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Pathogenetic substantiation of thiotriazoline use on the basis of disorders of proteolysis processes and protease inhibitors under conditions of contact dermatitis and experimental pneumonia

M. M. Regeda-Furdychko

Lviv Medical Institute

Abstract

The aim of our research was to to investigate the features of the proteinase-inhibitory system in guinea pig lungs in the dynamics of the formation of experimental contact dermatitis (ECD) and experimental pneumonia (EP) and to establish the correction of their disorders by thiotriazoline.

Materials and methods. The researches were carried out on 60 guinea-pigs which were divided into 6 groups. I group (control) were intact guinea-pigs, II group – were animals with an ECD and EP (4^{th} day), III group – were guinea-pigs on the 8^{th} day of the experiment, IV group consisted of animals with an experimental CD and EP (10^{th} day) and V group included guinea-pigs with an combined pathology (18^{th} day, without thiotriazoline using). The last sixth group included animals with an ECD and EP that were treated by thiotriazoline from the 8^{th} to the 18^{th} days of the experiment. Two periods of development of ECD and EP were distinguished: early (4^{th} and 8^{th} days of experiment) and late (10^{th} and 18^{th} days).

Experimental contact dermatitis was simulated by method of VA Volkovoj (2010). EP was called by the method of VN Shlyapnikov, TL Solodov (1998). Thiotriazoline was

administered intramuscularly at a dose of 100 mg per 1 kg of weight daily from the 8th to the 18th days of the experiment. The condition of proteinase-inhibitory system was determined by lysis of the azoalbumin, azokasein and azokolagen and maintenance content of α1-protease inhibitor (α1-PI), α2-macroglobulin (α2-M) by method of Veremeenko K.N., Goloborodko O.P. (1988).

Results and discussion. It is established that under the conditions of development of experimental contact dermatitis and experimental pneumonia there are changes in the proteinase-inhibitory system, which is manifested by activation of proteolysis. There was an increase in the level of azoalbumin, azocasein and azocollagen, especially on the 18th day of the experiment and depression of protease inhibitors. This led to the formation of proteinase-inhibitory imbalance before treatment.

The use of thiotriazoline led to the correction of proteolysis (their reduction) and the growth of protease inhibitors in the lungs with the development of contact dermatitis and experimental pneumonia, which indicated its corrective effect on impaired proteinase-inhibitory system markers and its appropriate pathogenetic justification.

Key words: contact dermatitis; pneumonia; proteinase-inhibitory system; thiotriazoline.

Патогенетичне обґрунтування застосування тіотриазоліну на основі порушень процесів протеолізу і інгібіторів протеаз за умов розвитку контактного дерматиту і експериментальної пневмонії

М. М. Регеда-Фурдичко

Львівський медичний інститут

Мета нашого дослідження - з'ясувати особливості процесів протеїназо-інгібіторної системи в легенях морських свинок у динаміці формування експериментального контактного дерматиту (ЕКД) та експериментальної пневмонії (ЕП) та встановити корекцію їх порушень тіотриазоліном.

Матеріал і методи дослідження. Дослідження здійснювали на морських свинках, поділених на 6 груп. До І групи (контроль) відносили інтактні морські свинки, до ІІ- тварини з ЕКД та ЕП (4-а доба), до ІІІ – морські свинки на 8-у добу поєднаного модельного процесу, до IV - тварини на 10-у добу, V - мурчаки на 18-у добу ЕКД та ЕП

до лікування та VI група - морські свинки з ЕКД і ЕП після лікування тіотриазоліном з 8-ї по 18-ту доби експерименту впродовж 10 діб. Умовно виділяли два періоди розвитку експериментального контактного дерматиту та експериментальної пневмонії: ранній і пізній. Ранній період включав групу тварин на 4-у та 8-у доби експерименту. Пізній – морські свинки на 10-у та 18-у доби ЕКД та ЕП.

Модель контактного дерматиту моделювали на морських свинках за методом Волковой В.А. (2010). ЕП викликали за методом В. Н. Шляпникова, Т. Л. Солодова (1998). Тіотриазолін вводили внутрішньом'язово дозою 100 мг на 1 кг маси щодня з 8-ї по 18-ту доби експерименту. Протеїназо-інгібіторну систему визначали за загальною протеолітичною активністю – за лізисом азоальбуміну, азоказеїну і азоколагену та інгібіторів протеолізу за вмістом альфа 1- інгібітора протеїназ (α1-ІП), альфа-2-макроглобуліну за методом Веремеенко К.Н., Голобородько О.П. (1988).

Результати дослідження та їх обговорення. Встановлено, що за умов розвитку експериментального контактного дерматиту та експериментальної пневмонії відбуваються зміни протеїназо-інгібіторної системи, які проявляється активацією протеолізу. Виявлено зростання рівня азоальбуміна, азоказеїна та азоколагена, особливо на 18-у добу експерименту і депресію інгібіторів протеаз. Це спричиняло формування протеїназо-інгібіторного дисбалансу до лікування.

Використання тіотриазоліну призводило до корекції показників протеолізу (їх зниження) та зростання інгібіторів протеаз в легенях за умов розвитку контактного дерматиту та експериментальної пневмонії, що свідчило про його коригуючу дію на порушені маркери ПІС та його доцільне патогенетичне обґрунтування .

Ключові слова: контактний дерматит; пневмонія; протеїназо-інгібіторна система; тіотриазолін.

Pneumonia is one of the most common diseases of the bronchopulmonary system, which leads to significant economic and social damage: temporary disability, the disability of patients, high material costs for treatment.

Contact dermatitis is also an important problem, especially for dermatologists. It is known that the combined pathology leads to significant changes in physiological processes in the body, reduces adaptive reserves, affects the course of the underlying disease, complicates diagnosis and is more difficult to treat [6].

The proteinase-inhibitory system is an important system of the body that controls homeostasis, changes in which lead to a number of diseases. Proteolysis is closely related to

the body's defense systems - blood clotting, fibrinolysis, kininogenesis, immune responses, the creation of biologically active peptides and hormones, and more. The literature indicates that the pathogenesis of many diseases is associated with changes in proteolytic activity [5]. The use of pathogenetic therapy, in particular antioxidant, antihypoxant and immunocorrector of thiotriazoline is important for the correction of metabolic disorders in contact dermatitis (CD) and pneumonia.

The aim of our research was to to investigate the features of the proteinase-inhibitory system in guinea pig lungs in the dynamics of the formation of experimental contact dermatitis (ECD) and experimental pneumonia (EP) and to establish the correction of their disorders by thiotriazoline.

Materials and methods. The researches were carried out on 60 guinea-pigs (males). The weight of each one was 180-220g. They were divided into 6 groups for 9 animals each of them, except the first (15 animals). I group (control) were intact guinea-pigs, II group – were animals with an ECD and EP (4^{th} day), III group – were guinea-pigs on the 8^{th} day of the experiment, IV group consisted of animals with an experimental CD and EP (10^{th} day) and V group included guinea-pigs with an combined pathology (18^{th} day, without thiotriazoline using). The last sixth group included animals with an ECD and EP that were treated by thiotriazoline. For the purpose of detailed analysis and interpretation of proteinase-inhibitory system indicators in different days of the experiment, two periods of development of ECD and EP were distinguished: early (4^{th} and 8^{th} days of experiment) and late (10^{th} and 18^{th} days). The chosen days of ECD and EP were due to the classical stages of the inflammatory process.

Experimental contact dermatitis was simulated by method of VA Volkovoj (2010). EP was called by the method of VN Shlyapnikov, TL Solodov (1998). Thiotriazoline was administered intramuscularly at a dose of 100 mg per 1 kg of weight daily from the 8^{th} to the 18^{th} days of the experiment due to the fact that during this period there are significant changes in metabolic processes and on the basis that this drug has immunocorrective, membrane-stabilizing, antioxidant properties.

The condition of proteinase-inhibitory system was determined by lysis of the azoalbumin (breakdown of low molecular weight proteins), azokasein (breakdown of high molecular weight proteins) and azokolagen (collagenolysis) and maintenance content of α1-protease inhibitor (α1-PI), α2-macroglobulin (α2-M) by method of Veremeenko K.N., Goloborodko O.P. (1988). The study material was collected under ether anesthesia. Numerical results were adapted with static method using Student’s criteria.

Results and discussion. We found an increase in the content of azoalbumin in the lungs on the 4^{th}, 8^{th}, 10^{th} and 18^{th} days of ECD and EP by 35.8%, 53.0%, 74.0% and 76.5%, respectively ($p \leq 0.05$) compared with the control, indicating the activation of proteolysis, which dominated in the late period of the experiment.

The study of azocasein in the lungs also showed an increase throughout the research (4^{th}, 8^{th}, 10^{th} and 18^{th} days), including an increase of 42.6%, 68.2%, 78.0% and 80.4, respectively ($p \leq 0.05$) compared with the first group of animals, which indicated an acceleration of protein lysis.

It was found that the level of azocollagen increased rapidly in animals of II, III, IV and V groups by 69.5%, 108.6%, 104.3% and 108.6 ($p \leq 0.05$) respectively, in ECD and EP, compared with controls, which indicated the activation of collagenolysis in the lungs.

Increased proteolytic activity in these combined pathologies caused a shift in the inhibitory defense system. The concentration of α2-macroglobulin, as well as α1-protease inhibitor in the lungs does not change significantly on the 4^{th} day of the experiment against a group of intact animals. Later from the 8^{th}, 10^{th} and 18^{th} days, namely, we record a decline in α2-M by 23.5%, 68.6% and 69.6% ($p \leq 0.05$) and α1-IP, respectively, 30.4%, 68.7% and 68.8% ($p \leq 0.05$) compared with intact animals, indicating depletion of the inhibitory potential of the protection in the lungs.

Thus, the results of our studies indicate an increase in proteolytic processes in conditions of reduced inhibitory potential in the lungs, which prevailed on the 18^{th} day of development of these experimental models of diseases.

The use of thiotriazoline for 10 days (from the 8^{th} to the 18^{th} days) leads to a decrease in the content of azoalbumin, azocasein and azocollagen in the lungs by 23.0% ($p_1 \leq 0.05$), 29.7% ($p_1 \leq 0, 05$) and 29.1% ($p_1 \leq 0.05$) and increased the level of α2-M by 54.8% ($p_1 \leq 0.05$) and α1-IP by 47.4% ($p_1 \leq 0.05$) in this combined pathology compared with a V group of animals, who were not prescribed this drug, on the 18^{th} day of the experiment.

Thus, the data obtained by us make it possible to state the corrective effect of thiotriazoline on the disturbed processes of the proteinase-inhibitory system in the lungs under the conditions of formation of combined pathology - ECD and EP and indicate its pathogenetic justification.

Conclusions. The results of the research allow us to conclude that ECD and EP are accompanied by changes in the state of the proteinase-inhibitory system, which is manifested by the activation of proteolysis (increasing levels of azoalbumin, azocasein and azocollagen) on the background of the exhaustion of protease inhibitors. It grounds the application of

thiotriazoline in the development of ECD and EP. Therefore, these results indicate that it is possible to use thiotriazoline in combination therapy for inflammatory processes in the lungs and skin and its pathogenetic justification.

References

1. Veremeenko K.N., Goloborodko A.P., Kyzym A.Y. (1988). Proteolysis in norm and at pathology. K .: Health, 200p. (in Ukrainian)

2. Volkova V.A., Kuchynska I.V., Tiupka T.I. Study of the therapeutic efficacy of a new ointment with a lipophilic complex of the Tremulin aspen bark under conditions of non-allergic contact dermatitis in rats. Pharmacology and drug toxicology. 2010;7–12.

3. Hozhenko A.I., Kovalska L.A., Kucher O.V. Clinical and pathogenic grounds for complex therapy of ChOLD and concomitant gastropathology. Aktualni problemy transportnoi medytsyny 2013; 3 (33): 88-94.

4. Shlyapnikov VN, Solodova TL Experimental models of acute pneumonia caused by opportunistic bacteria and their associations: Method. recommendations: Saratov Medical Institute, 1988. 33 p.

5. Neporada K.S., Beregova T.V., Sukhomlyn A.A., Gordienko L.P., Mykytenko A.O. Development of proteolytic imbalance in the tissues of the oral organs. Medical Forum. (12). 2017.103-106.

6. Tramper-Stranders G.A. Childhood community-acquired pneumonia: a review of etiology and antimicrobial treatment studies. Paediatr Respir Rev, 26 (2018), pp. 41-48