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Review

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Problems of Nutritional and Metabolic Therapy of Patients with Intestinal Fistulas

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ABSTRACT Intestinal fistulas remain a multidisciplinary, often life-threatening problem of clinical medicine. Such patients in the process of their conservative and surgical stages of treatment remain in a state of systemic metabolic dysfunction for a long time, which is usually accompanied by phenomena of trophological insufficiency of varying severity. In this regard, one of the most important areas of treatment for this category of patients is nutritional-metabolic therapy (NMT), aimed at minimizing the consequences, and, if possible, stopping the catabolic orientation of metabolism, which will help stabilize the trophological status of patients and improve the results of their treatment. NMT of patients with intestinal fistulas still remains a very complex and insufficiently resolved problem that requires further study. This article discusses the features and controversial issues of NMT for this category of patients, as well as a rational choice of nutritional accesses and optimal energy and protein supply when implementing clinical nutrition depending on the anatomical affiliation of the fistula and the degree of its production.

Keywords: intestinal fistula, intestinal failure, nutritional support

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AO – abdominal organs
BM – body mass
EN – enteral nutrition
ENM – enteral nutritional mixtures
GIT – gastrointestinal tract
IF – intestinal fistula
II – intestinal insufficiency
NMT – nutritional-metabolic therapy
NS – nutritional support
PN – parenteral nutrition
SGA — Subjective Global Assessment
SIF – small intestinal fistulas
SIR – systemic inflammatory response
TF – trophic failure
UIF – unformed intestinal fistulas
WEH – water-electrolyte homeostasis

An intestinal fistula (IF) is a defect in the intestinal wall that communicates with the body surface or the lumen of another hollow organ. According to various sources, the prevalence of IF currently accounts for 0.5–8.7% of all patients after abdominal surgery (AS). [1, 2]. The incidence of small intestinal fistulas (SIF) as a complication of surgical interventions is 0.1–18% in acute AS pathology and 0.2–2% in trauma [3]. At the same time, unformed intestinal fistulas (UIF) occur with a frequency of 1–2% of all postoperative complications in AS diseases [4]. In 24.5–58.7% of cases, unformed SIF occur after emergency surgical interventions for acute adhesive intestinal obstruction [5]. The greatest number of patients are young and middle-aged (25–60 years), which increases the social significance of the problem and the need to improve treatment methods for such patients. The overall mortality rate for external IF ranges from 5 to 20% [6, 7]. At the same time, there is a significant difference in mortality rates between formed (4%) and unformed IF (71.7%), which against the background of frequently developing peritonitis can increase to 82–90% [8–13].

In 75–85% of cases, the main cause of small intestinal fistulas are complications of surgical interventions on the abdominal cavity. Small intestinal fistulas can also be a consequence of complicated inflammatory bowel diseases (5–50%), acute pancreatitis (3–10%), oncological diseases of the gastrointestinal tract (GIT) (2–15%), and duodenal ulcers (3–6%) [14].

Treatment of patients with IF remains a complex task to date, due to both the lack of a unified management strategy and the frequent development of complications associated with fistulas, often life-threatening. Among the latter, the most frequently observed are: various infectious complications, including sepsis; severe disturbances of water-electrolyte homeostasis (WEH) and acid-base balance (ABB); long-term persistent phenomena of systemic inflammatory response (SIR) and concomitant systemic metabolic dysfunction; intestinal failure syndrome (IFS), often accompanied by progressive trophic failure (HF) and

immunosuppression. At present, it should be recognized that treatment of patients with IF requires a multidisciplinary approach in specialized multidisciplinary hospitals, and organizational issues of their treatment and rational routing are not sufficiently developed.

The treatment tactics of IF include conservative and surgical stages. One of the most important components of medical care for this category of patients is the relief of SIR, infectious complications and long-term persistent systemic metabolic dysfunction in the form of hypermetabolism-hypercatabolism syndrome, which is usually accompanied by insulin and anabolic resistance, as well as disruption of the endogenous trophic chain of the body, which is manifested by disruption of digestion processes, development of mitochondrial insufficiency and partial blockade of intracellular synthetic processes [15, 16]. This leads to the development of progressive protein-energy and micronutrient deficiency, increasing sarcopenia, a decrease in reparative processes, immunosuppression and the addition of various infectious complications. In this regard, one of the significant areas in the management of such patients at all stages of their treatment is the timely appointment and implementation of optimal nutritional support (NS) (clinical nutrition) by using known methods of substrate provision (oral sipping, tube and (or) parenteral nutrition (PN)) using special nutritional mixtures (solutions) of various directions.

It should be noted that at present, clinical nutrition can and should be considered as pharmacological nutrition, which allows for a certain pathogenetically justified effect on the impaired structural, functional and metabolic processes of the body, which, in essence, is an independent type of medical care called “nutrition-metabolic therapy” (NMT) [15].

Among the factors that will in some way influence the tactics of NMT in patients with IF , it is necessary to take into account their anatomical affiliation, localization (high or low), type of opening (internal or external, single or multiple), level of fistula production (low up to 200 ml, average 200–500 ml or high more than 500 ml), method of fistula control, presence or absence of access to the distal part of the gastrointestinal tract, with its significant length, development of infectious complications and severity of SVR, state of organ functions and, above all, the digestive system, as well as trophological status and severity of the patient's condition.

Clinical manifestations of fistulas directly depend on their localization and development variant. The more proximal the fistula is and the greater the volume of irreparable losses through the fistula, the more often violations of the VEG and KOS are observed, as well as TN phenomena and infectious complications, which together often predetermine the outcome of the disease. Significant clinical differences, disease prognosis and treatment tactics are also determined by the variant of fistula development (controlled or uncontrolled). Uncontrolled fistulas always occur with more pronounced phenomena of systemic metabolic dysfunction and often require an individual approach when performing NMT.

One of the important problems in the treatment of patients, especially with small intestinal fistulas, is the frequently developing SI syndrome, which is understood as a decrease in the functional capacity of the small intestine below the minimum, leading to disturbances in the processes of intracavitary and parietal hydrolysis, as well as the absorption of nutrients, water and electrolytes, which is accompanied by disorders of trophic and water-electrolyte homeostasis, as well as progressive TI, often requiring intravenous correction [17, 18].

The frequency of detected TN in patients with IF varies depending on the variant of development, height, level of location and number of fistulas and, according to different authors, ranges from 12.9 to 100%, reaching maximum values in NIF [3, 19, 20]. According to our data, TN phenomena in the form of marasmic kwashiorkor of varying degrees of exhaustion were observed in all 56 patients with NIF treated at the St. Petersburg Research Institute of Emergency Care named after I.I. Dzhanelidze from 2016 to 2023.

In surgical patients with pronounced signs of developing TN, postoperative mortality is observed

4–30 times more often than in patients with normal TS values [21]. In patients with formed and unformed IF, sepsis is observed in 25–83% of cases, which sharply increases the risk of death [22, 23].

The development of CI syndrome in combination with persistent chronic systemic inflammatory response leads to the development of mitochondrial dysfunction (insufficiency), which, against the background of frequently occurring forced adynamia in such patients, directly or indirectly contributes to the development of progressive sarcopenia and a decrease in rehabilitation potential [24].

DIAGNOSIS OF TROPHIC INSUFFICIENCY

All patients with IF should be considered to be at risk for developing TN, for the early diagnosis of which there is currently no ideal scale. In our opinion, 6 indicators recommended by ASPEN can be used as simple and accessible criteria for TN: insufficient energy intake, weight loss, muscle loss, subcutaneous fat loss, the presence of localized or generalized edema that can mask weight loss, and decreased muscle strength. The presence of two or more of these indicators indicates the presence of TN [25].

Many foreign authors use existing screening scales for early detection of patients with a high risk of malnutrition who require the appointment of NP: NRS 2002 - nutritional risk screening 2002, NUTRIC - nutritional risk in critical conditions or subjective global assessment (SGA). The SGA (Subjective Global Assessment) scale classifies patients into level A (good nutrition), level B (moderate underweight or suspected underweight) or level C (severe underweight) based on an analysis of the number of meals, dynamics of weight loss, functional assessment of muscle strength and physical examination [26].

Currently, TN is assessed based on a combination of somatometric and some laboratory parameters: body mass index, arm circumference, size of the skin-fat fold above the triceps, arm muscle circumference, content of total protein, albumin and transferrin in the blood serum, as well as the absolute number of lymphocytes, each of which has a point value [15].

Recently, instrumental methods for assessing the component composition of the body and determining muscle mass have become increasingly popular for assessing TS in seriously ill patients. Among them, the most well-known are bioimpedancemetry and radiation methods: dual-energy X-ray absorptiometry, computed tomography, magnetic resonance imaging, and ultrasound. Each of the methods allows for a quantitative and qualitative assessment of muscle mass and the dynamics of its changes during treatment. However, it should be noted that the above research methods have not yet found widespread use.

Isolated diagnostic assessment of the level of visceral proteins in the blood serum as indicators of existing TN does not have the required sensitivity and specificity. A decrease in the concentration of serum albumin, transferrin and prealbumins may be due to a persistent systemic inflammatory reaction and the observed perverted protein synthesis by the liver (increased seromucoid production and decreased albumin synthesis), which are often observed in patients with IF. Low serum albumin levels are not an entirely adequate parameter for assessing TS in the presence of severe SVR, but may have prognostic value. Several studies have demonstrated that the level of serum albumin correlates with increased patient mortality.

Gibbs J. et al. [27] in a review including 54 215 patients who underwent various cardiac surgeries demonstrated that hypoalbuminemia less than 30 g/l was the most independent predictor of their increased mortality. The same conclusion was reached by Fazio V. et al. [28], who noted a high mortality rate of patients (42%) with formed small intestinal fistulas, in whom serum albumin was less than 25 g/l compared to a group with zero mortality with serum albumin content of more than 35 g/l. Lu C. et al. [29] noted a significantly higher probability of spontaneous fistula closure (18.1 times more often) against the background of complete PN with an increase in serum albumin levels from 32 to 34.6 g/l, compared to a group where the serum albumin level was 29.6 g/l.

In another study, where 277 patients with formed TIF were analyzed, the level of serum albumin was not recognized as an independent prognostic factor for clinical outcomes [30]. Kuvshinoff BW et al., in a retrospective analysis of 79 patients with formed TIF, also did not reveal the prognostic significance of the level of serum albumin on patient mortality, but noted its correlation relationship, as well as transferrin, as a predictor of TIF closure. Among patients receiving PN, with a serum albumin content of 34 g / l and intestinal losses of less than 500 ml / day, 93.3% experienced spontaneous closure of the TIF compared to 30% of patients with hypoalbuminemia of 29 g / l and intestinal losses of at least 500 ml / day. Also, fistula closure was more often observed at serum transferrin concentrations of 200 ng/dl, as opposed to low levels (126 ng/dl) [31].

NUTRIENT ACCESSES

To date, the issues of rational nutritional access and optimal substrate provision for this category of patients, depending on the location and clinical variant (formed, unformed) of the TIF, remain controversial. Formed IF are characterized by the presence of a clearly defined fistula tract lined with granulation and scar tissue (tubular fistula) or close fusion of the intestinal mucosa with the skin (labial fistula). Unformed fistulas open into a wound in the abdominal wall or a purulent cavity and, as a rule, do not have a fistula tract. Formed fistulas have a more favorable course, usually not accompanied by severe general symptoms. Unformed fistulas, even low ones, occur against the background of intoxication due to the inflammatory process and often accompanying infectious complications.

The conservative stage of treatment of patients with TIF currently includes: determination of the anatomical affiliation with topical reference of the fistula location relative to the length of the intestine from the Treitz ligament, as well as assessment of existing intestinal losses; exclusion of distal obstruction and assessment of the length of the intestine below the fistula from the point of view of the possibility of performing fistuloclysis; diagnosis and treatment of infectious complications; assessment of the VEG and AOS with the relief of existing disorders, as well as assessment of the patient's TS with the choice of the most rational nutritional access and determination of the necessary, better personalized, volume of substrate provision of the body.

An important task of this stage is to determine how functional and suitable for enteral nutrition (EN) the small intestine sections are, both proximal and distal to the fistula. There is an opinion that to ensure relatively effective oral use of a gentle diet and modern well-balanced enteral nutritional mixtures (ENM), the required length of the functioning jejunum, where active hydrolysis of most nutrients and their absorption occurs, should be at least 75-100 cm from the ligament of Treitz. However, in clinical practice, maldigestion and malabsorption phenomena with high fistula losses can often be observed with a jejunum length proximal to the fistula of even about 120-150 cm, which often requires restriction of oral water intake (switching to xerophagy), food, as well as ENM and the appointment of additional PN [32].

In the 1960s and 1970s, most clinicians began to adhere to the principle of "complete rest" of the intestine, when in order to reduce the loss of intestinal secretions through the fistula, patients did not receive any oral food. NS was carried out only by prescribing a complete PN in the amount of: energy 30-40 kcal/kg and protein 1.88-2.5 g/kg per day [33, 34]. According to data, for example, by Chapman R. et al. [35], the use of PN with an energy value of 2000-3000 kcal in 30 patients with controlled TIF contributed to a decrease in mortality to 12%, and fistula closure was noted in 55% of patients.

Of interest are the data of Soeters PB et al. [36], who presented an analysis of the effectiveness of treatment of 404 patients with abdominal fistulas in three periods: the first - from 1945 to 1960, the second - from 1960 to 1970, the third - from 1970 to 1975. The authors noted that during the first period, the mortality rate of patients was 43%, while in the second period it was observed in 15% of cases. The difference in data in these periods is explained by the use of more adequate methods of PN. According to Traverso LW et al . [37], the use of PN allows to reduce the volume of intestinal losses through the

fistula by 30-50% and thereby reduce the loss of enzymes and reduce catabolism.

Based on the above data, it may seem that PN is the most preferred method of NS for patients with gastrointestinal fistulas. However, many researchers [11, 38, 39] are of the opinion that in patients with formed intestinal fistulas during NS, preference should be given, if possible, to EN using modern EPS, which provide and maintain intraluminal trophism and regenerative potential of the intestinal mucosa, thereby promoting faster closure of the fistula [40].

At present, it is absolutely clear that the NS of patients with IF should include all modern technologies of both PN and EN, aimed at achieving the required volume of their substrate supply. In all cases, preference should be given to a more physiological EP, and if it is impossible to properly implement it, prescribe additional, if necessary, complete PN in order to achieve and subsequently maintain a positive energy and nitrogen balance.

Basic principles of nutritional-metabolic therapy for patients with intestinal fistulas:

— stabilization of water and wastewater treatment plants;

- creation of functional rest for the fistula tract;

— substrate provision close to the patient's actual needs;

— ensuring mechanical and chemical protection of the gastrointestinal tract;

— pharmanutrient and pharmacological activation of anabolic processes.

The choice of one or another variant of NP for such a category of patients is carried out taking into account the localization of the fistula, the available products and the clinical variant of its manifestation. Along with this, it is important to have a clear idea of the length of the small intestine proximal and distal to the fistula to decide on the possibility of prescribing EN.

Factors that allow us to expect success of the conservative therapy: the presence of a formed (controlled) fistula, a large length of the fistula tract without its distal obstruction, low fistula production and the absence of active infection, as well as its iatrogenic nature.

In the presence of unformed (uncontrolled) fistulas opening into a laparotomy wound, the main option for the initial substrate provision of patients is usually PN. The decision on a possible transition to mixed or EN is usually made only after the fistula has been transferred to a controlled state and the possibility of creating intestinal nutritional access has appeared. In this case, it is necessary to have a clear idea of the length of the proximal and (or) distal sections of the small intestine, which is important, firstly, for choosing the necessary EPS and the rate of their introduction, and, secondly, when the length of the proximal controlled section of the jejunum is more than 100 cm and the appointment of gentle oral nutrition in combination with powdered EPS in a relative "xerophagy" mode.

In the case of formed (controlled) fistulas, the choice of nutrient access will be determined, first of all, by their localization and the volume of the actual output. The options for nutrient access and substrate provision for such patients that we recommend are presented in Table 1.

Notes:

1. For high-yielding (more than 500 ml/day) fistulas, active suppression of gastric secretion with hydrogen pump inhibitors; if Omeprazole 20–40 mg x 2 times a day is insufficiently effective, prescribe Pantoprazole or Rabeprazole 20 mg x 2 times a day.

2. In case of persistent large losses of intestinal contents through a proximal fistula (more than 1000 ml), it is indicated to prescribe drugs that slow down the propulsive activity of the intestine with an individual selection of the daily dose depending on the clinical situation (Loperamide up to 12 mg/day).

3. If large losses of intestinal contents (more than 1000 ml) persist, temporary administration of Somatostatin (Octreotide) 100 mcg x 3 times a day for 5–7 days is indicated; if the discharge through the fistula decreases to less than 500 ml and there is a further need to limit intestinal losses, administration of Octreotide-Depot 20–30 mg (effective for a month) is indicated.

Table 1

Options for nutritional access for substrate provision of patients with formed (controlled) intestinal fistulas

Localization of the fistula	Treatment tactics
Duodenum	– oral food intake is prohibited; moderate (up to 200–300 ml/day) fractional consumption of water in small sips is allowed to eliminate dryness of the mucous membranes of the oropharynx; – the main nutritional access is a gentle (silicone or polyurethane) nasointestinal tube (12–15 Fr), installed distal to the Treitz ligament by 20–30 cm; – in case of widespread purulent-destructive pancreatitis and the first laparotomic sanitation of the source of infection, the application of a jejunostomy is indicated for the implementation of tube feeding; – additional PN is prescribed only when it is impossible to provide the patient with adequate substrate through tube feeding, when there is poorly corrected intestinal dyspepsia, documented by total maldigestion according to coprogram data and manifested by rapidly increasing reduction in body weight (2% or more per week), as well as a decrease in the protein-synthetic function of the liver - increasing hypoalbuminemia (transferrinemia) or a decrease in transthyretin or cholinesterase levels; – when conducting additional PN, the administration of intravenously administered vitamin (Soluvit + Vitalipid or Cernevit) and microelement (Addamel) complexes is indicated.
Jejunum less than 50 cm from the ligament of Treitz	– oral food intake is prohibited; moderate (up to 300–500 ml/day) fractional consumption of water in small sips is allowed to eliminate dryness of the mucous membranes of the oropharynx; – if possible, install a Foley catheter or balloon stoma in the distal (relative to the fistula) section of the jejunum to perform tube feeding using polymeric, and if they are poorly tolerated (maldigestion) oligomeric EPS and perform fistuloclysis — fractional (30–50 ml x 4–5 times a day) introduction of intestinal contents from the proximal section of the intestine containing bile and pancreatic enzymes through a tube; – if it is impossible to provide nutritional access to the distal jejunum — prescribe a complete PN (including vitamin and microelement complexes) in the volume: energy 25–30 kcal/kg/day, protein at least 1.3–1.5 g/kg/day.
Jejunum ,50 to 150 cm from the ligament of Treitz	– limited oral intake of gentle food with elements of "xerophagy" (viscous porridges, omelettes, meat soufflés, jelly) and the addition of dry (preferably oligomeric) EPS (100–150 g/day — 400–600 kcal, 18–30 g protein) to side dishes, as well as separate water consumption limited to 500 ml/day to eliminate dryness of the oropharyngeal mucosa and (or) additional minimal oral intake of polymeric or oligomeric isoosmolar (280–300 mosm/l) isocaloric EPS by the sipping method, taking into account the individually tolerated volume (200–400 ml/day); – if possible, install a Foley catheter or balloon stoma in the distal (relative to the fistula) section of the jejunum — tube feeding with a choice of EPS based on tolerance + fistuloclysis (see above); – if adequate substrate supply through the gastrointestinal tract is impossible, additional PN is prescribed, including vitamin and microelement complexes, until energy supply is achieved in the amount of 30–35 kcal/kg/day, and protein is at least 1.5 g/kg/day.
Distal jejunum (more than 150 cm from the ligament of Treitz) or initial ileum	– an individual gentle diet with elements of "xerophagy" (viscous porridges, omelettes, meat soufflés, jelly) and the addition of dry polymeric or oligomeric EPS to side dishes (500–800 kcal, protein 20–40 g per day), as well as separate water consumption limited to 1000 ml/day (the guideline for the volume of discharge through the fistula is no more than 500–600 ml) or additional oral consumption of polymeric (oligomeric) iso-osmolar (280–300 mosm/l) EPS by the sipping method, taking into account their individual tolerance (600–800 kcal, protein 25–40 g per day); – if possible, install a Foley catheter or balloon stoma in the distal (relative to the fistula) section of the ileum — tube feeding with a choice of enteral PS based on tolerance + fistuloclysis (see above); – if adequate substrate supply through the gastrointestinal tract is impossible, additional PN is prescribed, including vitamin and microelement complexes, until energy supply is achieved in the amount of 30–35 kcal/kg/day, and protein is at least 1.5–2.0 g/kg/day.
Distal ileum	– an individual gentle diet with elements of "xerophagy" (viscous porridges, omelettes, meat soufflés, jelly) and the addition of dry polymer EPS (100–150 g/day) to side dishes, as well as separate water consumption limited to 1000 ml/day (based on the volume of discharge through the fistula); – if it is possible to install a Foley catheter or balloon stoma in the distal (relative to the fistula) section of the intestine — tube feeding using EPS as tolerated; – if adequate substrate supply through the gastrointestinal tract is impossible, additional PN is prescribed until energy supply reaches 30–35 kcal/kg/day, and protein – 1.5–2 g/kg/day.
Colon	– an individual gentle diet with elements of "xerophagy" (viscous porridges, omelettes, meat soufflés, jelly) and the addition of dry polymer EPS (up to 150 g/day) to side dishes or sipping with the consumption of iso-osmolar hypercaloric EPS (600 kcal, 24–40 g of protein per day), as well as separate water consumption limited to 1000–1500 ml/day (based on the volume of discharge through the fistula); – oral administration of the dipeptide alanyl-glutamine (Glutamine Plus) 10 g x 2 times a day.

Notes: Gastrointestinal tract; PN - parenteral nutrition; EPS - enteral nutritional mixtures

4. In cases of insufficient effectiveness of fistuloclysis (preservation of maldigestion phenomena), additional administration of enzymes through a tube (Creon, Pancitrate, Ermital, etc.) is indicated, and in case of fecal acholia, the administration of enzymes containing bile acids (Festal, Enzistal).

5. In the presence of severe intestinal dyspepsia (often a manifestation of bacterial overgrowth syndrome), which limits the possibility of implementing tube feeding, trans-tube intraintestinal decontamination is indicated for 7-10 days (Metronidazole 500 mg × 3 times a day or Rifaximin alpha 400 mg × 2-3 times a day or Nifuroxazide 200 mg × 4 times a day). In the event of antibiotic-associated diarrhea, Vancomycin 250-500 mg × 4 times a day should be administered through a tube. In all cases, intraintestinal decontamination should be combined with active enterosorption (smecta, polysorb, enterosgel, etc.) × 3-4 times a day and the introduction of metabiotics (Hilak Forte, Actoflor S). If there are a large number of fungi in the coprogram, intraintestinal antifungal therapy is prescribed (Pimafucin 100 mg x 4 times a day for up to 7 days or Nystatin 500,000 IU 6–8 times a day for up to 10 days).

6. In case of progressive trophic insufficiency and persistently negative nitrogen balance, additional administration of L -Glutamine is indicated: orally Glutamine Plus 10 g × 2 times/day or intravenously alanine-glutamine dipeptide (20% solution of Dipeptiven) 1.5–2 ml/kg/day.

Thus, when prescribing nutritional support, it is necessary to take into account the localization of the fistula and, in the case of an existing or emerging opportunity to use EN, to strive to use it as much as possible, as a more physiological, effective and relatively safe method of substrate provision of the body. The duration of fistula closure against the background of conservative therapy can vary from 10 weeks to 13 months [41]. Average terms of possible fistula closure are given depending on their localization, which can range from 30-40 days (large intestine) to 50-60 days or more (small intestine).

There are also controversial issues regarding the optimal energy and protein supply for this category of patients. According to Sobocki J. et al. [42], with daily fistula losses of up to 1 liter, approximately 2 g of nitrogen (12.5 g of protein) are lost with intestinal contents. To date, there is no clear evidence of the relationship between clinical outcomes of intestinal fistulas and protein or energy intake. Retrospective studies conducted between 1990 and 2016 report a target energy supply of 25–30 kcal/kg/day and protein intake of 1.5 g/kg/day [43–47]. In three recent review articles, the recommended empirical energy and protein supply for patients with "low-yielding" KS is 20–30 kcal/kg and 1.5 g/kg per day, and for "high-yielding" KS – 25–35 kcal/kg and 1.5–2.5 g/kg per day, respectively [1, 48, 49]. In our opinion, the empirical data on energy and protein supply for patients with intestinal fistulas, depending on their production, presented in Table 2 most rationally reflect their needs.

Table 2

Empirical data on energy and protein supply of patients with intestinal fistulas depending on their production

Volume of fistula discharge	Energy and protein supply
Up to 500 ml	Energy 25–30 kcal/kg Protein 1.2–1.5 g/kg
500-1000 ml	Energy 30–35 kcal/kg Protein 1.5–1.7 g/kg
More than 1000 ml	Energy 30–40 kcal/kg Protein 1.8–2 g/kg

It should be noted that patients with IF belong to the category of patients with frequently changing energy-plastic needs of the body at different stages of their treatment. We have not come across studies on the study and evaluation of the effectiveness of a personalized approach to NS in such patients by conducting indirect calorimetry and (or) determining average daily nitrogen losses. According to our data, the indicators of indirect calorimetry, usually carried out by a single 30-minute measurement, should not be absolutized, since they can vary significantly throughout the day, sometimes differing by 800-1000 kcal. On the other hand, this research method, unlike determining average daily nitrogen losses, is often not available in many medical and preventive institutions.

Determining nitrogen losses based on the daily urine urea content using the formula below, modified by us to take into account intestinal (drainage) losses, allows us to obtain data on the patient's personalized need for protein supply.

Nitrogen, g/day = (M × 0.033 × SD) + 4 g + (2.5 g × DrP) + 2 g (anabolism),

where: U — urea, mmol/l; DD — daily diuresis, l; DrP — drainage (intestinal) losses, l; 0.033 — coefficient of conversion of urine urea into nitrogen (0.028 × 1.2); 4 — extraurinary nitrogen losses, g; 2.5 — average nitrogen content in 1 l of drainage (intestinal) losses.

Protein requirement, g/day = nitrogen, g/day × 6.25 (no more than 2 g/kg).

It should be remembered that this method is not informative if the patient has liver and/or kidney failure [15].

By comparing the average daily nitrogen losses and indirect calorimetry readings in different categories of patients, we determined the optimal conversion factors for the obtained value of its losses to determine the optimal energy supply of the body per 1 g of nitrogen (Table 3).

Table 3

Determination of the personalized value of the optimal energy supply of the body based on the existing average daily nitrogen losses

Daily nitrogen losses, g/day	Conversion factor for required energy supply, kcal
<10	150
10 – <15	130
15 – <20	110
20 – <25	90
>25	75

An obligatory and important component of the NS for any category of patients is the proper (at least daily requirement) provision of the body with all essential micronutrients (vitamins and microelements). This area remains poorly studied. Some authors pay special attention to such micronutrients as vitamins C , B_1, B_6, B_9, B_{12} and microelements zinc, copper, selenium, and recommend using them in a dose 10 times exceeding the physiological need [50]. It should be noted that all balanced EPS of 1500 kcal contain a complete set of micronutrients corresponding to the daily requirement. When using a complete NS, even when using "three in one" containers, it is necessary to additionally administer water- (Soluvit) and fat-soluble (Vitalipid) vitamins or a complex containing both water- and fat-soluble vitamins (Cernevit), as well as microelements (Addamel).

The use of specialized EPS containing pharmaconutrients (arginine, glutamine, omega-3 fatty acids, nucleotides) in the treatment of patients with IF remains insufficiently studied. In a retrospective observational study that included 28 adult patients with postoperative small intestinal fistulas without signs of renal, hepatic failure and sepsis, 9 patients received oral glutamine (0.3 g/kg/day) in addition to PN, and 19 patients received only PN. In the group that received oral glutamine, a higher frequency of fistula closure, a shorter length of hospital stay and lower mortality were observed compared to the group that received only PN [51].

CONCLUSION

Thus, currently available approaches to nutritional-metabolic therapy of adult patients with intestinal fistulas remain controversial. The multifaceted nature of intestinal fistulas and the features of their clinical manifestations, as well as the heterogeneous patient population, create certain problems for choosing the optimal study design. Most of the literature on the problem under discussion is based on clinical studies conducted more than 20 years ago. The issues of tactics for choosing a particular type of nutritional support for patients with small intestinal fistulas in the context of their frequently developing anabolic resistance depending on the localization and nature of the existing intestinal fistula(s), as well as determining the required volume of optimal substrate provision using pharmaconutrients require further study.

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