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COMPARATIVE REVIEW

Peculiarities of nutritional support in patients with neoplasms of the hepatopancreatoduodenal zone as a component of intensive therapy in the postoperative period

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ABSTRACT

BACKGROUND: 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.

OBJECTIVE: To consider the features of nutritional support in patients with tumors of the hepatopancreatoduodenal zone in the early postoperative period.

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.

RESULTS: Under the provision of parenteral nutritional support, as per the applied screening protocols, a span of 10 to 12 days saw 17 patients sustaining a "normal" nutritional state, while 14 patients experienced a condition of "moderate malnutrition." Notably, one patient (3.2%) demonstrated a regression from the status of "severe malnutrition."

In the mixed nutrition group, within the same 10 to 12-day timeframe post-operation, there was a rise in the prevalence of patients classified as having "moderate malnutrition" according to the SGA and NRI scales by 10% and 6.7%, respectively. Remarkably, all indicators pointing to "severe malnutrition" were entirely eliminated as assessed by the mentioned nutritional evaluation scales ($p<0.005$).

CONCLUSION: A notable degree of effectiveness in stabilizing and upholding the nutritional condition of patients was attainable within the isolated parenteral nutrition group. This achievement was realized by elevating the count of patients classified under "moderate" and "normal" nutritional statuses, and concurrently diminishing the number of patients experiencing severe and moderate nutritional insufficiency, respectively. The mixed type of nutritional support in this case can be considered with a high degree of probability as an alternative replacement for parenteral nutrition, due to the statically similar indicators of the nutritional status of patients achieved in this study *(Fig. 4, Ref. 12)*. Text in PDF www.elis.sk

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

Abbreviations: ALAT–Alanine aminotransferase, ASAT–Aspartate aminotransferase, SGA–Subjective Global Assessment, NRI–Nutritional Risk Index, ASPEN–American Society for Clinical Nutrition and Metabolism, ESPEN–European Society for Clinical Nutrition and Metabolism

Introduction

Treating tumors located within the hepatopancreatoduodenal region and managing associated complications stands as a pivotal responsibility for both oncologists and intensivists. The significance of this subject stems from the growing count of individuals afflicted with abdominal cancer, necessitating supplementary

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external energy intake and correction of nutritional statuses during the postoperative phase. This surge in patient numbers persists despite advancements in non-invasive techniques for detecting tumors within the abdominal cavity and specifically the hepatopancreatoduodenal zone (1, 2). Notably, among all forms of malignant tumors, those found in the hepatopancreatoduodenal region hold a distinct position due to the emergence of complications like obstructive jaundice, liver insufficiency, and nutritional insufficiency during the perioperative period, all of which amplify the risk of mortality.

In order to identify nutritional insufficiencies, internationally recognized clinical nutrition associations such as ASPEN (American Society for Clinical Nutrition and Metabolism) and ESPEN (European Society for Clinical Nutrition and Metabolism) suggest employing screening methodologies. These approaches encompass patient surveys as well as the utilization of conventional anthropometric measurements and laboratory information. This comprehensive approach facilitates the evaluation of both nutritional status and the extent of any impairments present (3, 4).

Early identification of tumors in patients and the evaluation of their nutritional status at the outpatient level during the study have the potential to mitigate the risks associated with these complications. This can be achieved through the implementation of diverse screening techniques and assessment scales (e.g., Subjective Global Assessment, SGA; Nutritional Risk Index, NRI) to gauge the condition of patients, aiding in early nutritional intervention in conjunction with surgical treatment methods (4, 5). Preventing early postoperative complications proves to be highly effective, given that a substantial portion (up to 70–80%) of cancer patients experience varying degrees of nutritional deficits. These deficits can subsequently lead to complications during the postoperative phase due to pronounced hypercatabolism and the heightened demand for nutritional components by the body.

The selection of an appropriate nutritional approach remains a pertinent concern for numerous clinicians and researchers. This is especially true in cases involving intricate surgical procedures within the hepatopancreatoduodenal area, where tailored strategies are required. Unfortunately, the literature currently offers insufficient coverage on this matter, underscoring the necessity for further investigation and practical implementation in the realm of clinical oncology.

The primary objective of this study was to enhance the nutritional well-being of cancer patients who undergo surgical procedures within the hepatopancreatoduodenal zone due to malignant neoplasms. This was achieved through a comprehensive comparative assessment of the efficacy of three distinct nutritional support methods: isolated enteral, isolated parenteral, and mixed approaches, all conducted during the immediate postoperative period.

The study aimed to achieve the following objectives: To perform a comparative evaluation of the changes in nutritional deficits and nutritional statuses among patients who underwent surgery for malignant tumors located in the hepatopancreatoduodenal region. This assessment was carried out during the initial postoperative period while utilizing three different nutritional approaches: isolated enteral, isolated parenteral, and mixed nutrition.

To analyze the fluctuations in protein and carbohydrate metabolism, as well as the coherence of liver function in cancer patients who underwent surgical intervention for malignant tumors within the hepatopancreatoduodenal zone. This analysis was conducted in the context of the aforementioned types of energy supplementation during the early postoperative phase.

Material and methods

To address the defined objectives, a combination of methods was employed, including a prospective longitudinal parallel study and a retrospective analysis of treatment outcomes. This involved investigating a cohort of 91 patients diagnosed with malignant tumors in the hepatopancreatoduodenal region. The study encompassed both male participants (n=49) and female participants (n=44), all of whom were above the age of 18 years.

In accordance with the extent, severity, and distribution of the cancerous condition, appropriate surgical interventions were undertaken, categorized as either radical or palliative procedures. These surgical interventions included: 1) resection of various segments of the liver; 2) hemihepatectomy; 3) transhepatic drainage of the right and left hepatic duct; 4) bypass gastro-enteroanastomosis or cholecysto-enteroanastomosis with inter-intestinal entero-enteroanastomosis according to Brown; 5) gastro-pancreatoduodenal resection; 6) corporocaudal resection of the pancreas with splenectomy.

The predominant portion (84.7%) of the surgical procedures involved combined interventions targeting the intestines, liver, and pancreas concurrently. This trend was attributed to the considerable magnitude and progression of the oncological condition within this region, leading to a complete, albeit temporary, failure of intestinal function during the immediate postoperative phase.

Among certain patients (n=28, 30%), the illness was further complicated by obstructive jaundice, necessitating either preoperative or intraoperative relief of biliary tract obstruction. The average duration of jaundice following surgery was recorded as 15.5±3.3 days.

The first group (n=30) included patients who received enteral nutrition (EN) after surgery. The second group (n=31) included patients who received parenteral nutrition (PN) and the third group (n=30) included patients who received mixed nutrition (MP) as a variation of the partial parenteral nutrition technique. At the first stage, the clinical condition of patients was assessed according to the SGA and NRI screening protocols before surgery, on the 10th and 12th days after surgery.

A comparative assessment of the clinical effectiveness of various nutritional support methods was conducted as part of a comprehensive therapeutic approach following surgeries within the hepatopancreatoduodenal region. Furthermore, critical indicators of nutritional well-being were evaluated, including: Body mass index (weight measurements taken before surgery, on the 10th, and 12th days). Basal metabolic rate, computed using the

Harris–Benedict equation, relying on the patient's anthropometric details (gender, age, weight, and height).

Laboratory parameters encompassing blood lymphocyte count, total protein level, total bilirubin concentration, ALaT (alanine aminotransferase) level, and ASaT (aspartate aminotransferase) level. These parameters are conventionally used in assessing nutritional status (6, 7).

Within each patient group, postoperative nutritional support commenced from the second day onwards. This support was based on the average estimated energy requirement of 35 kcal/kg. Highly concentrated glucose solutions (10% and 20%) were employed to ensure the adequate energy supplementation during the postoperative phase without necessitating an escalation in the daily volume of support. Starting from the third day until patients were transferred to the specialized department, 20% glucose solutions were administered. To facilitate the absorption of separately administered glucose, short-acting insulin was introduced, with a dosage of 1 international unit (IU) of insulin for every 4 grams of dry glucose (6, 8).

Patients belonging to the isolated enteral nutrition group received nutrient blends through a nasogastric tube. Initially, these mixtures were administered at a rate of 25–35 ml per single feeding, reaching a daily total volume of 500–700 ml. Subsequent days saw an incremental volume increase of 10–20%, contingent upon successful assimilation. The frequency of mixture administration varied based on individual patient clinical conditions and laboratory examination findings. The infusion rate of the mixture did not surpass 125 ml per hour at maximum. This infusion process occurred over a span of 18–20 hours during the day, with a subsequent pause typically observed during the night hours.

Individuals in the mixed nutrition group were subjected to a combined nutritional regimen. Starting from the second day postoperatively, they were administered parenteral nutrition. Subsequently, as soon as signs of intestinal motility, the absence of vomiting, and significant gastrointestinal tract paresis were observed, patients transitioned to receiving nutrition either orally or via a nasogastric tube, following the specified protocol. In instances where gastrointestinal tract paresis was evident, the proportion of enteric (intestinal) nutrition was adjusted, favoring an increased contribution of parenteral nutrition to fulfill the daily caloric requirements (9).

Methods of statistical data analysis

The data collected in the study were subjected to analysis utilizing both descriptive and analytical statistical methods. Quantitative and qualitative metrics were examined. For laboratory parameters, pairwise comparisons were conducted based on the examination timing, employing the Wilcoxon T-test with a significance level denoted as α (adjusted for the Bonferroni correction). To analyze measurements taken at multiple time points, Friedman's test was employed.

The statistical significance level "p" that emerged from the analysis indicated whether the distribution conformed to a normal distribution pattern. If the value of "p" exceeded 0.05, it was deemed that the distribution aligned with a normal distribution. Conversely, if "p" was 0.05 or less, the distribution was regarded as deviating from a normal pattern. The predetermined level of statistical significance was set at a probability of error of 0.05.

Results

The nutritional condition of patients in all three groups was evaluated prior to surgery and during the 10–12 days following the surgical procedure. This evaluation was performed in reference to the clinical scales utilized for assessing nutritional status, namely SGA and NRI. The categorizations included normal, moderate, and severe malnutrition, as illustrated in Figures 1, 2, and 3.

From the provided data, it is evident that in the preoperative phase, based on the SGA scale, the first, second, and third groups exhibited normal nutritional status in 80%, 61.3%, and 56.7% of

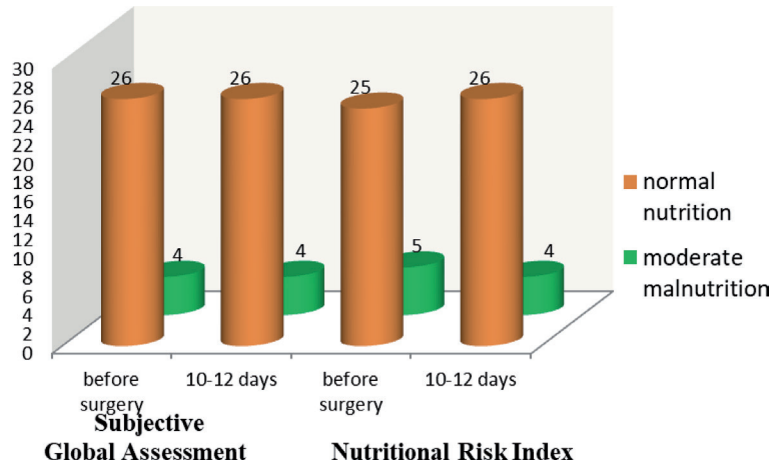

Fig. 1. Dynamics of the nutritional status of patients with enteral support.

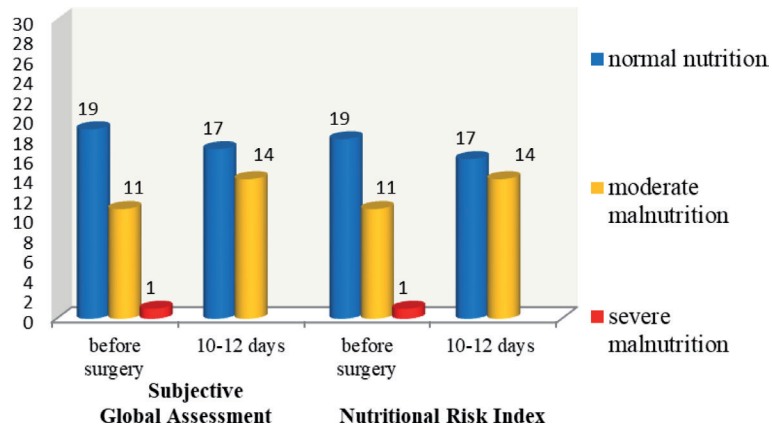

Fig. 2. Dynamics of the nutritional status of patients with parenteral support.

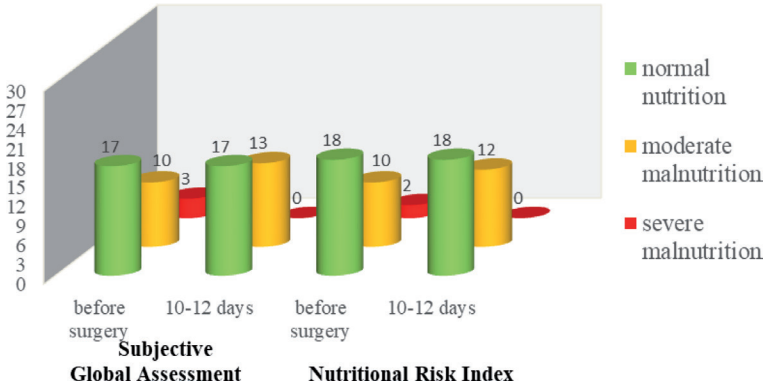

Fig. 3. Dynamics of the nutritional status of patients with a mixed type of nutritional support.

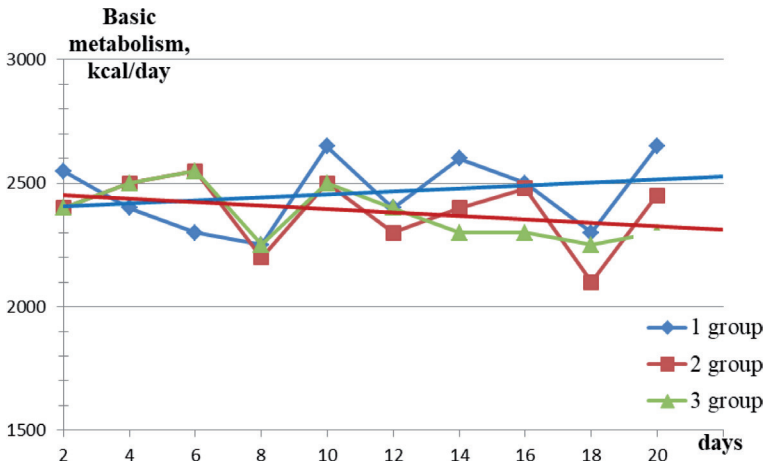

Fig. 4. Comparative analysis of the dynamics of the level of basal metabolism in patients of three groups in the early postoperative period.

the patients respectively. The remaining patients in these groups had varying degrees of malnutrition, categorized as "moderate" or "severe."

Evaluating the nutritional status before surgery using the NRI scale corroborated a predominantly "normal" nutritional status among the vast majority of patients across all groups (n=62), indicating true negatives (normal nutritional status) (1, 2, 5). Twenty-six patients demonstrated true positives (moderately malnourished), while 3 displayed severe malnutrition. The NRI data during this period exhibited a robust correlation with SGA scores ($p<0.005$).

During the 10–12th day of the postoperative period, patients in the first group maintained their SGA scale assessment results. However, the NRI assessment scale indicated a slight increase of "moderate malnutrition" by 3.3% per patient. Among patients receiving parenteral nutritional support, 17 individuals achieved a status of "normal nutrition", 14 experienced "moderate malnutrition," and notably, one patient (3.2%) exhibited regression from "severe malnutrition." In the mixed nutrition group, there was a complete eradication of "severe malnutrition" according to the provided scales ($p<0.005$). However, this was accompanied by an increase of 10% (SGA) and 6.7% (NRI) of patients with "moderate malnutrition.

In the patient groups receiving enteral and parenteral nutrition, the basal metabolic rate reached its initial values by the conclusion of the respective energy supplementation types (days 10–15). For the enteral group, this value was approximately 2500.1±353.4 kcal/day, and for the parenteral group, it was 2350.0±330.5 kcal/day. This trend indirectly affirmed the efficacy of the utilized nutritional support methods.

In the case of mixed nutrition, a noteworthy statistical convergence of basal metabolic rate with its baseline was achieved earlier, around 6-8 days into the postoperative period (2250.0±105.2 kcal/day). This observation suggests a more efficient coverage of energy requirements for patients in the mixed nutrition variant, compared to the isolated nutritional approaches ($p<0.03$) (Fig. 4).

The analysis provided above regarding the changes in basal metabolic rate among patients in the three groups highlights an earlier alignment of basal metabolic rate with its initial value in those following a mixed nutrition approach. This occurrence suggests a more rapid resolution of energy deficiency in patients post-surgery, even in the presence of an increased number of individuals with "moderate malnutrition."

This observation supports the notion that the significance lies not solely in the pace at which the calculated basal metabolic rate is restored, but rather in the effective outcome achieved through the chosen nutritional method in addressing nutritional deficits.

The assessment and subsequent analysis of average laboratory examination outcomes across patient groups, in a comparative context, revealed a relatively gradual decline in total blood protein levels by day 5 of the postoperative period. On average, this reduction amounted to 6.8±0.95% of the initial values. This decline could likely be attributed to heightened catabolism and concurrent protein losses, such as through exudation and drainage.

Interestingly, a noteworthy surge was observed at the conclusion of nutritional support, leading to average values elevating by approximately 8.47% in comparison to the initial values.

Specifically, a statistically significant increase in total blood protein levels was identified within the mixed nutrition group ($p=0.004$). In the enteral and parenteral nutrition groups, variations in the progression of total protein levels were found at levels of statistical significance trends: $p=0.108$ and $p=0.129$, respectively.

While analyzing the alterations in blood lymphocyte count, it's important to acknowledge that prior to the surgery, the relative level of blood lymphocytes was notably diminished in all three groups (25.9±3.7%). However, considering the surgical methods

and extent of the operation, along with the immune system's cellular and humoral responses, the progression of lymphocyte levels demonstrated a statistically significant increase during the postoperative period of 10–12 days.

By the 10th day of the postoperative period, there was a consistent upward trend in the blood lymphocyte levels across the first, second, and third groups. On average, these levels increased by 8.95% (p=0.000), 10.35% (p=0.003), and 10.91% (p=0.000), respectively.

In the comparative analysis of blood transaminase levels (ALaT and ASaT) among the studied groups during the 10–12th day of the postoperative period, a noteworthy trend emerged. Some patients exhibited an initial surge, often exceeding the normal values by several folds immediately after the operation. Subsequently, these elevated levels experienced a decline.

Particularly, the dynamic trends in blood transaminase levels were observed in most patients of the first group (n=23, 78.2%) by the 10th day. This was characterized by a reduction in ALaT and ASaT values, averaging around 32.1% and 40.15% respectively, in comparison to their initial preoperative levels.

In the second group, a significant reduction in blood transaminase levels was recorded in the majority of patients (81.6%, n=26). On average, by the fifth day of the postoperative period, these levels dropped by a statistically significant 72.2% compared to their baseline, and by the 10th day, the reduction remained significant at 66.7%.

Within the mixed nutrition group, by the fifth day of the postoperative period, a substantial decline in transaminase levels was observed, averaging a remarkable 72.6% reduction from the initial values (p=0.000). By the 10th day, these levels further decreased to 63.8% relative to the achieved value on the fifth day (p=0.008).

Regarding the evolution of total blood bilirubin levels, it's noteworthy that elevated levels persisted on the first day post-surgery. This could be attributed to temporary biliary tract edema and difficulties in bile outflow into the intestinal lumen. This resulted in a considerable surge of total blood bilirubin levels, exceeding the baseline by more than tenfold (p=0.000).

On average, during days 5–7 following surgery, all the studied groups exhibited a trend towards a 5–6-fold decrease in total blood bilirubin levels from their initial values. This trend persisted, with levels gradually returning to normal ranges by days 10–12. In some patients, these normalized values endured until their discharge from the hospital (p=0.004).

In terms of quantitative comparison, patients in the first group exhibited a modest decrease in total bilirubin levels by an average of 12.7% only by the 10th day after surgery (p=0.187). Meanwhile, the second group saw a more substantial decline in total blood bilirubin levels, with an average reduction of 40.09% by the 5th day and 45.0% by the 10th day from their initial preoperative values (p=0.002).

Conversely, patients in the third group experienced a slower regression of this indicator. Their total bilirubin levels decreased by an average of 20.0% by the 5th day and 44.0% by the 10th day of the postoperative period.

Discussion

Upon evaluating the study outcomes, particularly the shifts in nutritional status indicated by the NRI and SGA scales, it's important to highlight that a more favorable trend toward normalization of patients' nutritional status was observed with parenteral support. This is underpinned by the fact that the elevated count of patients with "moderate malnutrition" (increased by an average of 9.7%, n=3) on both scales can be attributed to the complete resolution of severe nutritional deficiencies. In other words, this increase in "moderately malnourished" patients did not come at the expense of an absolute rise in their number, but rather by addressing severe malnutrition.

A parallel outcome in terms of nutritional status stabilization was observed in the mixed nutrition group as well. This group exhibited a parallel increase in the number of patients with "moderate malnutrition," specifically by 10% and 6.7%, respectively. This shift was attributed to the complete reversal of severe nutritional deficiencies. Therefore, within this group, a similar situation was apparent where there was no absolute augmentation in the count of patients with "moderate malnutrition." However, it's noteworthy that this group demonstrated comparable indicators in laboratory examinations and an earlier restoration of basal metabolic rate compared to its initial value.

Patients who received isolated enteral support demonstrated the most favorable outcomes on the rating scales. There was merely a slight rise in the count of patients with "moderate malnutrition" by 3.3% (n=1) solely on the NRI scale in the postoperative period. Nonetheless, when compared to the other groups, there was no discernible eradication of moderate malnutrition to the benefit of patients with a "normal" nutritional status. In other words, the nutritional status dynamics within this group lacked clear trends.

The trajectory of basal metabolism level recovery, as indicated by the vector trends in the groups, underscores a gradual return to its initial level by only the 10-12th day of the postoperative period for those with enteral and parenteral support–2500.1±353.4 kcal/day and 2350.0±330.5 kcal/day respectively. Interestingly, a rapid trajectory towards the initial basal metabolism level (2250.0±105.2 kcal/day) was observed between days 6–8 after surgery in the mixed nutritional support group. However, this quick recovery did not necessarily correlate with a swifter return to self-feeding for patients and was not linked to the complete elimination of moderate nutritional deficiencies (in fact, an increase in patients with this level of nutritional disorder was observed).

Nonetheless, the alignment between the calculated basal metabolism level and the "energy intake" from the total volume of nutritional supplementation within the mixed nutrition and isolated enteral support groups seems to be linked to the preservation or restoration of parietal digestion in the gastrointestinal tract during the early postoperative phase. This occurs even in the presence of varying degrees of postoperative intestinal paresis.

Analyzing the protein metabolism dynamics unveiled that upon transferring patients from the intensive care unit to the specialized department, the mixed nutritional support exhibited more

pronounced and statistically significant improvements in the total blood protein levels.

In terms of the increase in blood lymphocyte levels across all groups, it's plausible to attribute this reaction to the surgical procedure itself. This response likely reflects the body's reaction to the trauma of surgery.

The elevation in blood lymphocyte levels could indirectly signify a favorable impact of this response on the immune status of patients undergoing all studied nutritional approaches during the postoperative period within this specific patient group.

Regarding the shifts in the levels of transaminases and total blood bilirubin among the patients in the three groups (n=91, 100.0%), there was a statistically significant rise in ALT and AST levels, along with a comparatively lesser increase in total blood bilirubin. These changes can primarily be attributed to the surgical intervention itself and its extent, the underlying hepatopancreatoduodenal zone condition, and the concurrent cytolytic syndrome in the presence of cholestasis.

Starting around 5–6 days and continuing until the 10–12 day mark of the postoperative period, a reduction in blood transaminase levels became evident. Notably, upon comparing the analyses of total blood bilirubin levels in all patient groups, a robust direct correlation was observed with the decrease in blood transaminase levels. This correlation appears to be attributed to the establishment of effective intraoperative bile outflow achieved through biliary tract drainage and the elimination of the cause of obstructive jaundice (the tumor).

Although the nature of nutritional support exerted a certain impact on the dynamics, particularly a reduction, in serum transaminases and total blood bilirubin levels, the surgical procedure itself also significantly contributed to these changes. The surgical intervention played a crucial role in facilitating improved bile outflow, eliminating the root cause of obstructive jaundice (tumor removal), and consequently decreasing the severity of the cytolytic syndrome as an outcome of the surgical procedure.

Conclusion

1. Throughout the entirety of the compared nutritional support approaches, as evaluated by the NRI and SGA nutritional status assessment scales, both parenteral and mixed types of nutrition exhibited superior efficacy in stabilizing the patients' clinical condition quantitatively. Furthermore, these approaches demonstrated the ability to reverse severe nutritional inadequacies when compared to the group receiving isolated enteral nutrition.

2. In the context of patients who underwent surgical procedures for malignant neoplasms of the hepatopancreatoduodenal zone, the mixed type of nutrition during the postoperative phase presents itself as a viable substitute for isolated parenteral nutrition. This is primarily attributed to the complete resolution of severe malnutrition and the ability to sustain the count of patients in the perioperative period with a "normal" nutritional status.

3. The restoration rate of the calculated basal metabolism level to its pre-surgery values, regardless of the type and nature of nutritional support, should not be solely regarded as the definitive criterion for assessing nutritional efficacy in the postoperative period. This is because there exists an unclear correlation between the dynamics of basal metabolism values and the resolution of varying degrees of nutritional deficiencies.

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