KARAGANDA STATE MEDICAL UNIVERSITY

Clinical trial protocol

“Nutritional support for patients operated on with malignant tumors of the hepotopancreatoduodenal zone in the early postoperative period”

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Brief Summary: A pressing concern involves the efficient and intensive treatment of complications arising from malignant tumors in the hepatopancreatoduodenal region. This matter is closely tied to rectifying energy deficits, addressing insufficient body weight, and restoring proper metabolic processes. This is particularly crucial post-surgery, as the process is hindered by significant hypercatabolism, heightened nutritional requirements, and the presence of intoxication syndrome.

Methods. An investigation was carried out on 91 individuals aged 18 years and older who were afflicted with malignant tumors situated in the hepatopancreatoduodenal area. These patients were categorized into three distinct groups, each receiving a different form of nutritional assistance.

The assessment encompassed various aspects of the patients' nutritional well-being, including outcomes from the screening protocol, body mass index, basal metabolic rate, and critical laboratory measurements such as blood lymphocyte count, total protein level, total bilirubin concentration, as well as ALaT and ASaT levels.

Keywords: nutritional status, nutritional deficiency, nutritional support, sips, oncology, nutrition, tumors of the hepatopancreatobiliary zone.

I. Purpose of the study and introduction.

Purpose of the study. Comparative analysis of the degree of influence of isolated enteral, isolated parenteral and mixed type of nutritional support on the nutritional status of cancer patients after operations performed in the hepatopancreatoduodenal zone in connection with malignant neoplasms in the early postoperative period.

Research objectives:
1. To conduct a comparative assessment of the dynamics of nutritional deficiency and nutritional status of patients operated on for malignant tumors of the hepatopancreatoduodenal zone in the early postoperative period during isolated enteral, isolated parenteral and mixed types of nutritional support.
2. To analyze the dynamics of the state of protein and carbohydrate metabolism, the consistency of liver function in cancer patients operated on for malignant tumors of the hepatopancreatoduodenal zone, against the background of isolated enteral, isolated parenteral and mixed type of nutritional support in the early postoperative period.
3. To determine the degree of effectiveness of these methods of nutritional support in this category of patients based on the totality of the results of assessing nutritional status and the dynamics of the level of basal metabolism in patients in the early postoperative period.

Introduction. Treatment of malignant tumors of the hepatopancreatobiliary zone is one of the most pressing problems in clinical oncology. Among diseases of the liver and extrahepatic biliary tract, the most severe can be considered those that are accompanied by persistent obstruction of the main bile ducts with the subsequent development of obstructive jaundice (MJ), the treatment of which is still controversial.

Despite the increased availability of various highly sensitive non-invasive methods for diagnosing tumors of these organs, the detection of cancer of these organs in the early stages of the disease has practically not increased. In the vast majority of cases, patients continue to be admitted to specialized hospitals only with the development of various complications of cancer of the pancreatoduodenal zone, such as obstructive jaundice, duodenal obstruction, hepatic-renal failure, tumor invasion of hollow organs and bleeding into the lumen of the gastrointestinal tract (Patyutko Yu.I., Kotelnikov A.G., 2007).

43-87% of patients with malignant neoplasms of various localizations have pronounced disturbances in body composition, which correlate with the prevalence of the tumor process and are aggravated during combined treatment. This is based on disturbances in protein, carbohydrate and fat metabolism caused by the systemic effect of the tumor on the body. Violation of nutritional status has a significant impact on the outcome and prognosis of the disease, inevitably increases the duration and cost of treatment, contributes to an increase in mortality and the number of complications, such as infection, slower wound repair, immunosuppression, hemocoagulation disorders, decreased concentrations of blood plasma proteins and a number of enzymes, metabolic disorders medications, decreased tolerance to surgical treatment, radiation and chemotherapy. BUT. Stadley showed that when depleted patients lost 20% of their initial body weight, mortality after surgery reached 33%, and in non-depleted patients -3.5%. According to B.R. Bistrian, G.L. Blakburn, with a 5% decrease in body weight during hospital stay, the length of stay increases by 2 times, and the frequency of complications increases by 3.3 times. J.L. Mullen and G.P. Buzby (1980) showed that impaired nutritional status in surgical patients leads to an increase in postoperative complications by 6 times, and mortality by 11 times, while timely administration of adequate nutritional therapy to such depleted patients reduces the number of postoperative complications by 2-fold. 3 times, and lethality - 7 times.

In this regard, the importance of accurately assessing the nutritional status of patients is obvious, which is the first step in treating and preventing further progression of malnutrition. A variety of methods are used to assess a patient's nutritional status. The use of enteral nutrition in the postoperative period contributes to the rapid elimination of intestinal paresis, early activation of intestinal motility, improved regeneration of the intestinal mucosa and activation of its absorption function.

The possibility of preventing excessive microbial contamination of the gastrointestinal tract, a preventive effect against acute erosive and ulcerative injuries, stopping the catabolic direction of metabolism, normalizing the immune status, reducing the number of infectious complications, reducing the time of stay of patients in the hospital were also noted [Bakhman A L, 2001, ShcherbakovaGN, 1996, KostyuchenkoAL, 2001, GrämlichL, 2004, MertesN, 2000, KomplanL, 1999]. There are difficulties in developing protocols and methods for assessing nutritional status and the effectiveness of enteral nutrition in the early postoperative period in patients with hepatopancreatobiliary diseases.

To solve the problems of perioperative nutritional support during extensive surgical interventions on the abdominal organs, aimed at eliminating metabolic disorders and fully meeting the energy-plastic needs of the body, as well as to eliminate preoperative nutritional deficiency, both parenteral and enteral nutrition are used [Levit D.A., 2008, Davidson, W., 2004, Olofsson B., 2007, Awad S., 2012].

II. Criteria for selecting study participants.

1. Number of participants. (91 patients), will be divided into 3 groups

1. The first group (n=31) included patients who received enteral nutrition (EN) after surgery.
2. The second group (n=30) included patients receiving parenteral nutrition (PN).
3. The third group (n=30) receiving mixed nutrition (MN), as is commonly considered the method of partial parenteral nutrition, in the early postoperative period.

2. Gender distribution

The study will include both genders.

3. Age.

Age from 20 to 75 years.

4.Nationality (ethnicity).

The racial and ethnic distribution of participants was not significant, so the study included individuals of varying national and ethnic backgrounds.

5.Criteria for inclusion.

- patients or relatives who consented to participate in the study (informed consent).
- patients with concomitant diseases (cardiovascular disease, liver and kidney dysfunction, lung diseases) that may complicate the course of the operation and the postoperative period, or patients who have previously undergone various operations.

6. **Criteria for exclusion.**

-age up to 20 years, pregnant and lactating
- patients with an unstable condition, unstable hemodynamics or severe concomitant pathology in the acute stage.

7. Vulnerable groups.

The study did not include participants who are considered to be in a vulnerable group.

III. Methods and procedures

Study plan:

1) Content analysis of medical documentation.

IV. 2) Obtaining informed consent;

3) Biochemical studies: transaminases, thymol test, urea, creatinine, study of total protein and its fraction, state of nitrogen metabolism, blood glucose level, body mass index

4) Study of the acid-base state and gas composition of the blood.

5) Control of tests before and in the early postoperative period against the background of ongoing nutritional support (determining quantitative ratios of fat mass, water and dry matter in patients before surgery and in the early postoperative period).

6) Determination of the immunological state before and after surgery as part of nutritional nutrition.

1. Methods and procedures.

At the first stage, modern ideas about methods for assessing nutritional status and methods of nutritional support in the early postoperative period of patients operated on for malignant tumors of the hepatopancreatoduodenal zone were studied.

At the second stage, taking into account the need to select the optimal method of nutritional support in the early postoperative period, patients underwent an intragroup and intergroup comparative analysis of the main clinical and laboratory indicators, reflecting the most satisfactory dynamics of plastic processes regarding the type of nutritional support: enteral, parenteral and mixed.

To solve these problems, a prospective, longitudinal, parallel study and retrospective analysis of the results of treatment of 91 patients with malignant tumors of the hepatopancreatoduodenal zone who underwent the following operations were carried out:

1) resection of various segments of the liver;
2) hemihepatectomy;
3) transhepatic drainage of the right and left hepatic duct;
4) bypass gastroenteroanastomosis or cholecystoenteroanastomosis with interintestinal enteroenteroanastomosis according to Brown;
5) gastro-pancreatoduodenal resection;
6) corporecaudal resection of the pancreas with splenectomy.

The study was carried out on the basis of the KGP at the RVC “Multidisciplinary Hospital No. 3 of the city of Karaganda”. Venue: intensive care unit.

To identify nutritional deficiencies, there are screening methods recommended by the international clinical nutrition associations ASPEN (American Society for Parenteral and Enteral Nutrition - ASPEN) and ESPEN (European Society for Parenteral and Enteral Nutrition - ESPEN), including questioning patients, using standard anthropometric and laboratory data, which makes it possible to assess nutritional status and the degree of its impairment.

At the first stage, the clinical condition of the patient was assessed using the Nutritional Risk Screening (NRS, 2002), Subjective Global Assessment (SGA) and Nutritional Risk Index (NRI) protocols before surgery and on the 5th, 10th, 15th day after surgery .

A comparative assessment of the clinical effectiveness of the use of types of nutritional nutrition in a complex of therapeutic measures after these operations in the hepatopancreatoduodenal zone was carried out.

Some nutritional status indicators available for determination at the Oncology Clinic were assessed - body mass index (weight measurements were carried out before surgery, on the 5th, 10th and 15th days), basal metabolic rate (calculated using the Harris-Benedict equation, based on anthropometric data of the patient (gender, age, weight and height).), laboratory parameters: blood hemoglobin, lymphocytes, total protein, serum albumin, serum transferrin, total bilirubin and direct, ALT, AST, which are related to the traditional method for assessing nutritional status.

Additionally, we assessed the duration of postoperative gastrostasis, the timing of the onset of intestinal motility, the appearance of stool, the return to a normal diet, the length of patients' stay in the ICU, the readmission of patients to the ICU and the duration of the postoperative bed-day, and the incidence of complications was calculated.

2. Data analysis and monitoring.

Statistical processing of the obtained data will be carried out using the application package STATISTICA version 7.0, taking into account computational methods recommended for biology and medicine. Statistical research methods include: calculation of median and mode, standard deviation. To determine the reliability of the obtained indicators, Student's t-test will be used. Also calculate the pairwise correlation coefficient according to Pearson.

3. Data storage and confidentiality.

Confidentiality is ensured by encrypting the personal data of the subject with a digital code. Storage of information about patients is carried out in writing in the registration journal of the research topic, in electronic form on a computer in the databases of Microsoft Excel and STATISTICA 7.0 programs. The head and executor of the research topic have access to the data. The results of the research, without indicating personal data, will be used to write a doctoral dissertation, the results of the research will be published in print and electronic publications and reported at conferences.

IV. Risk/benefit assessment

1. Degree of risk.

When conducting research, the degree of risk is minimal. Before the study, participants will be interviewed to explain the purpose and methods of the study. Minimal risk means that the likelihood and magnitude of harm or discomfort expected in the study is no greater than would normally be encountered in everyday life or while receiving routine physical or psychological tests. The study will be conducted in compliance with all requirements and safety measures.

2. Potential risk.

During the study, exacerbation of pre-existing, chronic diseases is possible. In this case, the patient is excluded from the study and all necessary support and correction measures are taken.

3. Protection from risk.

This procedure is introduced voluntarily and participants or other legal representatives of the patient have the right to refuse the examination. In order to exclude exacerbations of pre-existing chronic diseases, a thorough medical history will be taken and concomitant pathology taken into account.

4. The potential benefit for the participant is the possibility of early nutritional support in cancer-surgical patients, receiving timely recommendations on lifestyle management, prevention, treatment and rehabilitation.

5. Alternatives for the participant.

Participants have the right to refuse the proposed research method. In this case, treatment will be carried out using the traditional method. Without the written consent of the participant or legal representatives, the patient cannot be included in the study.

V. Identification of Study Participants, Recruitment and Consent

Before each study, patients are explained the goals and objectives of the study, informed of their right to refuse examination at any stage, and written consent to undergo treatment is obtained.

1. Methods for identifying participants and recruiting them.

The subjects will be selected by a continuous method during screening and patients with cancer pathology will be randomly selected.

2. Consent process.

The consent process will be carried out by the researcher in the form of written consent after explaining to the participants the purposes and methods of the study, as well as all potential risks, in accordance with the norms of the standard of Good Clinical Practice (GCP).

3.Participant's condition.

It is necessary to obtain informed consent from the patient in person. If it is not possible to obtain informed consent, the patient is not included in the study.

4.Understanding.

After the goals and objectives of the study have been explained and potential benefits and risks have been discussed with the participant, the participant will be asked to sign an informed

consent form. The patient may refuse to participate in the study if he wishes. Children and incapacitated adults will not be included in the study.

5.Consent forms.

The informed consent form is presented in Appendix 1 to this protocol.

6. Documentation of consent.

Informed consent, in two copies, is voluntarily signed by the study participant and the research physician, and one copy remains with the research subject, the second is stored in the study file and the registration journal of the research topic.

7. Participation price.

There is no cost of participation for patients.

8.Participation fee.

There is no payment to the participant.

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Informed consent form for participation in a clinical trial

Head of the study: Kani Zhumkenovich Musulmanbekov

Responsible researcher: Davanov Sherzad Kurbanalievich

To solve the problems posed to the researcher it is necessary: a comparative assessment of various methods of parenteral (infusion) nutritional support. The patient has the right to refuse the proposed studies.

The criteria for interrupting the participation of individual study participants is: the presence of concomitant somatic pathology, in case of patient refusal from the study.

The patient receives treatment in full according to the Medical and Economic Standard.

All information received is strictly confidential and is not subject to disclosure.

The patient can receive additional information about the progress of the study by calling:

Written consent of the patient to conduct the above studies

I,_____, live at ,
tel. identification
No., issued by the physician-researcher _____
About the nature of the planned clinical
research_____

I received written and oral information about the goals, objectives, and nature of the upcoming clinical trial.

I had the opportunity to discuss with the researcher all the questions that interested me and get clarification on them.

I voluntarily agree to take part in a clinical study, I am informed that I have the right to refuse or at any time to stop participating in this study, without explaining the reasons for my decision.

I agree to follow the instructions, cooperate in good faith with the research doctor and immediately inform him of any kind of disturbance in my health or changes in my well-being.

I agree that the information obtained during the clinical trial will be used for scientific purposes.

I have been advised that if my health is harmed as a result of my participation in a clinical trial, I will be compensated by the investigator. The amount or terms of compensation may be revised if I am at fault for the deterioration in my health.

Received a signed and dated copy of the study participant's informed consent to participate in the clinical trial.
On three (3) pages.

Signature of study participant date

I confirm that I have explained in detail the purpose and possible risks of the clinical trial to the participant
research_____
Signature
responsible researcher_____
Date of_____

I confirm that I have witnessed the explanation given by the research physician to the study participant and the fact of signing the informed consent.

FULL NAME.

independent witness_____
Signature
Independent witness_____date_____

Signature
Research director_____date_____

Karaganda Medical University

Report

"Nutritional support for patients operated on with malignant tumors of the hepotopancreatoduodenal zone in the early postoperative period"

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Karaganda 2020

Report

№ MUK_NutS-HPD-PO_2017 from March 17, 2020

Karaganda Medical University

This study was approved by the Karaganda Medical University of the city of Karaganda of the Republic of Kazakhstan. Research and Ethics Committee of February 12, 2020 Protocol №4. All methods were carried out in accordance with ethical principles and rules approved by the ethics committee.

The clinical trial period was started in January 2017 and completed in March 2020

Purpose of the study: To improve the nutritional status of cancer patients after operations performed in the hepatopancreotoduodenal zone in connection with malignant neoplasms, through a comprehensive comparative analysis of the effectiveness of isolated enteral, isolated parenteral and mixed type of nutritional support in the early postoperative period.

Scientific hypothesis

Complete and comprehensive nutritional support for patients operated on for malignant neoplasms of the hepatopancreatoduodenal zone, in the form of various approaches and methods of delivering nutrients to patients in the early postoperative period, allows to improve the functional activity of the gastrointestinal tract of patients, stabilize the level of carbohydrate, protein, basal metabolism, accelerate transfer to full enteral nutrition and reduce the length of stay in the intensive care unit and, ultimately, in the hospital.

Research objectives:

1. To conduct a comparative assessment of the dynamics of nutritional deficiency and nutritional status of patients operated on for malignant tumors of the hepatopancreatoduodenal zone in the early postoperative period during isolated enteral, isolated parenteral and mixed types of nutritional support.

2. To analyze the dynamics of the state of protein and carbohydrate metabolism, the consistency of liver function in cancer patients operated on for malignant tumors of the hepatopancreatoduodenal zone, against the background of isolated enteral, isolated parenteral and mixed type of nutritional support in the early postoperative period.

3. To determine the degree of effectiveness of these methods of nutritional support in this category of patients based on the totality of the results of assessing nutritional status and the dynamics of the level of basal metabolism in these patients in the early postoperative period.

Researched 91 patients, will be divided into 3 groups:
1. The first group (n=31) included patients who received enteral nutrition (EN) after surgery.
2. The second group (n=30) included patients receiving parenteral nutrition (PN).
3. The third group (n=30) receiving mixed nutrition (MN), as is commonly considered the method of partial parenteral nutrition, in the early postoperative period.

Clinical research program:

The study was carried out on the basis of the KGP at the RVC “Multidisciplinary Hospital No. 3 of the city of Karaganda”. Venue: intensive care unit.

To identify nutritional deficiency, there are screening methods recommended by the international clinical nutrition associations ASPEN (American Society for Parenteral and Enteral Nutrition - ASPEN) and ESPEN (European Society for Parenteral and Enteral Nutrition - ESPEN), including questioning patients, using standard anthropometric and laboratory data, which makes it possible to assess nutritional status and the degree of its impairment.

At the first stage, the clinical condition of the patient was assessed using the Nutritional Risk Screening (NRS, 2002), Subjective Global Assessment (SGA) and Nutritional Risk Index (NRI) protocols before surgery and on the 5th, 10th, 15th day after surgery .

A comparative assessment of the clinical effectiveness of the use of types of nutritional nutrition in a complex of therapeutic measures after these operations in the hepatopancreatoduodenal zone was carried out.

Some nutritional status indicators available for determination at the Oncology Clinic were assessed - body mass index (weight measurements were carried out before surgery, on the **5th**, **10th** and **15th** days), basal metabolic rate (calculated using the Harris-Benedict equation, based on anthropometric data of the patient (gender, age, weight and height).), laboratory parameters: blood hemoglobin, lymphocytes, total protein, serum albumin, serum transferrin, total bilirubin and direct, ALT, AST, which are related to the traditional method for assessing nutritional status.

Additionally, we assessed the duration of postoperative gastrostasis, the timing of the onset of intestinal motility, the appearance of stool, the return to a normal diet, the duration of patients' stay in the ICU, the repeated admission of patients to the ICU and the duration of the postoperative bed-day, and the incidence of complications was calculated.

Methods of statistical data analysis

All patients hospitalized for special treatment with a verified diagnosis of a malignant neoplasm were subjected to the study in the abdominal department of the KGP at the Regional Oncological Dispensary, Karaganda.

The quantitative and qualitative indicators obtained during the study were analyzed using descriptive and analytical statistics methods. For statistical processing of qualitative (diagnosis codes, dichotomous data) and quantitative variables: symptom intensity, severity, frequency of occurrence, we used the calculation of the median level (Me) with 25%-75% quartiles (Q25; Q75) and the calculation of the arithmetic mean (M) with error (m) and 95% confidence interval (95% CI), standard deviation (s). Quantitative variables were checked for normality of distribution using the Kolmogorov-Smirnov test, as well as the module of Skewness and Kurtosis for quantitative variables $|\leq 2|$. Differences in the 3 groups of patients for quantitative variables corresponding to a normal distribution were identified using the Student's t test for unrelated groups, first for 3 or more groups, and then in pairs for each pair using the Student's t test. Differences for rank variables, or quantitative but not normally distributed for unrelated groups, were determined by the Kruskal-Wallis test or median test for 3 groups, and then pairwise or non-parametric Mann-Whitney test for each of the 3 pairs (groups 1 and 2, groups 1 and 3, groups 2 and 3), and for related groups (dynamic observations) by the Kendall test for 3 groups and then by the Wilcoxon test (Wilcoxon) for each of the 3 pairs (baseline, after 5 days and after 10 days).

Correlation was performed for quantitative variables according to Pearson and for rank variables according to Spearman. Statistical processing of the results was carried out using the Statistica program version 10.

Results and discussion. The nutritional status of patients in all three groups before surgery and during the 10-12 days of the postoperative period according to the methods of assessing nutritional status NRS, SGA and NRI was assessed as normal, moderate and severe malnutrition

As can be seen from the presented data, in the preoperative period, according to the SGA assessment, 24 patients in the enteral group, 19 patients in the parenteral group, and 17 patients in the mixed group had normal nutritional status before surgery, with variations relative to patients with moderate to severe malnutrition. Assessment of nutritional status before surgery using the NRI scale allowed us to confirm the nutritional status of the vast majority of patients in all groups as relatively normal

Thus, in 62 of the 91 patients examined, the NRI was assessed as true negative (normal nutritional status), in 26 as true positive (moderate malnutrition), and in 3 as severe malnutrition. Data from the NRI method during this time period had a strong correlation with the results of the SGA scale ($p < 0.005$).

On the 10-12th day of the postoperative period in patients of the “enteral” group, the results of the assessment on the SGA scale remained unchanged; according to the NRI rating scale, there was an increase in “moderate malnutrition” per patient (25%).

With parenteral nutritional support, 17 patients had “normal nutrition”, 14 patients had moderate malnutrition, with regression of “severe malnutrition” in 1 patient. In the mixed nutrition group, there was a complete elimination of signs of “severe malnutrition” by 100% according to the given scales ($p <0.005$).

In patients of all study groups, throughout the entire period of nutritional support, fluctuations in the level of basal metabolism were observed in average values of 335.89±53.6 kcal/day (13.44%) from the initial value - 1-2 days of the postoperative period and were due to variability body mass index and the dynamics of the temperature curve after surgery.

In patients in the groups with enteral and parenteral nutrition, by the end of these types of energy subsidies (days 10-15), the level of basal metabolism was observed to approach its initial values - 2500.1±353.4 kcal/day and 2350.0±330.5 kcal/day days accordingly. With a mixed type of nutrition, there was a statistically significant decrease in the level of basal metabolism by 6.78% (2250.0±105.2 kcal/s), which allows us to conclude that patients’ energy costs are more effectively covered with this option of nutritional support in a comparative aspect with isolated types nutrition ($p<0.03$).

This fact was obviously associated with the preservation/restoration of parietal digestion in the gastrointestinal tract in the early postoperative period, despite postoperative intestinal paresis of varying degrees, and the involvement of nutrients in anabolic processes with parallel “covering” of the required daily caloric intake by parenteral administration of mixtures.

Evaluation and subsequent analysis of the results of laboratory examination in groups of patients in a comparative aspect showed a relatively slow and gradual decrease in the level of total blood protein by the 5th day of the postoperative period, on average, by 6.8±0.95% of the initial values, which,

apparently , was due to increased catabolism and ongoing protein losses (exudation, drainage, etc.) with a fairly significant increase by the end of nutritional support.

Thus, a statistically significant increase in the level of total blood protein was noted in the mixed nutrition group ($p = 0.004$). In the groups with enteral and parenteral nutrition, differences in the dynamics of total protein levels were found at the level of a statistical trend: $p=0.108$ and $p=0.129$, respectively.

When analyzing changes in the number of blood lymphocytes, it should be noted that before the operation the relative value of lymphocytes in the groups was significantly reduced (25.9±3.7%), but taking into account the methods and volumes of the operation, the tension of the cellular and humoral parts of the immune system, the dynamics of their level was expressed in the form of a statistically significant increase in the level of lymphocytes in the postoperative period by 10-12 days.

Thus, there was a steady increase in the level of blood lymphocytes by the 10th day of the postoperative period in all groups, on average by 8.95% ($p = 0.000$), by 10.35% ($p = 0.003$), by 10.91% ($p = 0.000$) respectively.

This dynamics reflects the positive effect on the immune status of patients of the combined use of parenteral and enteral types of nutritional support in the postoperative period in this group of patients.

A comparative analysis of the dynamics of ALT and ASAT values in all patients in the study groups on the 2-3, 6-8, 10-12 days of the postoperative period reflected an excess of their normal values after surgery in some patients tens of times in the first day of the postoperative period. These changes can be explained, first of all, by the surgical intervention itself and its volume, the underlying disease of the hepatopancreatoduodenal zone and the associated cytolytic syndrome against the background of cholestasis [9,10,11].

In terms of assessing the dynamics of blood transaminase levels, in the majority of patients in the first group (78.2%), by the 5th and 10th days there was a decrease in ALT and AST values, on average, by 32.1 and 40.15%, respectively.

In the overwhelming number of patients in the second group (81.6%, n=26), a statistically significant decrease in the level of these blood transaminases was also recorded, on average by 72.2% by the fifth day and 66.7% by the 10th day of the postoperative period from level of their initial indicator.

With a mixed type of nutritional support, by the 5th day of the postoperative period, the average significant decrease in transaminases was, on average, up to 72.6% of the initial values ($p = 0.000$); by the 10th day of the postoperative period, their level decreased to 63.8% from the previous achieved value of 5 days ($p=0.008$).

When comparing analyzes of the level of total blood bilirubin in patients of all nutrition groups, there was a strong direct correlation with a decrease in the level of blood transaminases, which, apparently, was also due to the creation of sufficient intraoperative bile outflow due to drainage of the biliary tract and elimination of the cause of obstructive jaundice (tumor).

However, high values of total blood bilirubin that persisted on the first day after surgery were due to temporary swelling of the biliary tract, which caused the excess of the norm by more than 10 times ($p = 0.000$).

On days 5-7, there was a tendency towards a 5-6 fold decrease in its level from the initial values, which gradually decreased to normal values by days 10-12 and in some patients persisted until discharge from the hospital ($p = 0.004$).

In comparative quantitative terms, in patients of the first group, a decrease in the level of total bilirubin was recorded, on average, by 12.7% only by the 10th day after surgery ($p = 0.187$). In the second group, there was a decrease in the level of total blood bilirubin by the 5th day, on average, by 40.09% and by the 10th day by 45.0% from its initial values (preoperative period), ($p = 0.002$).

In patients of group 3, there was a slower regression of this indicator: a decrease, on average, by 20.0% by the 5th day and by 44.0% by the 10th day of the postoperative period [1,5,12].

Conclusion:

1. According to the NRI nutritional status assessment scales, the SGA mixed type of nutritional support at the time of transfer of patients to the specialized department and upon completion of this area of intensive therapy in the specialized department by 12-15 days of the postoperative period showed higher effectiveness in stabilizing the condition and maintaining the patients' caloric intake in a comparative aspect with the group of isolated enteral nutrition and parenteral nutrition.

2. Throughout the entire period of isolated enteral, parenteral and mixed nutritional support, all patients (100%) showed a relatively constant level of total blood protein.

3. In patients of all three groups, throughout the entire period of nutritional support, fluctuations in the level of basal metabolism were observed, which was due to the variability of body mass index and the dynamics of the temperature curve after surgery. In patients in the groups with enteral and parenteral nutrition, by the end of nutritional support (days 15-20), the level of basal metabolism was observed to approach its initial values. With a mixed type of nutrition, a statistically significant decrease in the level of basal metabolic rate was observed, which suggests a more effective coverage of the energy costs of patients with this option of replenishing nutritional ingredients.

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