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The effect of the combination of thiotriazoline and corvitin on the values of some parameters of the cellular and humoral immune system during the experimental reproduction of allergic alveolitis under immobilization stress

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Abstract

The purpose of the study was to determine the effectiveness of the combination of corvitin and thiotriazoline for the correction of levels of T- and B-lymphocytes, circulating immune complexes (CIC) of the blood of male guinea pigs (GP) if experimental allergic alveolitis (EAA) and immobilization stress (IS) are combined. The study was performed on 50 male GP weighing 180-210 g. EAA was reproduced by the method of O.O. Orekhov, Yu.A. Kyrylov. The production of IS was carried out by the method of P.D. Horizontov. The content of T- and B-lymphocytes in the blood was determined by the method of E.F. Chernushenko, L.S. Kogosova. CIC were detected by the method of Haskova V., Kaslik J., Math J., Matejckava M. The withdrawal from the experiment was carried out by the method of decapitation after previous administration of nalbuphine hydrochloride in the experimental group (EG) of intact GP; in the EG of EAA and IS during the study days corresponding to the stages of development of IS: 1st – anxiety, 14th – resistance, 24th – exhaustion; EG of EAA with IS on the 24th day after pharmacocorrection with the above-mentioned combination of drugs. There was a progressive decrease in the level of T-lymphocytes by 33,47% ($p<0,01$), 36,23% ($p<0,01$) and 39,62% ($p<0,01$), an increase in B-lymphocytes by 27,82% ($p<0,01$),

131,13% (p<0,01) and 44,37% (p<0,01), an increase in CIC by 41,15 % (p<0,01), 46,62% (p<0,01), and 50,78% (p<0,01) on the 1st, 14th and 24th days respectively, compared to the indicators of the control group under the combination of EAA and IS. An increase in T-lymphocytes by 40% (p<0,01), a decrease in B-lymphocytes by 24,31% (p<0,01), and a decrease in the level of CIC by 26,08% (p<0,01) were observed in the EG using corvitin and tiotriazoline relative to the corresponding indicators of the EG with a combination of EAA and IS without pharmacological interventions on 24th day of the experiment. The results indicate an immunocorrective effect of the combination of corvitin and thiotriazoline which is manifested by activation of the cellular and suppression of the humoral link of immunity of GP exposed to EAA and IS.

Key words: allergic alveolitis; immobilization stress; corvitin; thiotriazoline; T-lymphocytes; B-lymphocytes; circulating immune complexes.

Вплив комбінації тіотриазоліну та корвітину на значення деяких параметрів клітинної та гуморальної системи імунітету при експериментальному відтворенні алергічного альвеоліту в умовах іммобілізаційного стресу

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Резюме

Метою дослідження є вивчення ефективності комбінації корвітину та тіотриазоліну щодо корекції рівнів Т- та В-лімфоцитів, циркулюючих імунних комплексів (ЦІК) крові самців морських свинок (МС) при експериментальному поєднанні алергічного альвеоліту (ЕАА) та іммобілізаційного стресу (ІС). Дослідження виконано на 50 самцях МС, масою 180-210 г. ЕАА відтворено методом О.О. Орехова, Ю.А. Кирилова, ІС – методом П.Д. Горизонтова, визначення вмісту Т- і В-лімфоцитів крові – методом Е.Ф. Чернушенко, Л.С. Когосової, а ЦІК - методом Haskova V., Kaslik J., Math J.. Виведення з експерименту проводилось методом декапітації після застосування налбуфіну гідрохлориду у дослідній групі (ДГ) інтактних МС; у ДГ з ЕАА та ІС в доби дослідження, відповідно стадіям розвитку ІС: 1 доба – тривоги, 14 – резистентності, 24 – виснаження; у ДГ з ЕАА та ІС – на 24 добу після фармакокорекції

вищевказаною комбінацією препаратів. У ДГ з ЕАА та ІС (1, 14, 24 доби) виявлено прогресуюче зниження рівня Т-лімфоцитів відповідно на 33,47% ($p<0,01$), 36,23%($p<0,01$) і 39,62% ($p<0,01$), збільшення В-лімфоцитів на 27,82% ($p<0,01$), 131,13% ($p<0,01$) і 44,37% ($p<0,01$) та ЦІК на 41,15% ($p<0,01$), 46,62% ($p<0,01$), і 50,78% ($p<0,01$) порівняно з показниками ДГ інтактних МС. У ДГ з застосуванням корвітину та тіотриазоліну спостерігалось зростання вмісту Т-лімфоцитів на 40% ($p<0,01$) та зниження В-лімфоцитів на 24,31% ($p<0,01$) і ЦІК на 26,08% ($p<0,01$) порівняно з відповідними параметрами ДГ з ЕАА та ІС без фармакологічних втручань на 24 добу експерименту. Одержані результати підтверджують імунокоригуючий ефект комбінації корвітину та тіотриазоліну у вигляді стимулювання клітинної та ослаблення активності гуморальної ланки імунітету при ЕАА та ІС.

Ключові слова: алергічний альвеоліт; іммобілізаційний стрес; корвітин; тіотриазолін; Т-лімфоцити; В-лімфоцити; ЦІК.

Introduction. Allergic alveolitis is an important problem in modern medical science, the study of which lies on the border of various disciplines, namely: allergology, immunology, pulmonology, therapy, professional pathology, pathophysiology. This is an immunologically mediated disease, the basis of which is the formation of allergic reactions of type III and IV according to Gel and Coombs. This pathology is characterized by damage to alveoli, interstitial structures of lung tissue and terminal bronchioles. In different countries of the world, the share of allergic alveolitis is 0.5-19% among all diseases of allergic origin and about 3% of established diagnoses of hospitalized patients with a pulmonological profile [1 - 6, 12].

As is known, immune-complex allergic reactions of type III play the most important role in the initial stages of the formation of allergic alveolitis (7), since the basis of its pathogenesis is the production of antibodies as a result of the introduction of antigens into the body and the formation of circulating immune complexes upon their subsequent arrival. It is B-lymphocytes, transforming into plasma cells, that provide the synthesis of antibodies, and, as a result, the development of allergic reactions of type III hypersensitivity, while the value of T-lymphocytes lies in the development of type IV hypersensitivity reactions, namely, CD4+T-cell delayed-type hypersensitivity and CD8+-T cell cytotoxicity. This necessitates a more detailed study of the peculiarities of changes in the parameters of the immune system in this disease [8 - 13].

Since modern man is forced to live under the influence of stress, it deserves special attention to study the nature of deviations in indicators of immune status, which can occur both in this pathology and in various diseases, and their combination can worsen the course of the main disease. Therefore, it is worth focusing more on the changes in the immune system under stress. The vast majority of studies emphasize the tendency to activate the humoral link of the immune system in the form of increased proliferation, differentiation of B-lymphocytes and synthesis of antibodies, and suppression of the cellular link, which was manifested by a decrease in the proliferation and activity of T-lymphocytes. Assuming the possible development of abnormalities of the immune status in allergic alveolitis under conditions of stress, the question arises of the need to correct the indicated combined pathology with drugs with immunomodulatory properties, in connection with which the combination of corvitin and thiotriazoline was chosen for the experiment.

The purpose of the work is to evaluate the effectiveness of the combination of corvitin and thiotriazoline for adjusting the level of blood T- and B-lymphocytes, circulating immune complexes under the conditions of experimental reproduction of allergic alveolitis during immobilization stress.

Research materials and methods. The study of changes in the parameters of the cellular and humoral link of immunity (T- and B-lymphocytes, circulating immune complexes) was carried out on 50 male guinea pigs, weighing 180-210 g, divided into 5 experimental groups: the first group - intact experimental animals (control) - 10 guinea pigs; the second, third and fourth groups, in which the experimental setting of allergic alveolitis and immobilization stress was performed, also contained 10 experimental animals each, which were removed from the experiment on the 1st, 14th and 24th days of the study, respectively; the fifth experimental group included 10 guinea pigs with experimental allergic alveolitis and immobilization stress and administration of corvitin (produced by the Borshchagiv Chemical and Pharmaceutical Plant) at a dose of 40 mg/kg intraperitoneally and thiotriazoline (produced by PJSC "Galichpharm") at a dose of 50 mg/kg intramuscularly for 10 days (from 14 to 24 days) to withdraw guinea pigs from the experiment, the method of decapitation was used after preliminary administration of nalbuphine hydrochloride (LLC "Yuria-Pharm", Ukraine) at a dose of 182 mg/kg intraperitoneally in time. Experimental modeling of allergic alveolitis was carried out by the method of O.O. Orekhov, Y.A. Kirilov [14]. Translated with www.DeepL.com/Translator (free version)For the experimental setting of immobilization stress, the method of P.D. was applied. Horizontova [15]: the animals were fixed on the operating table on their backs by their limbs for 3 hours. Determination of the level of T- and

B-lymphocytes in the blood was carried out according to the method of E.F. Chernushenko, L.S. Kogosova [16], and circulating blood immune complexes - by the method of Haskova V., Kaslik J., Math J. [17]. Statistical processing of the obtained results was carried out according to the Student's method.

Research results and their discussion. n the conditions of experimental modeling of allergic alveolitis under immobilization stress, a progressive increase in the level of B-lymphocytes and circulating blood immune complexes and a decrease in the content of T-lymphocytes were observed. Thus, on the 1st day from the beginning of the study, the level of T-lymphocytes decreased by 33.47% ($p<0.01$), on the 14th - by 36.23% ($p<0.01$), and on the 24th - by 39.62% ($p <0.01$) compared to the corresponding indicators of the group of intact animals (Fig. 1). The content of B-lymphocytes after 1 day increased by 27.82% ($p<0.01$), on the 14th - by 31.13% ($p<0.01$), and on the 24th - by 44.37% ($p<0.01$) relative to the indicators of the control group (Fig. 1). The level of circulating blood immune complexes increased by 41.15% ($p<0.01$) after 1 day, while on the 14th day - by 46.62% ($p<0.01$), and on the 24th - by 44.37% ($p<0.01$) compared to the values of similar parameters in the group of intact guinea pigs (Fig. 1).

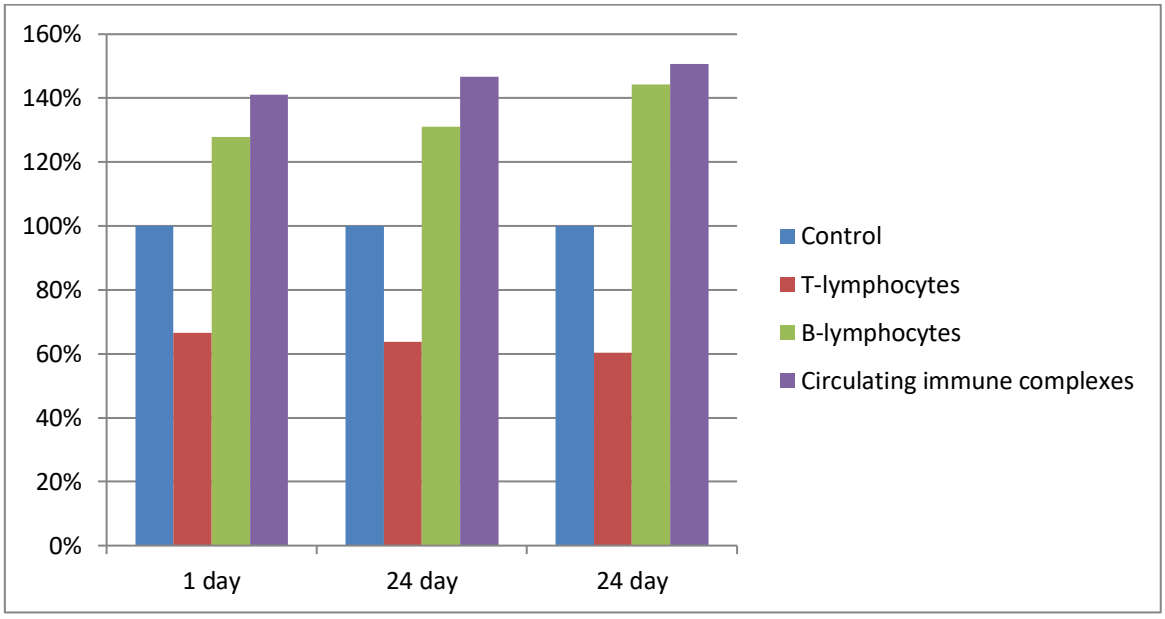

Fig. 1. Shift in the parameters of the cellular and humoral link of the immune system in male guinea pigs in the dynamics of the development of an experimental combination of allergic alveolitis and immobilization stress (in % of control)

It costs to underline that content of T-cell of blood arrived at the most subzero values, and arrived at B- lymphocytes and circulatory immune complexes the greatest values on 24

times of experiment, that became the bright display of progress of cellular inactivation and stimulation humoral links of immunity at this combined pathology. Therefore, during the experimental modeling of allergic alveolitis and immobilization stress, a gradual decrease in the level of blood T-lymphocytes was observed, which indicates a tendency to suppress the cellular link of immunity, and an increase in the content of blood B-lymphocytes and circulating immune complexes, which confirms the presence of signs of activation of the humoral link of the immune system systems.

As a result of the introduction of thiotriazoline (produced by PJSC "Halychpharm") at a dose of 50 mg/kg intramuscularly and corvitin (produced by "Borshchagiv Chemical and Pharmaceutical Plant") at a dose of 40 mg/kg from the 14th to the 24th day, in animals with experimental allergic alveolitis and immobilization stress, an increase in the level of blood T-lymphocytes by 40% ($p<0.01$), a decrease in B-lymphocytes by 24.31% ($p<0.01$) and circulating immune complexes by 26% ($p<0.01$) was found. 08% ($p<0.01$) compared to the values of similar parameters of the group of experimental animals with experimentally combined pathology without the use of any pharmacological means on the 24th day of the experiment (Fig. 2).

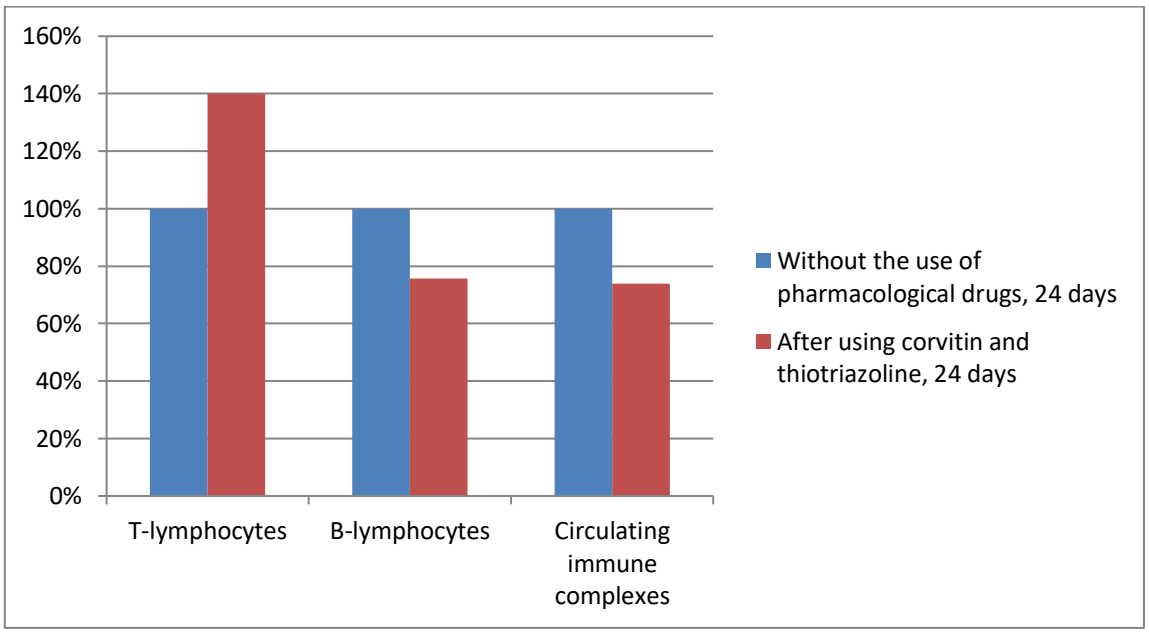

Fig. 2. Changes in the state of the cellular and humoral link of the immune system in the blood of male guinea pigs on the 24th day of experimental reproduction of the combination of allergic alveolitis and immobilization stress without any pharmacological interventions and after the use of a combination of corvitin and thiotriazoline (in % relative to the indicators of the group of animals without pharmacological correction)

Therefore, the obtained results confirm the existence of a corrective effect of the combination of thiotriazoline and corvitin on immunological status in the direction of cellular stimulation and inhibition of the activity of the humoral link of the immune system in experimental allergic alveolitis under conditions of immobilization stress.

Conclusions. Animals subjected to experimental modeling of allergic alveolitis under conditions of immobilization stress showed a tendency to progressive activation of the humoral link of the immune system in the form of a gradual increase in the level of B-lymphocytes and circulating immune complexes of the blood, and suppression of the cellular link of immunity, which was characterized by a pronounced decrease in the content of T-blood lymphocytes. After a ten-day use of the combination of corvitin and thiotriazoline, on the 24th day of the experiment, a decrease in the content of B-lymphocytes and circulating immune complexes of the blood and an increase in the level of T-lymphocytes was observed, which allows us to assert the ability of the above-mentioned combination of pharmacological drugs to stimulate cellular and inactivate the humoral link of the immune system, which indicates about a pronounced immunocorrective effect.

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