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THE STATE OF NITRIC OXIDE IN THE BLOOD SERUM AND ON THE AFFECTED AREAS OF THE SKIN IN PATIENTS WITH CUTANEOUS LEISHMANIASIS

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RESUME
This article presents the results of studies of the state of nitric oxide in blood serum and affected areas of the skin in patients with cutaneous leishmaniasis in comparison with the indicators of healthy individuals.

Keywords. cutaneous leishmaniasis, nitric oxide, blood vessels.

INTRODUCTION

In recent years, special attention has been paid in dermatological practice to the study of the role of free radical reactions in the pathogenesis of many dermatoses [1,2,3]. It was noted that monocytes, macrophages, polymorphonuclear and endothelial cells generate an excess of activated oxygen forms, which is one of the most important causes of destruction of the epidermis and dermis, as well as microcirculatory, vascular and rheological disorders of the blood with the development of the inflammatory process [14].

Currently, nitric oxide (NO) is considered as the first representative of a new class of signaling molecules that carry out intercellular communication and regulation of many functions in different tissues and body systems [13]. Nitric oxide is one of the most important biological mediators in the human body [12]. The content of NO largely determines the state of lipid peroxidation, which reflects the protective and adaptive reaction of the body at the cellular level. The accumulation of free radical oxidation products has a damaging effect on cell membranes, including the membranes of immunocompetent cells, which, in turn, leads to disruption of many organs [11].

To date, nitric oxide (NO) is recognized as the most important mediator mediating a surprisingly wide range of various physiological and pathophysiological processes. Nitric oxide regulates the tone of small and medium-sized blood vessels, promotes relaxation of smooth muscles, has anticoagulant properties, inhibits platelet activation, mediates immune response and neurotransmission [16].

The concentration of NO is the main factor determining its biological effect. At low concentrations (<1 μm), direct effects of nitric oxide mainly prevail, aimed at maintaining homeostasis of the cardiovascular and nervous systems. At high concentrations (>1 μm), indirect effects due to the formation and subsequent action of a highly reactive compound, peroxynitrite, become predominant [10,15].

Excessive production of nitric oxide, leading to the formation of peroxynitrite and mediating the indirect effects of NO, is often pathological in nature. These effects lead to modification of various macromolecules, including proteins, lipids and nucleic acids [8]. With an excess of N0, iron-containing mitochondrial

enzymes are inactivated and cell growth and reproduction are inhibited. In the cardiovascular system, excess NO increases vascular permeability, which causes tissue edema, and also has a direct cardiotoxic effect, leading to persistent generalized vasodilation and a pronounced drop in blood pressure (BP). The development of septic shock is also associated with an excess of NO, when a large number of microbes circulating in the blood sharply activate the synthesis of NO in the endothelium, which leads to a prolonged and strong expansion of small blood vessels and to a significant decrease in blood pressure, which is difficult to respond to therapeutic effects. The same phenomena have been described in hemorrhagic, traumatic, anaphylactic, thermal and cardiogenic shock [7].

Thus, this problem is of great scientific and practical interest and allows us to attribute this problem with good reason to the field of activity of the dermatovenereological service, given the growth of cutaneous leishmaniasis in our region and will solve the epidemiological, pathogenetic, therapeutic and other aspects of this disease.

Nowadays, the study of the influence of an infectious factor on various biochemical processes in the body is of particular interest. In recent years, special attention has been paid in medical practice to the study of the role of free radical reactions in the pathogenesis of many pathologies [2,4,6,9].

One of the representatives of free radical oxidation is nitric oxide (NO), a signaling molecule that carries out cellular communication and regulation of many functions in different tissues and body systems [1,3,5,17].

THE PURPOSE OF THE STUDY

To study the regulatory effect of nitric oxide (NO) on metabolic processes in the aspect of possible effects on the formation of clinical course and complications in cutaneous leishmaniasis**.**

MATERIAL AND METHODS OF RESEARCH

Nitric oxide in blood serum was studied in 119 patients with cutaneous leishmaniasis. Of these, 38 patients had a tubercular form of cutaneous leishmaniasis, 52 – ulcerated leishmaniomas, 22 – ulcerated leishmaniomas with tubercles with lymphangoitis and 7 – metalleishmaniasis. The control group consisted of data from 12 practically healthy individuals.

Nitric oxide in the affected areas of the skin was studied in 45 patients with cutaneous leishmaniasis. Of these, 14 patients were diagnosed with a tubercular form of cutaneous leishmaniasis, 18 with ulcerated leishmaniomas and 13 with ulcerated leishmaniomas with tubercles with lymphangoitis. The control group consisted of data from 10 patients in whom the material was taken from a healthy area of the skin.

The results of the nitric oxide study showed that in patients of the general group with cutaneous leishmaniasis, there was a significant increase in the level of nitric oxide in the blood serum compared to the data of the control group and averaged 15.18 ± 0.33 mmol/l versus 9.50 ± 0.27 mmol/l in the control ($p < 0.001$) (Table 1).

Table 1 Indicators of nitric oxide content in blood serum in patients with cutaneous leishmaniasis (M±m)

Study groups	Number of examined patients	Serum NO level, mmol/l
Control group	12	9,50 ± 0,27
General group of patients with cutaneous leishmaniasis	119	15,18 ± 0,33*
Tubercular form of cutaneous leishmaniasis	38	11,87 ± 0,27*
Ulcerated leishmaniomas	52	14,72 ± 0,17*
Ulcerated leishmaniomas	22	19,51 ± 0,38*
with tubercles of insemination with lymphangoites	7	23,00 ± 0,67*

Note: p is the reliability of the data in relation to the control * - p<0,001

When studying the NO content in patients with cutaneous leishmaniasis, depending on the clinical forms, it was revealed that in the blood serum of patients with tubercular form of cutaneous leishmaniasis, the level of nitric oxide was on average 11.87 ± 0.27 mmol/l, with ulcerated leishmanioma -14.72 ± 0.17 mmol/l, with ulcerated leishmanioma with tubercles with lymphangoitis – 19.51 ± 0.38 mmol/l and with metalleishmaniasis – 23.00 ± 0.67 mmol/l versus 9.50 ± 0.27 mmol/l in the control group, which indicates a statistically significant increase in the content of nitric oxide in patients of the examined groups ($p<0.001$) compared with the data of the control group (Table 1). It should be noted that a more pronounced increase in this indicator was detected in patients with ulcerated leishmaniomas with tubercles of insemination with lymphangitis and metalleishmaniasis.

The data obtained indicate that with cutaneous leishmaniasis, a violation of nitric oxide production is detected in the blood serum and this has a negative effect on the course of this dermatosis.

In subsequent studies, we studied the state of nitric oxide indicators on the affected areas of the skin in patients with cutaneous leishmaniasis.

Table 2 Indicators of nitric oxide content in the affected areas of the skin in patients with cutaneous leishmaniasis (M±m)

Study groups	Number of examined patients	NO level in the affected areas of the skin, mmol/l
Control group	10	3,23 ± 0,10
General group of patients with cutaneous leishmaniasis	45	12,11 ± 0,33*
Tubercular form of cutaneous leishmaniasis	14	9,80 ± 0,29*
Ulcerated leishmaniomas	18	12,12 ± 0,28*
Ulcerated leishmaniomas	13	14,59 ± 0,35*

Note: p is the reliability of the data in relation to the control * - p<0,001

A study of the content of nitric oxide showed (Table. 2) that in patients of the general group with cutaneous leishmaniasis, a significant increase in the concentration of nitric oxide in relation to the indicators of the control group was detected in the affected areas of the skin and averaged 12.11 ± 0.33 mmol/l versus 3.23 ± 0.10 mmol/l in the control ($p <0.001$).

The study of the content of nitric oxide on the affected areas of the skin in patients with cutaneous leishmaniasis, depending on the clinical forms, revealed that in all examined groups of patients there was a significant increase in the content of nitric oxide compared with the data of the control group ($p < 0.001$) and on average it was 9.80 ± 0.29 mmol/l in the tubercular form of cutaneous leishmaniasis, with ulcerated leishmanioma – 12.12 ± 0.28 mmol/l and with ulcerated leishmanioma with tubercles of seeding with lymphangoites – 14.59 ± 0.35 mmol/l at 3.23 ± 0.10 mmol/l in the control (Table 2). The data obtained show that a more pronounced increase in this indicator was observed in patients with ulcerated leishmaniomas and with ulcerated leishmaniomas with tubercles of infection with lymphangitis.

The results of the study show that with cutaneous leishmaniasis, a violation of nitric oxide production is also detected in the affected areas of the skin and this has a negative effect on the course of this dermatosis.

Thus, with cutaneous leishmaniasis, a violation of nitric oxide production is detected both in general and at the local level, and a more pronounced increase in this indicator is detected in patients with complicated forms of cutaneous leishmaniasis. The increased content of nitric oxide in patients with a complicated course of cutaneous leishmaniasis may be explained by inflammatory degradation of connective tissue structures and endogenous intoxication, developing mainly due to increased decomposition of nitrogenous compounds. This in turn indicates the need to include in the complex of therapy of patients with cutaneous leishmaniasis

drugs regulating the production of nitric oxide and in the future can be used in the development of complex methods of therapy of patients with cutaneous leishmaniasis.

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