Currently parenteral nutrition is a recognized supplement of surgical treatment. Often this therapy enables a surgical procedure to be conducted without putting the patient at risk of unnecessary complications related to malnutrition (1). Administration of proper nutritive facilitates quicker recovery in the postoperative period and in cases of radical intestinal resection, nutritional treatment not only enables survival, but also recovery to preoperative fitness level which also implicates return to work (2).

The most important aim of nutritional treatment is to suppress destruction of body proteins. This can be achieved through administration of exogenous amino acids, but also through administration of adequate amount of energy. Starting this type of therapy, one must consider patient’s current clinical situation, his nutritional status, co-morbidities and mainly his metabolic ability (3). Except for obvious benefits of nutritional treatment, it must be emphasized that this therapy is not without risks. It not only requires administration of neutral intravenous fluids that can be detrimental, but in reality a big interference with human metabolism.

Is there a gold standard, one formula that can be used in anyone or at least in majority of patients? Of course, not. Formulations used in the parenteral nutritional treatment are drugs and obviously drugs require to be sued at proper dosages to provide proper therapeutic effect. As we know, these dosages need to be adjusted in individual patients. However, there is a “standard” requirement for these substances, however it must be emphasized that it varies under different clinical settings. This knowledge is necessary for proper nutritional treatment (3).

Increased protein-energy requirement in hospitalized patients usually results from a disease, injury, surgical procedure, fever or infection. Along with increased energy requirement, also protein demand increases and varies according to clinical situation of a patient. The more severe is the patient condition, the bigger disproportion between protein catabolism and energy requirement – increase of protein demand exceeds increase of energy requirement. Optimal nutritional treatment should predominantly cover energy requirement and nitrogen (protein) demand in different patient groups (4).

It is also important to notice that the above mentioned therapeutic effects results not only from amount of components of a nutritional mixture, but also from their quality. The origin of calories that the main nutritional components are converted to, directly results from reasons for which this therapy is conducted and diseases that the patient suffers from. It must be emphasized that the success of nutritional treatment, unlike any other therapy, to a large extent depends on the method of administration of a nutritional mixture (5).

Of course, we must remember that our aim is to treat patients in a manner closely approximating the physiological setting. If possible, gastrointestinal tract should be used in the nutritional treatment at any possible level (6).
However, this paper concerns patients in whom it is not possible and the only route for administration of nutritives is a parenteral route (7).

The aim of this paper is to demonstrate “standard” conditions and clinical situations that require non-routine therapeutic measures and to present recommendations for optimal parenteral nutritional treatment in the context of energy and protein requirement in these clinical states.

1. Nutritional treatment program

Adequate “nutritional program” should be established when a need for parenteral nutritional treatment is found. Such program involves not only an adequately prepared nutritional mixture, but also route and duration of its administration and method of achievement of a full therapeutic dose. For this purpose we must have adequate patient data. Patient weight and height are required to calculate adequate requirement for individual components of a nutritional mixture. Adequate measuring equipment to measure tissue bioimpedance, enables quite precise calculation of muscle mass and this parameter can be used in further analyses. However, most sites do not have such equipment and it seems to be little need for its widespread use. Current body weight is sufficient in most clinical settings.

When we have this information, we start to prepare a nutritional mixture from calculating protein demand that is 6 – 8 g protein per kilogram of body weight. In nutritional treatment, to standardize protein dosing, due to varied sources, the dose is expressed as nitrogen gram (g N). It facilitates quantitative approach to requirement for this basic component of a nutritional mixture. Adequate measuring equipment to measure tissue bioimpedance, enables quite precise calculation of muscle mass and this parameter can be used in further analyses. However, most sites do not have such equipment and it seems to be little need for its widespread use. Current body weight is sufficient in most clinical settings.

Glucose is an essential energetic material due to the fact that some tissues always need it (glucose-dependent tissues). Therefore when we prepare a nutritional mixture, we must always include this source of energy. One gram of glucose provides approximately 4 kilocalories. When we calculate per cent requirement for energy from this source, we obtain dose of a second component of nutritional mixture. However we must remember that excessive glucose supply has adverse effects, in particular when the therapy is prolonged. Excess glucose is converted to fat. Prolonged excessive glucose supply results in fatty liver. Daily glucose dose should not exceed 300 g. To facilitate its use by tissues, adequate amount of a short acting insulin may be added to a nutritional mixture (1 unit per 5 – 10 g of glucose).
Such management reduces the risk of insulin resistance accompanying nutritional treatment.

In view of the above mentioned limitations and to provide adequate amount of energy, second “high energy” component must be added. Fat emulsion plays such role. 1 gram of fat emulsion provides approximately 9 kilocalories. It provides relatively high amount of energy in a small volume. Fat emulsion is not only a source of energy but its components are structural materials. As with glucose, excessive amounts of fat emulsion, especially when given on a long-term basis, may have detrimental consequences. Liver is affected the most and its injury may manifest as a transient increase of aminotransferases through transient jaundice until its severe failure. To reduce toxic liver effects of the lipids, it is important to adjust their dose to metabolic abilities of the patient. These abilities increase with treatment. Therefore, protein and energy requirement and lipid contents of the nutritional mixture are reached slowly, and patient condition and abilities are assessed at each step.

When our aim is to maintain nutritional status of the patient (e.g. in the perioperative setting) or when we treat a patient with mild or intermediate malnourishment, qualitative composition of both amino acids and fat emulsion is of secondary importance. Completeness of a nutritional mixture is most important. The mixture should be prepared to provide any nutritional components at adequate amounts. We must not forget about daily requirement for vitamins, trace elements and ions (7, 11) (tab. 1). Only mixtures that include all these substances may be referred to as complete (12).

2. Severe malnutrition

It is a condition that clearly requires proper management. Of course we must attempt to clarify causes of deep malnourishment. There are multiple potential causes of this condition. Therefore its management should be individualized. It must be emphasized that the best and safest way to correct nutritional deficiencies is through the gastrointestinal tract. However, malnourishment is a systemic condition that affects any organ, including the gastrointestinal tract (13). Very commonly, gastrointestinal tract becomes dysfunctional in severely malnourished patients and parenteral route must be used. In such patients, despite eagerness to provide excessive amounts of nutritives and calories which is supported by large deficiencies, one must take into account metabolic abilities of the body. Administration of excessive amounts of energy, in particular originating from glucose, may result in refeeding syndrome due to phosphate – vitamin deficiency, i.e. multiorgan failure. Therefore supply must be limited and dose of energy should be gradually increased, the slower the deeper are nutritional deficiencies. Energy deficiency affects any organ and the metabolism is slow. Therefore it is useless to administer excessive amounts of nutritives since they cannot be metabolized. This is particularly the case with fat emulsions that at the early stages of nutritional treatment in severely malnourished patients can be metabolized only to a small degree or not metabolized at all and put a needless load on the patient and can cause adverse effects (hypertriglyceridemia, hyperbilirubinemia).

<table>
<thead>
<tr>
<th>Microelements and vitamins</th>
<th>Enteral</th>
<th>Parenteral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium</td>
<td>30 μg</td>
<td>10-15 μg</td>
</tr>
<tr>
<td>Copper</td>
<td>0,9 mg</td>
<td>0,3-0,5 mg</td>
</tr>
<tr>
<td>Fluorine</td>
<td>4 mg</td>
<td>0,95-1,49 μg</td>
</tr>
<tr>
<td>Manganese</td>
<td>2,3 mg</td>
<td>60-100 μg</td>
</tr>
<tr>
<td>Molybdenum</td>
<td>45 μg</td>
<td>19-25 μg</td>
</tr>
<tr>
<td>Selenium</td>
<td>55 μg</td>
<td>20-60 μg</td>
</tr>
<tr>
<td>Zinc</td>
<td>11 mg</td>
<td>2,5-5 mg</td>
</tr>
<tr>
<td>Vitamin B_{12} (thiamin)</td>
<td>1,2 mg</td>
<td>3 mg</td>
</tr>
<tr>
<td>Vitamin B_{6} (riboflavin)</td>
<td>1,3 mg</td>
<td>3,6 mg</td>
</tr>
<tr>
<td>Niacin</td>
<td>16 mg</td>
<td>40 mg</td>
</tr>
<tr>
<td>Folic acid</td>
<td>400 μg</td>
<td>400 μg</td>
</tr>
<tr>
<td>Panthotenic acid</td>
<td>5 mg</td>
<td>15 mg</td>
</tr>
<tr>
<td>Vitamin B_{6} (pyridoxinw)</td>
<td>1,7 mg</td>
<td>4 mg</td>
</tr>
<tr>
<td>Vitamin B_{12} (cobalamine)</td>
<td>2,4 μg</td>
<td>5 μg</td>
</tr>
<tr>
<td>Biotin</td>
<td>30 μg</td>
<td>60 μg</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>90 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>900 μg</td>
<td>1000 μg</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>15 mg</td>
<td>5 μg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>15 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>120 μg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Na</td>
<td>60-80 mEq</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>30-60 mEq</td>
<td></td>
</tr>
<tr>
<td>Ca</td>
<td>4,6-9,2 mEq</td>
<td></td>
</tr>
<tr>
<td>Mg</td>
<td>8,1-20 mEq</td>
<td></td>
</tr>
<tr>
<td>Pi (PO4)</td>
<td>12-20 mEq</td>
<td></td>
</tr>
</tbody>
</table>
fore one must avoid excessive supply of these components at the start of nutritional treatment and often nutritional mixtures are used that lack fat emulsions. On the other hand, phosphate and vitamins B supply, in particular vitamin B1, are very important components of this therapy (14, 15).

A nutritional mixture is gradually enriched with improvement of patient’s condition and good tolerance of the treatment, reaching a standard requirement. It is important to include current body weight instead of target body weight in calculations of target protein requirement. This also prevents excessive supply.

3. Malignancy

Cause of malnutrition is an additional factor that modifies the patient management. Malignancy, in particular end-stage malignancy, is accompanied by severe malnutrition (16). In malignancies, malnutrition very often results in preoperative complications. Therefore, when an elective procedure is planned and malnutrition is diagnosed, nutritional treatment should be initiated, often at a cost of delay of the surgical procedure (17, 18). In such cases composition of the nutritional mixture should also be adjusted to the underlying illness. It is emphasized that patients with malignancies require increased percentage of calories from lipids due to poor metabolism of lipids by tumor cells. Also quality of fatty acids may be of potential relevance. Polyunsaturated omega-3 fatty acids may potentially reduce inflammation that may be responsible for increased severity of malnutrition on anorectic-cachectic disease (19). However, addition of these fatty acids may be important only at the beginning of the treatment of cachectic patients and their permanent use in the nutritional mixture does not provide clear benefits (20).

4. Obesity

Malnutrition may be present in all patients, including those who due to their appearance are not expected to be malnourished. Obese patients, especially subjects with BMI above 25, are as often malnourished as underweight patients. Delay of nutritional intervention that is often observed, results in rapid progression of abnormalities related to malnutrition. Unfortunately, loss of body weight is observed relatively late. Until this time reduction of plasma protein pool (reduction of albumin concentration) predominates, accompanied by impairment of immunity related to reduction of lymphocyte count and reduction of muscle mass that reduces strength and immobilizes the patient. All these mechanisms result in various complications, in particular in patients in perioperative period.

When considering requirement for nutrients in obese patients, we must remember that current body weight should not be used since otherwise excessive supply of both proteins and calories can result. Target body weight should be used instead.

5. Inflammatory bowel disease

Nonspecific inflammatory bowel diseases include Crohn disease and ulcerative colitis. Etiology of these diseases is unclear. Except for abnormalities of immune response of genetic origin, role of environmental factors is emphasized. Inflammation dominates in both diseases (21, 22) and, depending on affected bowel segment, results in nutritional deficiencies.

Nutritional treatment in these diseases is of limited use and essentially is limited to cases of severe malnutrition that often accompanies these diseases or when the gastrointestinal tract cannot be sued due to complications (23). Some authors report good clinical results of so called bowel rest, i.e. complete parenteral nutrition in patients with Crohn disease, in particular at early stages of disease exacerbations. Nutritional treatment must be used most commonly in patients qualified to surgical treatment (24, 25).

In the context of diseases of inflammatory etiology, one must remember that certain nutrients affect immune response, including: arginine, glutamine, polyunsaturated fatty acids, nucleosides.

Due to potential immunosuppressive effects of omega-3 polyunsaturated fatty acids, that could be useful in these diseases. However immunomodulating substances can both stimulate or inhibit immune system depending on condition of immunocompetent cells and therefore it is impossible to establish when immunomodulating nutrition is absolutely
Nutritional treatment a various clinical setting – practical considerations

indicated, and when absolutely contraindi-
cated (26, 27).

Nutritional treatment may lead to delay of surgical treatment in some patients, provide better conditions for bowel wound healing, sometimes for fistula closing (Crohn disease) (28).

When treating such patients, in particular patients with Crohn disease, one must remember about vitamin deficiencies, in particular vitamin B deficiency, due to involvement of terminal segment of the ileum where vitamins B are absorbed. Very often abnormalities of calcium phosphate metabolism are observed, resulting from abnormalities of vitamin D metabolism. Bowel inflammation is also associated with chronic bleeding which leads to use of vitamins and elements required for erythropoiesis. In such patients deficiencies of vitamin B₁₂ and folic acid as well as iron should be corrected.

6. Renal failure

Malnutrition is very common in renal disease, in particular in patients with end stage renal failure who require renal replacement therapy. Nutritional treatment of patients undergoing dialysis therapy does not require any special modification of nutritional mixture however fluid restrictions must be kept in mind. Volume of nutritional mixture must be adjusted to water elimination ability of the body. One must remember that peritoneal dialysis results in bowel changes and prolonged peritoneal dialysis therapy may lead to gastrointestinal insufficiency and development of malabsorption syndrome (or multilevel intestinal obstruction due to changes in the intestinal walls). Therefore nutritional status should be assessed in such patients as often as possible and if abnormalities are found, adequate measures should be instituted. Proper and early initiation of nutritional treatment provides the patients with maximum benefits. If nutritional abnormalities progress, renal impairment progresses too, in particular metabolic abnormalities due to accompanying abnormalities of calcium and phosphate metabolism. When there are advanced metabolic abnormalities, nutritional treatment is particularly difficult and often unrewarding (29).

Nutritional treatment is most difficult in patients with end stage renal failure who do not require renal replacement therapy. Excessive protein supply may lead to progression of renal changes in these patients and make early initiation of dialysis therapy necessary. Therefore the nutritional mixture should cover minimum nitrogen requirement. Excessive fat supply may be associated with marked hypertriglyceridemia due to their impaired elimination from blood.

7. Intensive therapy

Patients from intensive care units usually have increased energetic requirements. This is due to metabolic condition that underlies their disorders. Postoperative trauma, sepsis, burns are associated with marked stress that causes pronounced hormonal abnormalities including e.g. increased release of catecholamines, thyrotropic hormone and as a consequence, of thyroid hormones, adrenocorticotrophic hormone and glucocorticoids and mineralocorticoids (30). These abnormalities result in dominance of catabolic processes, inhibition of glycolysis and increase of gluconeogenesis, resulting in hyperglycemia. Peripheral tissues are resistant to insulin which facilitates the above mentioned phenomena or underlies them. These abnormalities eventually result in reduced endogenous amino acid synthesis, increased proteolysis, increased nitrogen elimination, resulting in negative nitrogen balance. Sodium and water retention play an important role in the patomechanism of stress related diseases, resulting on other, serious consequences (31, 32).

The above mentioned abnormalities show that nutritional mixture needs to be adjusted during nutritional treatment of such patients (vast majority). Protein supply should be increased in such patients due to its increased use and reduced production, resulting in negative nitrogen balance.

Fight against hyperglycemia is also one of the priorities of the treatment of patients in poor condition. The mixture should not contain excessive amounts of glucose. Often patients hospitalized in these departments have respiratory insufficiency except for their underlying disease. Excessive supply of glucose results in increased production of carbon dioxide which intensifies preexisting respiratory abnormalities. In such cases ration of energy obtained from glucose and lipids should be equal. It also
provides adequate nonprotein energy to the patient. Such energy cannot be provided using glucose as a sole source of energy (33).

In such cases nutritional treatment should be supplemented with intensive insulin therapy to maintain physiological glucose level. Similar effects may be achieved by adequate selection of glucose dose for an individual patient. If continuous insulin treatment is given, the nutritional mixture need not to be supplemented with insulin; otherwise this is indicated in any intensive care patient. In all cases blood glucose should be monitored very often, in particular at an early stage of nutritional treatment (33, 34).

Eventually, volume of nutritional mixtures must be mentioned. Excessive water supply results in fluid transfer to the extravascular space, leading to edema which markedly worsens patient prognosis. Volume of a nutritional mixture should be closely adjusted to patient needs, preferably based on reliable fluid balance. For majority of patients, fluid overload is of great importance, in particular when urine output and/or heart failure is present. Some patients may particularly rapidly decompensate following administration of excessive amounts of fluid and develop systemic edema, including pulmonary edema, which markedly worsens patient prognosis.

Therefore intensive care patients should receive a nutritional mixture characterized by increased nitrogen amount, reduced glucose amount and moderate volumes.

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