https://www.proconference.org/index.php/usc/article/view/usc16-01-023
DOI: 10.30888/2709-2267.2022-16-01-023

UDC УДК 616-02:613.65]-092.9:612.017.11

INFLUENCE OF CHRONIC IMMOBILIZATION STRESS ON THE PARAMETERS OF NONSPECIFIC HUMORAL IMMUNITY IN RATS

Pavlova O.O.
d.t.s., prof.
ORCID: 0000-0002-0570-3931
Sirenko V.A.
c.med.n
Kharkiv National Medical University, Kharkiv, Nauky Avenue 4, 61022

Abstract. *The role of the imbalance of regulatory cytokines in the blood of rats under conditions of chronic immobilization stress, compared with the control, in the implementation of immune mechanisms of pancreatic damage was considered, where it was established: a predominant increase in the content of IL-12, a decrease in IL-4 in rats, which indicates participation of both specific (Th 1) and activation of nonspecific (macrophage) cellular immunity, which is possibly associated with increased production of Th1-lymphokines that stimulate excessive migration of macrophages - effector cells, immune response modulators, sources of regulatory cytokines to the site of damage where an excess of cytokines can potentiate the development of chronic pancreatitis in the future*

Keywords: *chronic immobilization stress, cytokines, immunologic reactivity, pancreas.*

Introduction

The high pace and tension of life experienced by a modern person in connection with responsible work, mental overload, instability of the social situation, and uncertainty about the future, often lead to the development of neuroses, which are characterized by a violation of the management of the functioning of internal organs, primarily organs digestion [1]. Chronic stress poses a threat to health and life [2]. The influence of stress causes the development of systemic and local protective reactions in response to damage The mechanisms of adaptation to stress and its numerous manifestations in young people are not yet sufficiently developed, and in the elderly and the elderly, they are exhausted.

Scientists, under conditions of experimental stress of different durations on rats, found structural changes in various organs, including the pancreas. This process involves the immune and neuroendocrine systems, the interaction of which is provided by the immune system mainly by cytokines, which are produced as a result of the complex interaction of T cells and macrophages [3,4,5]. With their help, you can trace the direction of the implementation of the immune response.

Taking into account the possibility of damage to organs and tissues associated with the influence of stress factors, as well as the lack of information on the role of nonspecific immune responses in the pathogenesis of post-stress damage to the pancreas, there is no doubt about the importance of continuing research in this direction. [2].

The objective of the study is to determine the content of IL-12 and IL-4 cytokines and their ratio in the blood serum of the rats that were on chronic immobilization stress

The volume of the study included experiments on 30 nonlinear rats (WAG/G Sto population). The animals were divided into groups: the rats which were isolated for

47.0±6.1 days every day (except Sundays) in special pen cages for immobilization. The duration of immobilization of the rats was different every day to prevent the possibility of their adaptation to immobilization, which could reduce the degree of impact on the body (20 specimens), and the rats of the control group (10 specimens).

All the procedures on the animals and also the removal of the animals from the experiment by decapitation were made under anesthesia with the use of thiopental narcosis. The levels of interleukin-4 (IL-4) and interleukin-12 (IL-12) in the blood serum were determined by the immune enzymatic method using the sets of reactants of BEST Vector and the sets of reactants of (Elisa Kit). The results of the study are processed by means of the analysis package of Microsoft Excel and Biostat.exe -2008 computer program.

The results of the study and their discussion. The important regulatory role of cytokines is known. IL-4 induces the proliferation of T-helpers of the 2-nd type (Th2) which mediate the reactions of humoral immune response (stimulation of B-lymphocytes and production of antibodies) and is also an antagonist of gamma interferon inhibiting the proliferation of T-helpers of the 1-st (Th1) type [2], while IL-12 enhances the proliferation and differentiation of T-helpers of the 1-st (Th1) type which mediate the reactions of cellular immunity and at the same time inhibit the proliferation of T-helpers of the 2-nd type (Th2) [4, 7, 8].

It was found that in animals subjected to chronic immobilization stress, there is a significant increase, more than 3 times, in the content of IL-12, and at the same time, in the majority of animals of the studied group, there is a decrease in the content of IL-4 compared to the control. To find out the degree of proportionality of the change in the level of IL-12 and IL-4, we determined the ratio of IL-12/IL-4. It was established that its level in rats is significantly increased compared to that in animals of the control group (by 3.7 times) (Table 1).

Table 1 Cytokine content in the blood of rats subjected to chronic immobilization stress (in % of the Standard)

Indicators (pg/ml)	control (n=10)	Rat (n=10)
IL-12	9,57±0,42	28,04±0,73*** *($p_{1,2}$<0,001)*
IL-4	1,98±0,19	1,51±0,12 * *($p_{1,2}$<0,001)*
IL-12/IL-4	5,3±0,59	19,43±1,26*** *(p_1<0,001)*

*Notes. 1. ***p < 0,001, *p < 0,05 (comparison with the control group).*

This indicates that rats that have experienced chronic immobilization stress have the most pronounced cytokine imbalance, as the level of the IL-12/IL-4 indicator is 3.5 times higher in them than in animals of the control group. The nature of the change in the level of IL-12 (increase) and IL-4 (decrease) gives reason to note that in the rats of the study group, the immune response to stress-induced damage to the pancreas is realized by the activation of cellular immunity reactions against the background of a decrease in the activity of humoral response reactions [1, 2, 3, 7].

Summary and conclusions

Were received the experimental data obtained are indicative of the fact that chronic immobilization stress of rats is the essential risk factor for the development of pathology of the pancreas with secretory failure.

1. In rats who were on chronic immobilization stress the signs of imbalance of regulatory cytokines with the prevalence of IL-12 content, the reduced IL-4 level was revealed that indicates the attraction of a nonspecific cellular link of immunity to the pathogenesis of the pancreas damage.

2. The imbalance of regulatory cytokines in rats is possibly associated with increased production of Th1 lymphokines, which stimulate excessive migration of macrophages - effector cells, sources of regulatory cytokines to the focus of injury, where their excess can potentiate the development of chronic pancreatitis in the future.

References:

1. Omel′chenko OYE. Stresostiykist′ orhaniv travlennya, zminy lipidnoho spektru krovi u shchuriv pry vysokokaloriynomu kharchuvanni, immobilizatsiynomu stresi ta yikh poyednanomu vplyvi.[Stress resistance of digestive organs, changes in blood lipid spectrum in rats with high-calorie diet, immobilization stress and their combined effects]. Visnyk problem biolohiyi i medytsyny. 2015, No. 2, pp. 177−181.

2. Reznikov AG. Endokrinologicheskiye aspekty stressa. [Endocrinological aspects of stress], Mezhdunarodnyy endokrinologicheskiy zhurnal. 2007;(4):11-17. 2007, No. 4, pp. 11−17.

3. Datsyuk O.I. Discitokinemiya yak prediktor efektyvnosty startovoyi infuziynoyi terapiyi v kompleksi peredoperatsiynoyi pidgotovky hvoryh na gostryi pankreatit [Discitokinemia as a predictor of efficiency of starting infusional therapy in a complex of preoperative preparation of patients with acute pancreatitis], Klinichna hirurgiya, 2016, No. 5, pp. 41−44.

4. Klinicheskaya immunologiya i alergologiya s vozrastnymi osobennostyami: uchebnoye posobiye [Clinical immunology and allergology with age peculiarities: manual], 2-e izd., K., VSI «Medicina», 2012, 520 p.

5. Interleukin-12 as a predictor of outcome in patients with severe acute pancreatitis / P. Gregorić, K. Doklestić, S. Stanković [et al.] // Hepatogastroenterology. – 2014. – Vol. 61, N 129. – P. 208−211.

6. T-cell populations in chronic pancreatitis / S. Mansour, C. D. Johnson, J. Sanderson [et al.] // Pancreatology. – 2015. – Vol. 15, N 4. – P. 311−312. − DOI: 10.1016/j.pan.2015.04.009.

7. T-helper cell-mediated islet inflammation contributes to β-cell dysfunction in chronic pancreatitis / R. Talukdar, M. Sasikala, P. Pavan Kumar [et al.]// Pancreas. 2016. – Vol. 45, N 3. – P. 434−442. − DOI: 10.1097/MPA.0000000000000479.

8. Lee, B., Adamska, J. Z., Namkoong, H., Bellin, M. D., Wilhelm, J., Szot, G. L., ..& Habtezion, A. (2020). Distinct immune characteristics distinguish hereditary and idiopathic chronic pancreatitis. *The Journal of clinical investigation*,2020; 130(5):2705-2711.http//doi.org/10.1172/JCI134066

sent: 02.02.2023