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CLINICAL AND IMMUNOLOGIC PARAMETERS OF PATIENTS WITH ANASTOMOSIS AFTER MINIGASTRIC BYPASS SURGERY

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ABSTRACT

Background: Bariatric surgery is a leading treatment for obesity and type 2 diabetes mellitus, with minigastric bypass emerging as a popular option. This study aims to investigate the changes in cellular immunity in patients with postoperative anastomosis after minigastric bypass.

Methods: This open prospective clinical study included 152 obese patients who underwent minigastric bypass. Patients were divided into a main group (n=76) with postoperative anastomosis and a comparison group (n=76) without anastomosis. Leukocytes, lymphocytes, and their subpopulations were measured using hematology analyzers, rosette formation, and flow cytometry. Cytokine production (TNF-α, IL-2, IL-10, and IFN-γ) was assessed by sandwich immunoassay and immunofluorescence.

Results: In patients with anastomosis, leukocyte counts increased significantly postoperatively, peaking at 13.24x10^9/L on day 3. Lymphocyte counts dropped initially but recovered by day 14. T-helper cells increased progressively, while T-suppressors initially decreased, then doubled by day 14. B-lymphocytes decreased initially but returned to baseline by day 14. In patients with severe anastomosis, proinflammatory cytokine TNF-α production was significantly higher, indicating an intense inflammatory response.

Conclusion: Patients with postoperative anastomosis exhibit significant alterations in cellular immunity, characterized by fluctuations in leukocytes, lymphocytes, and increased proinflammatory cytokine production. These findings suggest that immune monitoring is crucial for managing complications after minigastric bypass surgery.

KEYWORDS: minigastric bypass, anastomosis, immunity.

INTRODUCTION

One of the most advanced areas of modern medicine is bariatric surgery, which accounts for up to 35% of other surgical procedures in developed clinics in developed foreign countries (1,3,5). This is due to the fact that today obese people with metabolic syndrome and insulin resistance are more likely to develop type 2 diabetes mellitus and its complications, with damage to vital organs (brain, heart, kidneys, etc.) (2,4,6,8).

Since promising and highly effective therapeutic agents for the treatment of type 2 diabetes mellitus are still under development, bariatric surgery (also known as metabolic surgery), in light of the above, remains the only effective treatment for not only obesity but also type 2 diabetes mellitus (7,9).

Currently, of the known bariatric surgery options for the treatment of obesity and type 2 diabetes mellitus, the most commonly used are gastric bypasses: biliopancreatic bypass (10,12,14), Roux bypass (1,4), and minigastric bypass (11,13,15).

Minigastric bypass surgery in bariatric surgery is considered a relatively "young" surgical treatment option for obesity and type 2 diabetes mellitus (3,7). The effectiveness of this type of surgery is attributed to its relative simplicity and rapidity in performance, with fairly effective treatment outcomes (16,17). This is confirmed by the presence of information on rapidly growing statistics regarding the use of minigastric bypass. For example, in the early 2000s, the incidence of minigastric bypass among all bariatric surgeries was only 0.73-1.02%, but in 2022 it increased to 4.6% (2,7,9).

Along with the increase in the frequency of minigastric bypass, naturally, publications about complications of this type of bariatric surgery began to appear in the literature (4,6).

All this is due to a complete change in the anatomical view of the well-known and long-accepted conceptualization of gastric surgery. This should include such features of minigastric bypass as the creation of a specific shape of the gastric stump (3,5), preservation of the still functioning gastric gastrin-producing area, and a number of other technical features. At the same time, most objections to the use of minigastric bypass are summarized by the high incidence of bile reflux, anastomosis and its complications (bleeding, ulcer formation, etc.) (9,11). Statistical data show its development in patients after minigastric bypass from 17.4% to 24.9%. Such a high incidence of anastomositis and its complications after minigastric bypass has determined the main vector of our research.

Purpose of the study. Study of the nature and analysis of changes in the indicators of cellular immunity in patients with various forms of anastomosis after minigastric bypass surgery

MATERIAL AND METHODS

The study included 152 obese patients who underwent minigastric bypass surgery. The total volume of clinical material of this type of surgery amounted to 344 patients who were treated and examined in the multidisciplinary clinic of the Tashkent Medical Academy and in the private clinic "Karmen Plus" of Bukhara city. The study was an open prospective clinical study consisting of main and comparative groups.

A total of 76 (22.1%) out of 344 patients had various anastomoses after minigastric bypass. All of them made up the main group of patients. The criteria for inclusion of patients into the main group were: patients with body mass index 35 kg/m2 and more after minigastric bypass complicated by anastomosis, aged from 18 to 75 years; availability of written informational consent of the patient for participation in the study. The criteria for non-inclusion of patients in the main group were: absence of anastomositis in the postoperative period after minigastric bypass; presence of decompensated chronic somatic pathology; patients with any uncontrolled psychiatric disease; patients who underwent minigastric bypass as a repeat operation after preliminary unsuccessful longitudinal gastric resection. The criteria for exclusion of patients from the main group were: taking medications affecting the patient's immune system in the postoperative period; pregnancy in the postoperative period; patient's refusal to participate in the study.

From the remaining 268 (77.9%) patients, a comparison group was formed in the same number of patients after minigastric bypass. Selection to the comparison group was strictly randomized. The criteria for inclusion of patients in the comparison group were: patients with a body mass index of 35 kg/m2 or more after minigastric bypass surgery, not complicated by anastomositis, aged from 18 to 75 years; availability of written informational consent of the patient for participation in the study. The criteria for non-inclusion of patients in the comparison group were: presence of anastomositis in the postoperative period after minigastric bypass; presence of decompensated chronic somatic pathology; patients with any uncontrolled psychiatric disease; patients who underwent minigastric bypass as a repeat operation after prior unsuccessful longitudinal gastric resection. The criteria for exclusion of patients from the main group were: development of anastomositis in the postoperative period, taking medications affecting the patient's immune system in the postoperative period; pregnancy in the postoperative period; patient refusal to participate in the study.

Thus, as the nature of patient selection showed, a total of 152 patients after minigastric bypass took part in the study. The main group consisted of 76 patients with postoperative anastomositis after minigastric bypass. The comparison group consisted of 76 patients who did not have postoperative anastomositis in the postoperative period.

In the majority of patients (59,2%) obesity was accompanied by type 2 diabetes mellitus. Of the total number of patients, 40.8% were between 41 years and 50 years of age. In the same proportion (25% each) were patients in the age categories of 31 to 40 years and 51 to 60 years. There were 5.3% of patients under 30 years of age and 3.9% of patients over 60 years of age.

Among patients with obesity and type 2 diabetes mellitus, patients aged 41 to 50 years (27.6%) prevailed, whereas without type 2 diabetes mellitus - patients in the age category of 31 to 40 years (17.1%). Thus, the mean age of patients in both the main and comparative groups was 46.72±9.84 years.

Of the total number, female patients prevailed (64.5%) mainly among the cases with obesity only (35.5%). Among the patients with obesity and type 2 diabetes mellitus the male patients prevailed (30,3%).

The nature of distribution of patients by body mass index showed that in the majority of cases (59.7%) patients had it at 40 kg/m2 and above (92 patients). In the second place in number (22.7%) were patients with body mass index in the range from 35 kg/m2. to 39.99 kg/m2. The remaining 27 (17.5%) patients had a BMI ranging from 30 kg/m2 to 34.99 kg/m2. The mean level of BMI equated to 43.8±7.9 kg/m2.

A total of 224 comorbidities were diagnosed in 152 patients. There were 1.5 comorbidities per 1 patient. Ischemic heart disease was the leader (41.1%) among comorbidities. Arterial hypertension was detected in 36 (16.1%) patients. Joint diseases were diagnosed in another 6 (2.7%).

Type 2 diabetes mellitus was diagnosed in 90 (40.2%) patients. In the majority of cases (38.9%) diabetes mellitus had an anamnesis duration from 1 to 4 years. Slightly fewer (32.2%) had a history of 5 to 10 years. In 17 (18.9%) patients the duration of history of diabetes mellitus was less than 1 year, and only in 9 (10%) patients - more than 10 years.

Distribution of patients according to the level of ASA anesthesia risk scale showed prevalence of patients (53.9%) with ASA III (82 patients). In 48 (31.6%) patients the index of the anesthesia risk scale was equal to ASA II. Only in 22 (14.5%) patients the index of the anesthesia risk scale equaled ASA I.

The indicators of immunologic monitoring were studied specifically to reveal their role in the pathogenesis of anastomositis development and to develop methods of predicting the development of this type of postoperative complication in patients after minigastric bypass.

The following immunologic methods of research were performed: determination of leukocytes (x109/l), lymphocytes (x109/l), its populations (T-lymphocytes x109/l and B-lymphocytes x109/l), as well as subpopulations (T-suppressors x109/l and T-helpers x109/l) in peripheral blood.

Leukocytes were determined on a hematology analyzer. Lymphocyte counting was performed according to the standard technique by counting cells in the leukocyte formula. The method of spontaneous rosette formation was used to determine the content of T-B lymphocytes.

Quantitative determination of cytokine secretion (pg/mL) TNF-α, IL-2, IL-10 and IFN-γ was determined by sandwich immunoassay using standard monoclonal and polyclonal antibodies Immunologic studies of the second level included assessment of the maximum ability of T-lymphocytes and B-lymphocytes to produce TNF-α, IL-2, IL-10 and IFN-γ cytokines. For this study, T-lymphocytes (CD4+ and CD8+) as well as B-lymphocytes (CD19+) were identified by indirect Kupz immunofluorescence test using CD series monoclonal antibodies. For this purpose, separated cells were stimulated in phorbolmyristate acetate (PMA, 50 ng/mL, Sigma Aldrich, St. Louis, MO, USA) and ionomycin (1 μM, Sigma Aldrich) medium at 1x106 cells/mL for a total of 5 hours. After 1 hour of exposure, monensin (Golgistop, BD, Erembodegem, Belgium), which is an inhibitor of cytokine secretion, was added to this medium and the process was continued for another 4 hours.

After completion of the process of stimulating T cells and B cells to produce cytokines in the artificial medium, the cells themselves were visually assessed by a modified method based on the principles of flow cytometry according to the method of N.H. Litjens et al. For this purpose, cells were stained with antibodies identifying different subpopulations of T- and B-cells and including a marker to exclude dead cells. T-helper cells were identified as CD4+ (to assess IL-2 and IFN-γ production) whereas cytotoxic T cells were identified as CD8+ (to assess IL-2 and IFN-γ production). Similarly, different B-cell subpopulations were identified by CD19+ expression (to assess IL-10, TNF-α, IFN-γ and IL-2 production).

The ability of T and B lymphocytes to produce cytokines was investigated at distant times after minigastric bypass, that is, at 3 and 6 months after surgery.

RESULTS AND DISCUSSION

The average number of leukocytes in the blood of patients with anastomosis during the whole period of the study was 11.63±0.81 x109/l. Before the operation it was equal to 9,42±0,54 x109/l [CI: 8,88; 9,96], but already on the 3rd and on the 7th day after the operation the patients of the main group had moderate leukocytosis reaching up to 13,24±0,93 x109/l [CI: 12,31; 14,17] and up to 13,13±0,82 x109/l respectively ($p<0,05$). On the 14th day of the postoperative period, the mean leukocyte count in the blood of the patients in the main group decreased, equating to 10.72±0.95 x109/L.

The randomized analysis by the degree of anastomositis development can be noted that in patients of the I subgroup the initial number of leukocytes in the preoperative period was lower than in patients of the II subgroup ($p<0,05$). In patients of each subgroup the initial value of leukocytes in blood was lower than the average value for the whole period of the study (10.58±0.69 x109/l in the I subgroup and 12.67±0.93 x109/l in the II subgroup, respectively).

In patients of the I subgroup the general dynamics of the leukocyte count in the blood was characterized by their increase on the 3rd day [CI: 12.7; 14.32] with further decrease on the 7th day [CI: 10.16; 11.62] and on the 14th day [CI: 8.35; 9.89] of the postoperative period. At the same time, the patients of the II subgroup also showed an increase in the number of leukocytes in the blood, but this process was noted not only during 3 days [CI: 11,92; 14,02] but also during 7 days [CI: 14,46; 16,28] of the postoperative period. We registered the decrease of leukocytosis in patients of the II subgroup only on the 14th day after the operation [CI: 11,19; 13,45].

The mean value of lymphocytes for the whole period of the study amounted to 2.24±0.19 x109/l [CI: 2.06; 2.43]. The initial values of lymphocyte count in the patients of the main group in the preoperative period were higher than the average values and equaled 2.36±0.27 x109/l [CI: 2.09; 2.62]. The critical level of lymphocyte decrease in patients of the main group was noted by us on 3 days after surgery 1,8±0,11 x109/l [CI: 1,69; 1,91] - $p<0,05$. However, starting from 7 days of the postoperative period we registered a rise in the number of lymphocytes up to 1.98±0.14 x109/l [CI: 1.84; 2.12] - $p<0.05$ and up to 2.85±0.23 x109/l [CI: 2.62; 3.07] - $p<0.05$ on the 14th day of study.

In patients of both subgroups, the general dynamics of lymphocyte counts changed identically. The minimum values were observed among patients of subgroup I [CI: 1.6; 1.76] and subgroup II [CI: 1.77; 2.05] on the 3rd day after surgery. In the following terms of the postoperative period there was an increase in the number of lymphocytes, but on the 14th day its level among the patients of the II subgroup significantly exceeded (1.64 times) the initial values of the preoperative period ($p<0.05$).

The number of T-lymphocytes on the average in the patients of the main group for the whole period of the study had a low confidence interval [CI: 0,97; 1,25] and equaled 1,11±0,14 x109/l. The initial value of T-lymphocytes in patients of the main group exceeded the mean values up to 1.23±0.12 x109/l [CI: 1.11; 1.35]. Low values of T-lymphocytes number were noted among the patients of the main group on the 3rd [CI: 0,67; 1,01] and 7th [CI: 0,82; 1,08] day of the postoperative period (0,84±0,17 x109/l and 0,95±0,13 x109/l, respectively). On the 14th day of the postoperative period there was an increase in the number of T-lymphocytes up to the level of 1.43±0.14 x109/l [CI: 1.29; 1.57].

The minimum value of the number of T-lymphocytes was noted by us among the patients of the I and II subgroups on the 3rd day of the postoperative period. The confidence interval for the number of T-lymphocytes was higher among the patients of the I subgroup [CI: 0.74; 1.12] than among the patients of the II subgroup [CI: 0.59; 0.89]. The similar character of changes among the patients of the I and II subgroups of the main group was noted by us on the 7th day of the postoperative period - [CI: 1.03; 1.23] and [CI: 0.6; 0.92], respectively. However, on the 14th day after the operation we revealed mirror character of changes among the patients of I and II subgroups - [CI: 1,03; 1,23] and [CI: 1,55; 1,91] respectively.

Lymphocyte subpopulations, in particular T-helpers, in patients of the main group were characterized by progressive growth throughout the dynamics of the study. The initial value of T-helpers among the patients of the main group amounted to 0.47±0.02 x109/l; [CI: 0.45; 0.49], which was 1.4 times lower than the general average value of this lymphocyte subpopulation (0.64±0.03 x109/l; [CI: 0.61; 0.67]). Such disproportion in the number of T-helper cells is explained by the increase in their number during the whole postoperative period - from 0.57±0.03 x109/l [CI: 0.54; 0.59] on the 3rd day after the operation and to 0.65±0.04 x109/l; [CI: 0.61; 0.69] and to 0.88±0.03 x109/l; [CI: 0.85; 0.9] on the 7th-14th day after the operation period, respectively.

The difference in the number of T-helper cells between patients of I and II subgroups was significantly pronounced (1.9 times; $p<0.05$). The character of dynamics of changes in the number of T-helper cells was identical: both in I and II subgroups of patients in the postoperative period there was an increase in these types of cells, reaching their maximum value on the 14th day.

In patients of subgroup I the reliable values of the confidence interval fell on the preoperative period [CI: 0,59; 0,63] and on the 14th day of the postoperative period [CI: 0,9; 0,96] that testified to the strengthening of T-helper cells expansion in this period of the disease course. In patients of the II subgroup the confidence interval reliability in the postoperative period was distributed in the following chronology: on the 3rd day [CI: 0.5; 0.52], on the 14th day [CI: 0.8; 0.84] and on the 7th day [CI: 0.59; 0.65] after minigastric bypass surgery.

T-suppressors differed from other subpopulations of T-lymphocytes by low values in early terms after minigastric bypass among the patients of the main group. So, at the initial value of T-suppressors at the level of 0,46±0,06 x109/l [CI: 0,4; 0,51], already on the 3rd day after minigastric bypass there was a decrease of this index to 0,26±0,03 x109/l [CI: 0,23; 0,29], and on the 7th day after the operation the level of T-suppressors was at the level of 0,29±0,02 x109/l [CI: 0,27; 0,31]. At the same time on the 14th day after minigastric bypass we registered a twofold increase of T-suppressors up to 0.55±0.06 x109/l [CI: 0.49; 0.61]. Due to this, the mean T-suppressor level over the entire study period was 0.39±0.04 x109/L [CI: 0.35; 0.43].

The mean level of T-suppressors among patients of subgroup I equaled 0.32±0.04 x109/L [CI: 0.28; 0.35], and among patients of subgroup II - 0.46±0.05 x109/L [CI: 0.42; 0.51].

We noted a pronounced difference between the subgroups of patients with anastomositis first of all on 14 days after surgery (2.6 times more among the patients of subgroup II). A less pronounced difference was noted in the preoperative period (1.5 times more among patients of subgroup II) and on the 3rd day after surgery (1.4 times more among patients of subgroup I).

The overall dynamics of changes in the number of T-suppressors was characterized by minimal values in patients of the I subgroup on the 7th day after surgery [CI: 0.27; 0.31] and in patients of the II subgroup on the 3rd day after surgery [CI: 0.21; 0.23].

B-lymphocytes had close confidence interval values for the whole period of the study [CI: 0.24; 0.29]. The mean static value of B-lymphocyte count equated to 0.27±0.03 x109/L, respectively. The mean baseline value of B-lymphocytes among the patients of the main group was higher than the mean total value and reached 0.31±0.03 x109/l, respectively [CI: 0.28; 0.33]. At the same time, in the overall dynamics in patients with anastomositis after minigastric bypass there was a decrease in the number of B-lymphocytes on the 3rd day (0.2±0.03 x109/l; [CI: 0.17; 0.23]) and on the 7th day after surgery (0.24±0.03 x109/l; [CI: 0.21; 0.27]). Further on the 14th day of postoperative period we found an increase in the number of B-lymphocytes in peripheral blood up to (0,33±0,02 x109/l; [CI: 0,31; 0,34].

A similar pattern of dynamics was noted among the patients of the II subgroup with the average value for the whole period of the study up to 0.26±0.02 x109/l; [CI: 0.24; 0.28]. In patients of this subgroup the wave-like changes in the amount of B-lymphocytes content in peripheral blood varied, reaching its maximum peak on the 14th day of postoperative period exceeding its own initial values 1.6 times ($p<0.05$).

High differential values between patients of I and II subgroups were noted by us on the 3rd day 1,3 times and on the 14th day 0,8 times after the operation period. In general, the average value of B-lymphocytes among the patients of I and II subgroups was lower than the initial data (0,28±0,03 x109/l and 0,26±0,02 x109/l, respectively).

Thus, the study of the character and analysis of changes in the content of leukocytes, lymphocytes, T- and B-cells in blood in patients with different forms of anastomosis after minigastric bypass showed that at uncomplicated, catarrhal form of anastomosis zone lesion the growth of lymphocytes number in blood is not manifested by expressed changes in cellular immunity indices, whereas in complicated forms of this postoperative pathologic process there is an increase in the number of T-suppressors (2.2 times) and T-helpers (1.5 times) against the background of relative stability of the number of B-lymphocytes.

When the patients of the main group of patients were analyzed separately between subgroups according to the severity of anastomosis development, it can be noted that the minimum mean value of proinflammatory cytokine TNF-α was observed among patients of subgroup I [CI: 16.15 pg/mL; 19.55 pg/mL], whereas the maximum mean level of proinflammatory cytokine TNF-α was recorded among patients of subgroup II [CI: 31.43 pg/mL; 39.91 pg/mL]. The ability to produce the proinflammatory cytokine TNF-α among patients of subgroup II was 2-fold higher than that of patients of subgroup I ($p<0.05$).

There was a progressive increase in the production of proinflammatory cytokine TNF-α among patients with postoperative anastomositis. In the confidence interval of values in the postoperative period, the minimum value of the ability to produce proinflammatory cytokine TNF-α was observed among patients of subgroup I at 3 days after minigastric bypass (14.42 pg/mL), and the maximum value was observed among patients of subgroup II (41.07 pg/mL) at 14 days after surgery. As for the maximum difference between I and II subgroups of patients by the production of proinflammatory cytokine TNF-α, we can note its presence already 3 days after minigastric bypass in 2.2 times ($p<0.05$).

When the main group of patients was analyzed separately between subgroups according to the severity of anastomosis development, it can be noted that the minimum mean value of proinflammatory cytokine IL-2 was noted among patients of subgroup I [CI: 2.41 pg/mL; 3.15

pg/mL], whereas the maximum mean level of proinflammatory cytokine IL-2 was recorded among patients of subgroup II [CI: 4.9 pg/mL; 6.11 pg/mL].

In the confidence interval of values in the postoperative period, the minimum value of the ability to produce proinflammatory cytokine IL-2 was observed among patients of subgroup I at 3 days after minigastric bypass (1.85 pg/mL), and the maximum value was observed among patients of subgroup II (6.47 pg/mL) at this time. As for the maximum difference between I and II subgroups of patients ability to produce proinflammatory cytokines IL-2, we can note its presence already in 3 days after minigastric bypass in 3.0 times ($p<0.05$), and the minimum difference we noted in the term in 7 days after minigastric bypass in 1.4 times ($p<0.05$). 5tr4

The initial value of the level of anti-inflammatory cytokine IL-10 was characterized by high values in patients of subgroup I [CI: 0.95 pg/ml; 1.21 pg/ml] and minimal - among patients of subgroup II [CI: 0.15 pg/ml; 0.29 pg/ml]. The difference between I and II subgroups of patients was 4.9 times.

In patients of the I subgroup the dynamics of the postoperative period had a wave-like character. The minimum value of anti-inflammatory cytokine IL-10 productivity was observed at 3 days after the operation [CI: 0.45 pg/mL; 0.61 pg/mL], and the maximum at 7 days after the operation [CI: 1.17 pg/mL; 1.39 pg/mL]. Thereafter, there was again a decline at a period of 14 days [CI: 1.11 pg/mL; 1.27 pg/mL] after surgery.

The maximum decrease in the productivity of anti-inflammatory cytokines IL-10 was noted by us among the patients of subgroup II. The dynamics of changes was characteristic of the I subgroup of patients. In 3 days after minigastric bypass the productivity of anti-inflammatory cytokines IL-10 was critically low [CI: 0.06 pg/mL; 0.22 pg/mL]. However, starting from 7 days after surgery, we noted a 5.1-fold [CI: 0.63 pg/mL; 0.79 pg/mL] increase in the productivity of anti-inflammatory cytokine IL-10 compared to the previous term.

The mean value of anti-inflammatory cytokine IFN-γ was equal to 2.02±0.61 pg/mL [CI: 1.41 pg/mL; 2.63 pg/mL]. The maximum value of this index in the order of 2.31±0.74 pg/mL [CI: 1.57 pg/mL; 3.06 pg/mL] occurred in the preoperative period. Not counting the period of 14 days after the minigastric bypass surgery, when we noted the rise of anti-inflammatory cytokine IFN-γ productivity up to 2,21±0,98 pg/ml [CI: 1,23 pg/ml; 3,19 pg/ml], the general dynamics was characterized by gradual decrease of this index in the postoperative period.

In general, during the development of anastomositis in the postoperative period the production of anti-inflammatory cytokine IFN-γ decreased, which was apparently due to the suppression of functional activity of T- and B-cells.

Separate analysis showed that anti-inflammatory cytokine production was high in subgroup I patients [CI: 1.56 pg/mL; 3.48 pg/mL], whereas it was minimal in subgroup II patients [CI: 1.56 pg/mL; 2.62 pg/mL]. In general, in the preoperative period, the ratio of this cytokine productivity among patients with different forms of anastomosis was insignificant.

The dynamics of changes in the productivity of anti-inflammatory cytokine IFN-γ in the postoperative period after minigastric bypass in patients of the I subgroup throughout the study only increased, reaching its maximum peak 14 days after minigastric bypass.

The difference in the productivity of anti-inflammatory cytokine IFN-γ starts already 3 days after minigastric bypass. The difference between patients of I and II subgroups was 1.7 times ($p<0.05$).

The dynamics of changes in the production of anti-inflammatory cytokine IFN-γ in patients of the II subgroup reflected the general average picture of changes in all patients of the main group. The correlation difference in the decrease of anti-inflammatory cytokine IFN-γ production in the patients of the II subgroup in relation to the patients of the I subgroup in 3 days after the operation amounted to 1.7 times ($p<0.05$), and in 7 days after the operation it increased up to 8.2 times ($p<0.05$). The difference peaked at 12 months after surgery and amounted to 9.9 times ($p<0.05$).

Thus, the complicated forms of anastomositis develop with an increase in the productivity of proinflammatory cytokines TNF-a (2.3 times) and IL-2 (2.4 times) against the background of a decrease in the productivity of anti-inflammatory cytokines IL-10 (4.5 times) and IFN-y (9.8 times), which may indicate the role of immunologic imbalance in the pathogenesis of anastomositis development after minigastric bypass.

The ability of CD19+ B-cells to produce TNF-α allowed to reveal the growth in 3-6 months, i.e. in remote terms after minigastric bypass. Thus 3 months after minigastric bypass in patients who underwent anastomosis, the level of this proinflammatory cytokine was equal to 18.4±1.7 pg/mL, and in another 3 months (6 months after surgery) - 26.3±3.4 pg/mL ($p<0.05$). The mean value for this study period of proinflammatory cytokine TNF-α production amounted to 22.3±2.5 pg/mL. At that, in patients of subgroup I [CI: 28.5; 36.1] the increase of TNF-α in blood during 3-6 months after minigastric bypass was 2 times higher than in patients of subgroup II [CI: 17.3; 23.1].

Production of proinflammatory cytokine IL-2 by CD19+ B-cells in the remote period after minigastric bypass increased by 0.8 ng/mL (from 2.3±0.1 pg/mL 3 months after surgery to 3.1±0.1 pg/mL 6 months after surgery; $p<0.05$). In contrast to the dynamics of changes in the proinflammatory cytokine TNF-α, in this case, the productive activity of CD19+ B-cells was more than 2 times greater among patients of subgroup II (3.9±0.2 pg/mL) than in patients of subgroup I (1.5±0.03 pg/mL).

The mean level of anti-inflammatory cytokine IL-10 3 months after minigastric bypass in patients with anastomoses equaled 1.7±0.03 pg/mL, and after another 3 months it decreased to 1.6±0.04 pg/mL. The ability of CD19+ B-cells to produce the anti-inflammatory cytokine IL-10 was lower in patients of subgroup I (0.4±0.02 pg/mL) than in patients of subgroup II (2.9±0.06 pg/mL) - $p<0.05$. Such character of changes testified to the increased productive ability of CD19+ B-cells in patients with complicated forms of anastomosis even in remote terms after minigastric bypass. Anti-inflammatory cytokine IFN-γ had no special difference between patients of I and II subgroups. The average level of IFN-γ in blood 3 months after minigastric bypass was 2.5±0.1 pg/mL, and 6 months later - 2.4±0.1 pg/mL. In patients of the I subgroup during the study period in the remote period after minigastric bypass increased IFN-γ production, and in patients of the II subgroup - decreased by 0.3±0.01 pg/mL.

The capacity of CD4+ T-cells to produce proinflammatory cytokines IL-2 in the distant period after minigastric bypass in patients with anastomositis was high. At 3 months after minigastric bypass, the level of anti-inflammatory cytokine IL-2 equaled 12.65±2.57 pg/mL. After following another 3 months, its blood concentration increased to 14.95±2.91 pg/mL. On average, an increase of 2.3±0.34 pg/mL was noted. Such level of increase was 2 times more in comparison with changes in the ability of CD4+ T-cells to produce anti-inflammatory cytokines IFN-γ, the amount of which increased only by 1,0±0,11 pg/mL in the distant terms after minigastric bypass, which did not express an absolute reliable difference between the chronology from 3 to 6 months.

When analyzed separately according to the presence or absence of complications of anastomositis, we found that the ability to produce the proinflammatory cytokine IL-2 by CD4+ T-cells was higher among patients of subgroup II with a difference of up to 4.3±1.56 pg/mL ($p<0.05$), whereas among patients of subgroup I the difference in the ability to produce IL-2 was 0.3±0.89 pg/mL. Similarity of character was noted by us in relation to the productivity of anti-inflammatory cytokine IFN-γ. The high productivity of anti-inflammatory cytokine IFN-γ by CD4+ T-cells among the patients of the II subgroup, which amounted to 2,2±0,27 pg/mL ($p<0,05$), in the patients of the I subgroup had the opposite picture - the productivity of anti-inflammatory cytokine IFN-γ by CD4+ T-cells decreased by 0,2±0,05 pg/mL.

In patients with anastomositis in 3-6 months after minigastric bypass the ability to produce CD8+ T-cells of the studied cytokines was characterized by the increase of both IL-2 (by 0.1±0.06 pg/ml) and IFN-γ (by 4.1±0.4 pg/ml).

The average level of proinflammatory cytokine IL-2 production by CD8+ T-cells 3 months after minigastric bypass equaled 3.45±0.18 pg/mL, whereas 6 months after surgery this ability increased to 3.55±0.34 pg/mL. Although the difference in the concentration of this proinflammatory cytokine throughout the remote period after surgery was not reliable, it nevertheless characterized the stable activity of CD8+ T-cells. In patients of the I subgroup the ability of CD8+ T-cells to produce proinflammatory cytokine IL-2 decreased only by 0.1±0.06 pg/mL, whereas in patients of the II subgroup it increased at a reliable level up to 0.3±0.03 pg/mL ($p<0.05$).

Meanwhile, the ability of CD8+ T-cells to produce anti-inflammatory cytokine IFN-γ in remote terms after minigastric bypass only increased, and more significantly (10 times more) in patients with complicated forms of anastomositis than in patients with uncomplicated forms of this pathological process.

CONCLUSION

1. The nature and analysis of changes in the production of proinflammatory and anti-inflammatory cytokines in patients with various forms of anastomosis after minigastric bypass showed that in the remote period there was an increase in the ability of CD4+ T-cells to produce IL-2 and IFN-γ, which was comparable between the subgroups of patients ($p<0.05$).

2. The ability of CD8+ T-cells to produce cytokines in patients with uncomplicated form of anastomosis did not change, but in patients with complicated form of anastomosis there was a significant increase in the production of IFN-γ against the background of a relatively low proportion of IL-2 production.

3. The ability to produce TNF-α, IL-2 and IFN-γ in patients with anastomositis differed by significant ($p<0.05$), indicating a more significant role and activity of CD19+ B-cells in the distant period after minigastric bypass surgery.

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