergic reaction – immunological, pathochemical and pathophysiological [1, 4].

So, we can say that the results obtained by us should be taken into account in the treatment of patients with allergic diseases.

Conclusion

1. In sensitization and anaphylactic shock, there is a sharp violation of the activity of digestive enzymes of the pancreas.

2. Prophylactic long-term administration of zaditen significantly levels the disturbance in the spectrum of pancreatic enzymes in these pathologies.

3. In sensitization and anaphylactic shock the activity of Mg²⁺-dependent ATPase is increased. Zaditen, introduced in the process of causing these allergic reactions, markedly levels the induction of the activity of this enzyme.

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