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CHANGES IN A FUNCTIONAL CONDITION OF PROOXIDANT SYSTEM IN GUINEA PIGS' BLOOD IN EXPERIMENTAL ALLERGIC ALVEOLITIS AND THEIR CORRECTION WITH THIOTRIAZOLIN

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Abstract

The study shows that significant elevation of conjugated dienes and malondialdehude in the blood of guinea pigs depend on experimental allergic alveolitis duration was detected. Oxidative stress can arises from overproduction of reactive oxygen species(ROS) by metabolic reactions that use oxygen. ROS also affects the expression of several genes by upregulation of redox-sensitive transcription factors. Regulation of redox state is critical for cell viability, activation, proliferation, and organ function. Corrective effect of thiotriazoline on these indicators have demonstrated .

Key words: **experimental allergic alveolitis, malondialdehude, conjugated diens, thiotriazolin.**

Introduction

Hypersensitivity pneumonitis (HP) also known as exogenic allergic alveolitis, is an interstitial lung disease caused by repeated inhalation of organic antigens and low-molecular-weight inorganic particles[1]. It is a T-cell-driven disease that is histologically characterized by diffuse mononuclear cell infiltrates and loosely formed granulomas in the lungs. Sources of the offending antigen are many, and include bacterial, fungal, animal, or inorganic chemicals. Interestingly, despite ubiquitous exposure to these factors, only 5–15% of exposed individuals ever develop HP [2, 3]. The risk factors of HP are poorly characterized and often require a high index of suspicion to make a diagnosis. The disease presents in acute, subacute, and chronic forms, depending on the amount and duration of exposure, as well as individual level of susceptibility, with the chronic form often leading to fibrotic disease [4-8].

Histopathological examination of lung biopsies from patients with HP have shown B cells, but the exact role of these lymphocytes in HP pathogenesis has not been investigated [9]. The role of oxidative stress in pathogenesis of this pathology is poorly understand. The aim of our work was to investigate the changes in prooxidant system in experimental allergic alveolitis (EAA) development.

MATERIALS AND METHODS OF INVESTIGATION

All experiments on laboratory animals were conducted following the principles of bioethics according to the regulations of European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986), European Union Directive 2010/63/EU, Law of Ukraine № 3447-IV “On protection of animals from cruel treatment”, general ethic principles of experiments on animals, approved by the first national congress of Ukraine on bioethics (2001).

The experiment was conducted on 30 female guinea pigs weighing 0.18-0.20 kg. Experimental allergic alveolitis (EAA) was induced by the method of O.O. Orehov and Y.A. Kyrylov [10]. Prior, the animals had been immunized with Freund’s complete adjuvant (0.2 ml intramuscularly into a hind leg). In 2 weeks, 0.2 ml of 1% BCG solution was introduced intravenously every 10^{th} day. Decapitation was made on 24^{th}, 34^{th}, 44^{th} and 54^{th} days and took blood for observation. The content of conjugated dienes (CD) was determined by the method of V.B. Havrylov and M.I. Myshkorudina [11], malondialdehyde (MDA) – by E.N. Korobeinikov method [12].

Thiotriazolin was used for 10 days (from 44^{th} to 54^{th} days) intramuscularly at a dose of 100 mg / kg 1 time per day.

All digital results were statistically processed using arithmetical mean (M), margin of error of arithmetical mean (m), and Student's criterion "t". The calculations were performed using means of statistical and graphic analysis of electron tables Microsoft Excel (Microsoft office programs). Statistically reliable were the results with $p \leq 0,05$.

RESULTS OF INVESTIGATION AND THEIR DISCUSSION

Changes in blood content of CD were first analysed during the course of experimental HP. A significant increase of this enzyme level on the 24 th and 34 th days by 56,26% ($p<0,05$) and 67,74 % ($p<0,05$) respectively against the control group of animals was observed. Depend on duration of this experimental model of disease accumulation of reactive oxygen species in the blood was found. Thus, significant increasing of CD in late periods of this immune pathology on the 44^{th} and 54^{th} days by 80,32% ($p<0,05$) and 154,84% ($p<0,05$)was detected respectively, compared with the control group.

Because MDA is secondary product of lipid peroxidation we also analysed its` level in guinea pigs` blood with experimental HP. Again, gradual elevation of MDA content was detected. It was expressed on the 24^{th} 34^{th} and 44^{th} days after starting of antigen injection and increased by 58,00, % ($p<0,05$), 57,75% ($p<0,05$) and 70,25% ($p<0,05$) respectively compared with healthy animals. Peak of MDA content was noticed on the day 54^{th} after experiment start and was the highest expressed -130% ($p<0,05$) in contrast with control.

Together, these data demonstrate that excessive accumulation of reactive oxygen species takes place in experimental allergic alveolitis that couses damage of biostructures and worsens of course of this pathology.

Analysis of CD and MDA contents in the blood of guinea pigs after usage of thiotriazoline which has antioxidant abilities has showed elevated levels of both enzymes in the treated groups compared with the guinea pigs which didn`t reseave this drug.Thus, CD and MDA were increased by 47,96130% ($p<0,05$) and 44,68% ($p<0,05$) (Fig.1). Such result detects us that thiotriazoline has corrective effect on disturbed indicators of prooxidant system in this immune pathology.

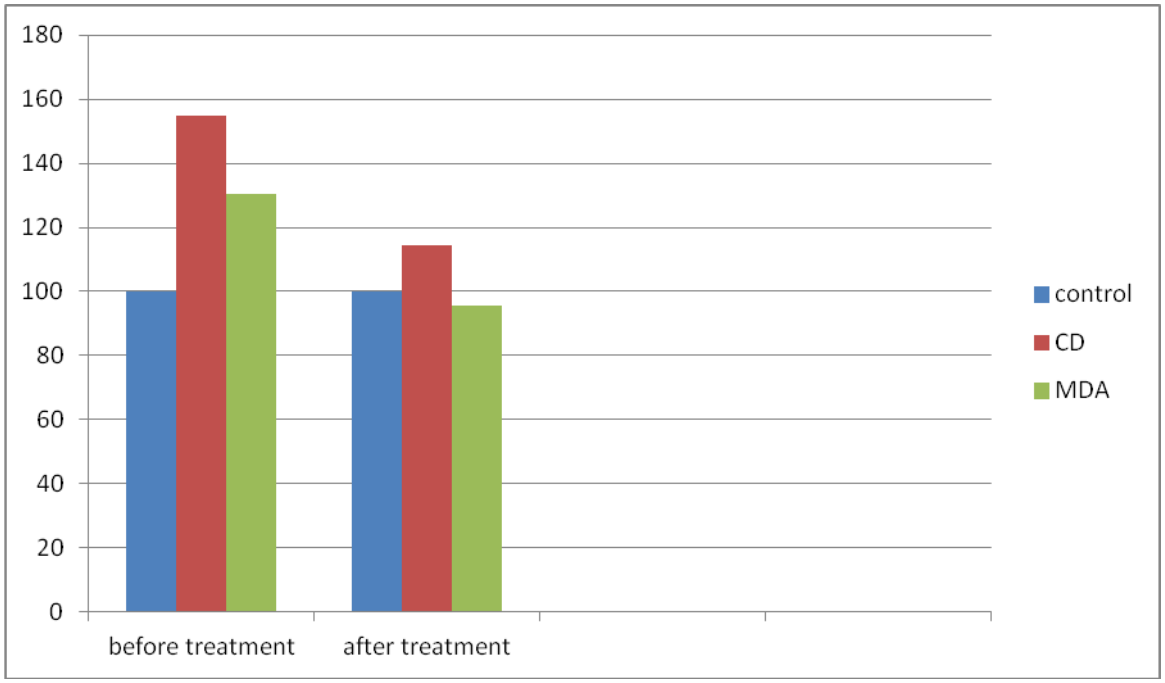

Fig.1. Condition of prooxidant system in the animals' blood in EAA (before and after treatment with thiotriazolin (in %).

CONCLUSIONS. Our findings indicate significant accumulation of lipid peroxidation products in the animals` blood during experimental allergic alveolitis and corrective effect of antioxidant-thiotriazolin on these markers.

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