

**CHARACTERISTICS OF PARAMETERS OF CELLULAR AND HUMORAL IMMUNITY
IN VARIOUS TYPES OF ANESTHESIA IN PATIENTS WITH DIABETIC FOOT
SYNDROME**

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ABSTRACT

Background: The choice of the optimal method of anesthesia for diabetic foot syndrome, as well as the study of its effect on the immune system is an important urgent problem. **The aim** of the study: to study in a comparative aspect the effect of general, epidural and conduction anesthesia on the state of cellular and humoral immunity in patients with diabetic foot syndrome (DFS). **Materials and methods** of research. 157 patients with diabetic foot syndrome who were on inpatient treatment in the department of purulent surgery of the Bukhara Regional Multidisciplinary Medical Center were examined, who made up 3 groups depending on the use of anesthesia methods: The first group consisted of 52 patients (33.2%) operated under general anesthesia (GA). The second group consisted of 51 (32.4%) patients who underwent epidural anesthesia (EA) during surgical interventions on the lower extremities. The third group consisted of 54 (34.4%) patients who underwent conduction anesthesia-stem blockade (PA). Quantitative study of lymphocytes with CD3, CD4, CD8, CD20 phenotype in peripheral blood was performed and the level of IgG, IgA, IgM in blood serum was determined by ELISA. **Results.** It was revealed that in patients with DFS there are changes in cellular and humoral immunity: the levels of CD3+, CD4+ cells are sharply reduced, the number of CD20+ lymphocytes is increased. IgA and IgG levels are elevated. Analysis of the studied indicators of the immune system before, intra and postoperative periods revealed that patients who underwent OA had deeper changes in the studied parameters than the initial ones. The indicators were slightly better in patients who underwent EA. **Conclusion:** In patients who underwent surgery with the use of PA, immunological parameters remained at the level of the initial data. Consequently, the use of PA is more gentle in relation to its effect on the parameters of the immune system.

KEYWORDS: diabetic foot syndrome, types of anesthesia, cellular and humoral immunity.

INTRODUCTION

One of the most important problems of modern diabetology, after coronarogenic complications, remains diabetic foot syndrome (DFS)^[1,2] which combines pathological changes in the nervous system, arterial and microcirculatory bed, immune system, which pose an immediate threat to the development of ulcerative necrotic processes and gangrene of the foot.^[7,12,13] Despite all attempts to improve the results of treatment of diabetic foot syndrome, the number of amputations and truncations of large segments of the legs is growing. Every hour in the world, 55 diabetic patients lose their lower extremity, which in turn is accompanied by a high mortality rate, treatment and rehabilitation costs.^[2,15] During the first 5 years after amputation, about 80% of patients who have undergone high amputation die. In 30-50% of cases, gangrenous lesion of the feet ends with

amputation of the limb.^[17,18,21] The great social significance of diabetes mellitus is that it leads to early disability. At the same time, the risk of developing gangrene of the lower extremities is 20 times greater than in patients without diabetes mellitus.^[3,4,6]

Modern means and methods of intraoperative anesthetic protection should ensure the normal functioning of all life support systems, have a high level of safety, be convenient and accessible to use, guarantee a high "quality of life" to the patient in the postoperative period, and also contribute to the fastest possible restoration of the structural and functional integrity of organs and tissues.^[8,20]

There is still a discussion in the literature about the choice of the optimal method of anesthesia for

amputation of a diabetic foot. A sufficient amount of data has been accumulated indicating the advantage of neuroaxial anesthesia in comparison with general anesthesia.^[7,10]

We have not met the literature data of the conducted studies on the effect of various methods of anesthesia on immunity in patients with diabetic foot syndrome. In addition, changes in the activity and capacity of the complement system, a number of humoral immune systems as markers of the adequacy of anesthetic provision have not been practically studied.^[5,8,11,14,19]

The aim of the study was a comparative study of the effect of general, epidural and conduction anesthesia on the state of cellular and humoral immunity in patients with diabetic foot syndrome.

MATERIALS AND RESEARCH METHODS

The study included 157 patients diagnosed with diabetic foot syndrome who were hospitalized in the department of purulent surgery of the Bukhara Regional Multidisciplinary Medical Center from 2012 to 2021. Among the patients, the predominance of men was noted (58.1%). The average age of the patients was 62.5 ± 7.5 years. Many patients (39.57%) were at the age of labor activity (from 45 to 60 years). In most cases of observation, patients suffered from type 2 diabetes mellitus (94.5%), where mainly moderate and severe degrees of severity of diabetes mellitus in the stage of subcompensation and decompensation were observed. 57.9% of patients had gangrene of the toes and 34.6% had gangrene of the distal parts of the foot.

Depending on the anesthesia performed, the patients were divided into 3 groups: Group 1 – 52 patients (33.2%) operated under general anesthesia (OA). The second group consisted of 51 (32.4%) patients who underwent epidural anesthesia (EA). The third group consisted of 54 (34.4%) patients whose anesthesia during surgical interventions on the lower extremities was performed by conduction anesthesia (CA) (stem-femoral-sciatic nerve blockade).

Immunological studies were carried out by quantitative study of the number of lymphocytes with CD3, CD4, CD8, CD20 phenotype in peripheral blood using monoclonal antibodies of the LT series (Sorbent LLP; Moscow, Russia), determination of IgG, IgA, IgM levels in blood serum by ELISA using the test system of Vector Best LLC (RF), according to the attached instructions. The control group consisted of 20 practically healthy people of the same age. Studies in patients were conducted before and after surgery.

The research materials were subjected to statistical processing using the Student's t-test, using the standard Windows 2000 statistical software package.

RESULTS AND ITS DISCUSSION

An analysis of the anamnestic data of the examined patients showed that by the nature of concomitant diseases, the patients of the designated groups were representative. The following nosologies were most common: Coronary heart disease, PICS, condition after undergoing ACVA, arterial hypertension, diabetic nephropathy, COPD.

The results of the study showed that, in general, in the group of patients who underwent general anesthesia, there was a relative instability of hemodynamic parameters at all stages of the operation. 7 (13.72%) patients had cardiac arrhythmia, 4 (7.8%) cases had uncontrolled hypotension, 11 (21.6%) patients had a duration of post-acute awakening, 3 (5.8%) patients had a hypoglycemic condition. In 5 (9.8%) cases, relaxant recurarization was observed, and 3 (5.8%) patients developed congestive pneumonia in the postoperative period. Moreover, in 2 (3.9%) cases, difficulties with tracheal intubation were noted.

Epidural anesthesia (EA) was performed according to a generally accepted method using a special set of "Espokan". The method of performing EA was as follows: in the patient's side position at the L2-3 level, puncture and identification of the epidural space was performed by the method of resistance loss. A spinal needle with a diameter of 18 G was carried out through Tuohy's needle, a hyperbaric solution of bupivacaine (marcain spinal heavy) was injected intrathecally at a dose of 40-52 mg. After removal of the spinal needle, an epidural catheter was carried out through the Tuohy needle 2-4 cm in the cranial direction, which was used for postoperative anesthesia. Exposure in the patient's side position for 15 minutes.

The results of the study showed that, in general, in the group of patients who underwent epidural anesthesia, 1 (1.9%) patient had unintentional damage to the root, which was accompanied by paresthesia of the lower limb, 5 (9.8%) patients had post-operative back pain, which persisted for 10-12 days after the operation, 3 (5.8%) patients had headache, which in 2 cases lasted more than a day, 1 (1.9%) patient had epidural hematoma, which was detected by computed tomography in the postoperative period, 4 (7.8%) patients had persistent hypotension against the background of severe intoxication and hypovolemia, 3 (5.8%) patients had inadequate anesthesia.

In patients of the third group operated under conditions of conduction (stem nerve blockade) anesthesia (PA), 14-15 minutes after the blockade of the nerve trunks, the effect of anesthesia was manifested, which persisted at all stages of the operation and no additional administration of analgesics was required. Hemodynamic parameters were fairly stable. At the same time, respiratory dysfunctions were not observed. The duration of analgesia in the postoperative period lasted from 7

hours to 11 hours. No serious complications were observed, but the following reactions were noted: headache developed in 2 (3.7%) patients after administration of a local anesthetic, nausea developed in 3 (5.5%), and muscle tremor was noted in 2 (3.7%) patients. These symptoms were regarded by us as a toxic effect of the anesthetic. In 5 (9.2%) patients, bradycardia was noted, which was stopped by the introduction of an atropine sulfate solution. It should be noted that regional anesthesia provided a complete blockade of nociception during surgical interventions on the lower extremities, as well as a smooth course of the postoperative period with

rapid activation of patients, that is, an early return to the usual meal intake and insulin therapy regimen, activity within the bed, verticalization in a sitting position.

All patients underwent routine noninvasive hemodynamic monitoring using DASH 3000 monitors: ECG, blood pressure, heart rate, SpO₂.

Analysis of the results of immunological studies in patients with diabetic foot syndrome-DFS showed that changes in cellular and humoral immunity are observed compared with the data of the control group (Table 1).

Table 1: Indicators of cellular and humoral immunity in the examined individuals.

Показатели	Cont.group, n=20	Patients with DFS, n=157
CD3+, %	53,8 ± 1,4	48,3 ± 1,2*
CD4+, %	34,2 ± 1,2	30,6 ± 1,1*
CD8+, %	22,6 ± 1,1	17,5 ± 0,8*
CD4 /CD8	1,51 ± 0,01	1,75 ± 0,01*
CD16+, %	13,4 ± 0,7	8,7 ± 0,6*
CD20+, %	24,5 ± 1,1	30,3 ± 1,0*
CD25+, %	21,3 ± 1,0	17,6 ± 0,7*
CD95+, %	25,6 ± 1,2	29,4 ± 1,1*
IgA, g/l	1,5 ± 0,07	2,43 ± 0,6*
IgM, g/l	1,2 ± 0,05	1,4 ± 0,2
IgG, g/l	8,3 ± 0,6	15,3 ± 1,0*

Note: * The values are valid with respect to the cont.group

(P<0,05-0,001)

As can be seen from Table 1, the level of T-lymphocytes (CD3+) and its subpopulations (T-helpers (P<0.01) and T-suppressors (P<0.05) was significantly reduced relative to the data of the control group. Changes in the content of subpopulation cells also affected the immunoregulatory index, which was significantly higher than the values of the control group (P<0.05). The number of lymphocytes with CD16 phenotype in patients with DFS was reduced, and the level of B-lymphocytes was significantly increased relative to the control group. Analysis of data on lymphocytes with activation markers - CD25 and CD95, showed their multidirectional change, the level of lymphocytes with a marker of early activation - CD25+-cells were significantly reduced, and lymphocytes with a marker of apoptosis were

significantly increased (P<0.05). As for humoral immunity, IgA and IgG levels were significantly elevated (P<0.01).

As you know, any operation is stressful for the body, including for the immune system. However, it turned out that anesthesia can also affect the parameters of the immune system in different ways. Analysis of the results of the study after the surgical procedure showed that general anesthesia applied during surgery in patients with DFS has an effect on both cellular and humoral immunity. As can be seen from the data given in Table 2, under the influence of general anesthesia, there is a significant decrease in the number of CD3+ cells (P<0,01).

Table 2: Dynamics of the studied parameters of the immune system depending on the applied anesthesia in patients with DFS.

Indicators	Before the operation, n=157	GA, n=51	EA, n=52	CA, n=54
CD3+, %	48,3 ± 1,1	44,2 ± 1,3*	45,4 ± 1,2	47,3 ± 1,5
CD4+, %	30,6 ± 1,1	26,3 ± 1,0*	27,5 ± 1,0*	29,4 ± 1,12
CD8+, %	17,5 ± 0,8	15,2 ± 0,7*	16,1 ± 1,0	17,9 ± 0,8
CD4 /CD8	1,75 ± 0,01	1,79 ± 0,02	1,77 ± 0,01	1,64 ± 0,02*
CD16+, %	8,7 ± 0,6	5,9 ± 0,4*	6,3 ± 0,5*	7,8 ± 0,8
CD20+, %	30,3 ± 1,1	35,7 ± 1,2*	33,8 ± 1,2*	31,2 ± 1,3
CD25+, %	17,6 ± 0,7	25,5 ± 0,9*	24,2 ± 0,8*	17,9 ± 0,7
CD95+, %	29,4 ± 1,0	34,5 ± 1,2*	33,1 ± 1,1*	28,4 ± 1,0
IgA, g/l	2,43 ± 0,06	2,61 ± 0,04*	2,59 ± 0,05*	2,37 ± 0,043
IgM, g/l	1,4 ± 0,02	1,34 ± 0,02	1,38 ± 0,02	1,3 ± 0,02
IgG, g/l	15,3 ± 1,0	16,7 ± 0,9	15,3 ± 0,9	15,3 ± 0,9

Note: * The values are valid relative to the group before the operation ($P < 0,05-0,001$)

The number of helper and suppressor cells is also reduced, as a result of which the immunoregulation index is increased ($P < 0.05$). And the number of cells with the CD25, CD95 and B-lymphocyte phenotype is higher than the initial data. The analysis of the data of patients who underwent surgery using EA was also changed, and most of the indicators were changed significantly. Analyzing the data of immunological parameters in patients who underwent surgery using PA, it was found that no significant changes were observed, except for the immunoregulation index, which was lower than in other groups ($P < 0.05$).

The number of NK cells in the postoperative period decreased significantly in all groups, but most pronounced in the OA group (PA - 17%; EA - 33%; OA - 42%).

According to the data given in Table 2, activation of cellular immunity is observed, which indicates the tension of regulatory systems and the development of unfavorable adaptation strategies, mainly in OA.

The humoral link of immunity (IgA, IgG, IgM of blood) is more resistant to the effects of surgical trauma and anesthesia. At the same time, a decrease in the level of immunoglobulins of classes A and G is observed both during epidural and general anesthesia.^[9,10]

According to a number of authors, in general surgical patients operated under general and epidural anesthesia, there is moderate immunosuppression of the cellular link of immunity (a decrease in the total number of lymphocytes in the blood, CD3+, CD4+, CD8+ cells).^[4,5] At the same time, statistically significant differences in all indicators of the immune status are revealed in patients with surgical pathology of the abdominal cavity operated under conditions of OA.^[6,9,16] This is not observed in patients who underwent surgery under general anesthesia. In these patients, immunosuppression in the postoperative period is further aggravated.^[9,18,19,20,21]

Thus, the studies conducted indicate that anesthesia has its effect on the immune system. However, the most sparing effect is provided by anesthesia during surgical interventions on the lower extremities in patients with diabetic foot syndrome, performed by conduction anesthesia (CA).

CONCLUSIONS

1. The use of general anesthesia during operations on the lower extremities in patients with diabetic foot syndrome, is accompanied mainly by the suppression of all links of cellular and humoral immunity.

2. The use of epidural anesthesia is accompanied by less tension of regulatory systems, which contributes to the conservation of protective resources of the body and the development of a favorable adaptation strategy. But a large number of complications associated with anesthesia limits its widespread use in patients with diabetic foot syndrome.
3. From the position of influence on cellular and humoral immunity, the method of choice for operations on the lower extremities in patients with diabetic foot syndrome is conduction anesthesia by stem blockade. This method of anesthesia has minimal complications that do not affect the vital functions of the body.

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