

Uncountered Effects of Immunomodulators

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Abstract

Certain shortcomings of clinical immunology at the present time are discussed, which leads to a reduction in the therapeutic use of immunomodulatory drugs, even despite their often high clinical effect and the imperfection of methods for specific target immunodiagnostics. Moreover, it is significant that their effect on the immune system is nonspecific. The non-immune systemic action of immunomodulators on various body systems is not taken into account. New methods for assessing the immune response are considered, which are not detected when using "stencil" methods.

Keywords: immunomodulators, immunodiagnostics, non-immune action of immunomodulators

Some doubt that is currently noted about the pathogenetic and diagnostic significance of pathological immune responses is apparently due to a certain obsolescence of the existing methodological base, because it detects mainly nonspecific changes in immune markers. The tendency to expand the panel of subtle methods for diagnosing a number of immune mechanisms, the insufficiently deep analysis of new approaches in immunotropic therapy, unfortunately, are of more theoretical than practical importance. There is a reduction in the therapeutic use of non-specific immunomodulators to a certain extent, despite their often high clinical effect, due to the lack of a specific justified ideology of immunocorrection, which should summarize the extensive accumulated information in this aspect. This narrowing of the arsenal of therapeutic agents occurs against the background of an increase in the proportion of chronic diseases with severe complications. And yet, apparently, certain doubts about the diagnostic value of the available methods for assessing immune disorders are justified, since they are largely based on ignoring the natural mechanisms of induction and regulation of immune and immunopathological reactions. It should be noted that it has long been clear that the problem of the definitions of "specificity" and "nonspecificity" used in immunology is far-fetched ^[1]. Thus, the induction of a specific immune response is mediated by an antigen and is regulated by a whole cascade of nonspecific mechanisms, which includes inflammation, regulatory peptides, specifically interferons, myelo peptides, thymomimetics, cytokines, fragments of immune globulins, endogenous hormones, low molecular weight products of nucleic acids, etc. Totally they are not able to trigger an immune response, but can modulate it. We should not forget the

functional unity of immunopathological reactions with disorders of lipid, protein, nucleic metabolism with the central nervous, endocrine, metabolic and other systems ^[2,3].

This is supported by an equally versatile, yet insufficiently known effect of immunomodulators on the body as a whole. And again, this is due to the incompleteness of the necessary information, although it is well known that low-molecular fragments of nucleic acids (oligonucleotides) activate tissue regeneration and repair, various metabolic reactions of the body, and provide detoxification of bacterial endotoxins, hormones, antibiotics, cytostatics, etc^[4]. Polysaccharides affect the blood coagulation system, thymomimetics regulate lipid metabolism, liver function, mylopeptides have an endorphin effect, etc. However, these effects are not taken into account or even assumed.

The standard assessment of the immunotropic action in general is reduced to the registration of quantitative changes in immune markers when compared with the "normal" immune parameters of healthy individuals. For this reason, a clinical immunologist has an extensive panel of immune markers that differ to a greater or lesser extent from the given reference ones, with vague information about the targets of action of various immunomodulators ^[5]. In this sense, it can be recalled that bone marrow myelopeptides stimulate humoral, and thymomimetics stimulate cellular immune links. However, if we talk about the specific characteristics of immune disorders in certain diseases, a certain feature of their course, the type of isolated microflora, stage, comorbidity, true and pseudo-allergic reactions, these problems have almost never been raised, as if they do not exist at all. The same applies to their relationship with genetic blood markers, the subtle mechanism of action of combined pharmacological and non-drug immunomodulation ^[6]. At the same time, a large empirical material has been accumulated on the use of multivariate immunocorrective therapy in the treatment of dozens of nosological forms. However, it is insufficiently analyzed and practically not generalized.

We are currently intensively working on this problem in order to sort out to some extent some of the unresolved issues in this area and try to find real relationships between a number of immune phenomena. To solve this complex problem, we have developed a universal method that allows us to evaluate the features of the immune response and its modulation, which are not detected when using "template" approaches. As such, the coefficient of diagnostic value was used, which allows, based on changes in the average values of indicators and their dispersion, to select key markers and with their help, taking into account the direction of dynamics (suppression, stimulation) from a given level and degree of changes, obtain a formula for immune system disorders (FISD) according to the dynamics from the norm, the formula of immunocorrection targets (FIT) according to the dynamics from the initial data after immunomodulation in this group of patients and the indicators bias formula (IBF) according to the dynamics of parameters in various treatment options ^[5,7,8,9]. The analysis of the terms of the formulas makes it possible to determine the links of the immune system involved in the pathological process, the vector and their severity ^[10,11,12]. A necessary condition for this analysis was the mathematical determination of the optimal number of patients in the group, i.e. observance of the rule of representativeness of the sample. Since the average values are not informative enough, because do not take into

account individual variations in the parameters in the generalized version; additionally, a frequency method was used to identify the number of patients in the compared groups with significantly changed markers; graphical, correlation-regressive, rank and other types of analyzes were performed [8,13,14,15]. The data obtained were processed by the methods of parametric and nonparametric variational statistics to determine the significance of differences. Performing extensive clinical immune studies in various nosological forms has shown the correctness of the developed approach, which is confirmed by numerous publications presented here.

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Conflict of Interest

None declared

Reference

- Zemskov VM, Pronko KN, Zemskov AM, Zemskova VA. Contradictions of clinical immunology: Nonspecific and specific mechanisms in immunogenesis. *Clinical Practice (Therapy)*. 2019, 16(3): 1161-1172.
- Zemskov VM, Neymann V, Zemskov AM, Pronko KN, Alekseev AA. Functional unity of the immune, endocrine and nervous systems. *Internat. J Case Studies*. 2020, 9(8): 19-23.
- Zemskov VM, Zemskov AM, Pronko KN, Neymann V, Demidova VS, Zemskova VA, Barsukov AA, Kozlova MN, Shishkina NS, Revishvili ASh. Immunometabolic aspects of pathological processes. *International Journal of Current Research and Review*. 2021,13(21), 7-13.
- Zemskov VM, Neymann VV, Pronko KN, Zemskov AM. Global role of low molecular weight nucleic Acids in biological systems. *Global Journal of Medical Research: C Microbiology and Pathology*. 2020, 20(2): 5-10.
- Zemskov AM, Esaulenko IE, Chereshev VA, Zemskov VM, Suchkov SV, Kozlov VA et al. Immunology. Electronic textbook. Moscow. Publishing House: GEOTAR-Media, 2016a: 265 copyright sheets. <http://www.studentlibrary.ru/ru/book/01-GEO-201601.html>).
- Zemskov VM, Pronko KN, Zemskov AM, Zemskova VA. Contradictions in the clinical immunology: polyfunctionality of genetic markers of blood for immune response. *International Journal of Current Research*. 2018, 10(7): 71595-71599
- Zemskov A.M., Zemskov V.M. An integral concept of regulating immune homeostasis". *J.Clinical and Experimental Pathology*. 2016, 6(2): 267.
- Zemskov AM, Esaulenko IE, Chereshev VA, Zemskov VM, Suchkov SV, Zemskova VA. The course of lectures on immunophysiology. Text book. Voronezh: Publishing House: Ritm, 2017: 1048p.
- Zemskov AM, Zemskov VM, Zemskova VA, Zoloedov VI, Kozlov VI, Dontsov AA, Dontsova EV. Handbook of clinical immunologist. "Theoretical, practical and applied aspects of clinical immunology at the present stage. Moscow. Publishing House: Triad-X, 2015:704p.

- Zemskov AM, Zemskov VM, Zemskova VA, Poletaeva IA. Principles of interpretation of laboratory diagnosis and infection treatment at the present stage. *Biology Bulletin Reviews*. 2020, 10(2): 140–149.
- Zemskov VM, Neymann V, Pronko KN, Zemskov AM. Some discussion problems of modern clinical immunology. *Biomarkers J*. 2020, 7(1) : 69-70.
- Zemskov AM, Zemskova VA, Zemskov VM. Unorthodox phenomena of clinical immunology. *Biology Bulletin Reviews*. 2020, 10(6), 534 – 542.
- Zemskov V, Zemskov A, Glukhov A. Diagnosis, treatment immune-dependent, immune-associated diseases (Fundamentals, characteristics, methods). Verlag, Palmarium Academic Publishing, Omni Scriptum GmbH & Co., Saarbrücken. 2014:640.
- Zemskov AM, Zemskov VM, Kulintsova YV, Dyadina KS. Non-target effects of pharmacological drugs. *International Journal of Current Research*. 2018. 10(01): 64731-64736.
- Zemskov AM, Chereshev VA, Revishvili AS, Zemskov VM, Popov VI, Zemskova VA. Problems of clinical immunology in 21st century—II: Natural and drug regulation mechanisms of immunological homeostasis. Moscow. Publishing House: Scientific Book. 2018: 286p.