Substrates for Enteral and Parenteral Nutrition

Module 7.2.

Substrates for Parenteral Nutrition

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Learning objectives:

- To know the components of tailored parenteral nutrition;
- To know the differences between different intravenous preparations;
- To understand the therapeutic options provided by the various preparations.

Contents:

1. Introduction
2. Protein sources in parenteral nutrition
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   4.3. Omega-3 fatty acid emulsions
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5. Micronutrients
6. Water and electrolytes
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Key messages:

- to ensure the proper function of the individual and his or her growth, exclusively parenteral nutrition must be complete and provide macronutrients (protein and energy) and micronutrients (electrolytes, trace elements, vitamins) together with water;
- the protein requirement for a healthy adult is 0.75–0.8g protein/kg body weight. Amino acids solutions always contain all essential amino acids, but non-essential amino acids may need to be delivered separately;
- glucose is the only carbohydrate used in parenteral nutrition nowadays; its provision should not exceed 4-5 mg/kg/min;
- fatty acids (FAs) are not only a source of energy, but also essential components of cell membranes, precursors for hormone synthesis and precursors for eicosanoids; lipids are now a basic constituent of PN admixtures;
there are various types of FA solutions, such as LCT, MCT/LCT, structured lipids, olive oil, and omega-3 PUFAs. The careful selection of lipid emulsion is important because this may improve the clinical outcome;

micronutrient supplementation at standard doses in artificial nutrition is recommended for all types of patients;

although the administration of electrolytes during PN depends upon the patient’s requirements, minimal amounts must always be administered on a daily basis.
1. Introduction

Some authors say that modern parenteral nutrition started in three major phases:

1. 1937: Elman used protein hydrolysates with glucose to feed patients via peripheral veins,
2. 1961: Wretlind created the very first safe lipid emulsion and infused it through peripheral veins,
3. 1968: Dudrick and his team administered complete parenteral nutrition via central veins (1).

Although Dudrick experienced many problems with lipid emulsion, and was forced to reduce its use for some years because of the FDA’s decision to withdraw Lipomul (a lipid emulsion manufactured in USA), he has always emphasized that modern parenteral nutrition (PN) has to be complete. In his words, to ensure the proper function of the organism and its growth, PN must include solutions providing macronutrients (protein precursors and energy) and micronutrients (electrolytes, trace elements, vitamins) together with water. In that form we have known PN for the last forty years.

2. Protein Sources in Parenteral Nutrition

Proteins are the basic nutrients enabling life on Earth and in building every cell in every organism. The minimum protein requirement in the diet is estimated to be 0.75 g protein/kg/body weight (b.w.), but that number changes with the age: for infants it is 0.9–1.0 g protein/kg/b.w., and for an adult 0.75–0.8 protein/kg/b.w. (2).

Proteins are built from amino acids. Among the latter there is a group, which must be delivered under all circumstances. These are the essential amino acids: isoleucine, leucine, lysine, methionine, phenyalanine, threonine, tryptophan and valine. The requirement for essential amino acids also decreases with age, but in a different proportion from the total protein: it falls from 43% for infants to 36% in children down to 19–20% for adults. Another important group of amino acids can become essential in particular conditions, such as trauma, burns or sepsis. They are called conditionally essential amino acids and include histidine, tyrosine, cysteine, glutamine and taurine.

2.1. Standard Amino Acid Solutions

Solutions of crystalline amino acids, which yield 4 kcal/g if oxidized for energy, are used as a protein source during parenteral nutrition. The first such solutions were created by Elman (1937), who administered a casein hydrolysate supplemented by tryptophan and methionine or cysteine (1).

These solutions always contain all essential amino acids, and the amount of non-essential varies depending on the admixture. Amino acids solution are available from different manufacturers in stock admixtures with concentration from 3% up to 20% (8.5% and 10% are the most popular).

Very rarely do solutions contain sufficient amounts of the conditionally essential amino acids. This is mainly due to pharmaceutical problems during the preparation of intravenous admixtures. For example, cysteine rapidly oxidizes to yield the dimer cystine which itself is very poorly soluble, and acidic conditions lead to reduction of the sulphonydryl group and the formation of H₂S. Tyrosine is also poorly soluble, and glutamine is unstable in aqueous solutions (2).
2.2. Special Amino Acid Solutions

Commercially available products may contain special amino acid patterns formulated for special disease states and conditions. For this reason they may also contain modified amounts of electrolytes and buffers. It should be always remembered that these admixtures should be reserved for patients who are expected to benefit clinically from their use. These formulations include:

a) amino acid solutions for renal failure – composed principally of essential amino acids, because, according to many authors, the non-essential ones can be physiologically recycled from urea. These solution are quite dilute (5-6.5%) despite the water restriction often needed in renal failure patients, and their electrolyte content is limited (some of them do not contain any electrolytes);

b) amino acid solutions for liver failure – these admixtures are designed only for hepatic encephalopathy patients (it is important to note that even substantial elevation of SGOT/AST, SGPT/ALT or other liver enzymes is not an indication for the use of these diets). They contain increased amounts of branched-chain amino acids (BCAA) and a decreased amount of aromatic amino acids (AAA) in comparison to standard admixtures. The use of such an admixture helps to protect the brain from increased transport of AAA to the brain and their transformation into pernicious neurotransmitters (3);

c) solutions for metabolic stress, hypercatabolism, trauma and burns – these admixtures are also based on an increased content of BCAA, because this is thought to be beneficial when there is increased muscle catabolism. Higher amounts of leucine, isoleucine and valine are thus provided. The results of clinical studies vary, and more research is needed for the evaluation of these solutions;

d) immunomodulators: glutamine.

Glutamine is an non-essential amino acid, which may become essential in stress conditions. It is a potent immunomodulator. Glutamine enhances activation and proliferation of lymphocytes and macrophages, and expression of interleukins 1 and 2 (IL-1 and 2) (2). It is also a preferred fuel source and a key player in the intermediary metabolism of the small bowel mucosa. Moreover intraluminal glutamine induces a variety of protective mechanisms against ischaemic insults, such as boosting antioxidant enzymes (e.g. glutathione and haem-oxgenase-1) or the anti-inflammatory transcription factor (4,5,6).

On the basis of current literature, glutamine administration has been recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) in the following patients: severe burns and/or trauma, all ICU patients in whom parenteral nutrition is needed, acute pancreatitis when PN is needed, and in patients undergoing major surgery. PN glutamine supplementation should be in doses of >0.2 g/kg/day to be effective (18). ESPEN recommended a dosage of 0.2–0.4 g/kg/day of L-glutamine (e.g. 0.3–0.6 g/kg/day alanyl-glutamine dipeptide). These solutions should be added to the parenteral bags before infusion. The total amino acid content in PN may be reduced by the amount of glutamine added to the all-in-one admixture, but under no circumstances should it replace the basic AA solution completely.

As free glutamine is unstable in aqueous solution unless it is bound to protein, parenteral glutamine (GLN) is often provided in dipeptide form, such as glycyl-glutamine (GLY-GLN) or alanyl-glutamine (ALA-GLN) (4,5).

To summarize, it should be emphasized that the needs for protein substrate must be fully covered during parenteral nutrition. As the ESPEN guidelines clearly state, ICU patients should be given approximately 1.3–1.5 g/kg ideal body weight/day, in conjunction with an adequate energy supply. In surgical patients, a daily nitrogen delivery equivalent to a protein intake of 1.5 g/kg ideal body weight (or approximately 20% of total energy requirements) is generally effective to limit nitrogen losses (6).
3. Carbohydrates

Carbohydrates (CHO) should cover 50-60% of total energy during artificial nutrition. Whereas polysaccharides, oligosaccharides (maltodextrins), sucrose and glucose can all be used for enteral nutrition, glucose (dextrose) is the only carbohydrate used in parenteral nutrition nowadays. It provides 3.4 kcal/g (not the 4 kcal/g so often quoted), and represents a convenient energy source. Of course, lipids also provide energy during PN, but as compared to the fatty acids, glucose has three unique properties related to energy metabolism: it can provide ATP in the absence of oxygen; it offers a higher oxidative efficiency (ATP/oxygen ratio) and it allows an anaplerotic flux providing Krebs-cycle intermediates and other compounds (6). Therefore, glucose represents an invaluable therapeutic option. Carbohydrates other than glucose, such as fructose and polyols (sorbitol and xylitol), were used in PN in the past, because they were thought to be beneficial for the stability of admixture and better tolerated by patients with diabetes mellitus (2). According to the latest studies, however, neither polyols nor fructose are superior to glucose in parenteral nutrition for diabetic patients, and compounding units and multi-chamber bags decrease substantially the risk of instability (7). Moreover, infusion of fructose and polyols can produce side effects, such as lactic acidosis, osmotic diuresis or liver injury in patients with aldolase deficiency (2,8,9). All of the above and the low price of glucose have combined to result in the use of glucose as the only carbohydrate in parenteral nutrition. From the metabolic perspective carbohydrates are not only an energy source, but they influence protein metabolism as well. Amino acids released from muscle breakdown represents a major source of endogenous substrates, while CHO metabolism, in turn, provides the carbon skeleton required for non-essential amino acid synthesis (6).

The basal requirement of glucose is usually estimated to be roughly 2 g/kg/day for an adult (6). It is important, however, to bear in mind that glucose can be metabolised by all cells of our body, but there are limits to this process relating to energy expenditure. Under stress conditions the rate of gluconeogenesis cannot be decreased by the administration of glucose; moreover, glucose uptake and oxidation is often impaired (2). For those reasons, large loads of glucose may represent an additional stress and it is safer to reduce them.

In physically inactive adults or bedridden patients, the oxidation rate is dependent on energy expenditure, and its maximal rate is approximately 4-5 mg/kg/min (2). Therefore in resting conditions the daily CHO intake should not exceed 7g/kg (or about 20 kcal/kg); it is, however, to some extent dependent on the nutritional regimen (2):
- during continuous feeding the rate of glucose infusion should not exceed the maximal rate of oxidation 4-5 mg/kg/min (corresponds to 0.25 – 0.3 g/kg/h);
- during cyclic artificial nutrition glucose the dosage should not be higher than 8-10 mg/kg/min (0.5 – 0.6 g/kg/h) at any time.

When infused at the higher rate, this exceeds the rate of oxidation and only about half of the administered glucose is oxidized, the remainder being stored in liver and muscle as glycogen to be used afterwards.

Therefore the maximal infusion rates should not therefore exceed 4-5 mg/kg/min in adult patients (2).

Intravenous glucose is available in stock admixtures with concentration from 5% (not used in PN) up to 70% (10%, 20%, 30%, 40% and 50% are the most popular).

4. Lipids

As fatty acids (FAs) are not only a source of energy, but also essential components of cell membranes, precursors for hormone synthesis and precursors for eicosanoids, lipids are normal constituents of PN admixtures. They should cover 20-40% of energy requirements; this proportion depends, however, not only on the clinical status of the patient, but also on the possibility of effective oxidation. The rate of the latter depends
not only on energy expenditure and the clinical situation, but also on hormonal status and the presence of other energy substrates, such as glucose (2).

The intestinal chylomicron was used as a model to create intravenous lipid emulsions. In that model, the core of the particle is made of triglycerides and some lipid-soluble vitamins, and the surface is made of phospholipids, free cholesterol, and the rest of lipid-soluble vitamins (2,9).

After being transported to the circulation and thus to tissues and organs, lipid particles are hydrolyzed, and there is then an exchange of neutral lipids (triglycerides and cholesteryl esters) with endogenous cholesterol-rich lipoproteins LDL and HDL, and uptake of remnant particles (enabled by vitamin E) (2,10). A knowledge of these processes is important to understand why various commercially available lipid emulsions may exert different clinical effects.

Fatty acids are classified according to structural characteristics including the length of the carbon chain, the presence and position of double bonds in the chain, and their configuration (i.e. cis vs. trans) (2). They may be classified as saturated (no double bonds) or unsaturated (one or more double bonds). The latter can be divided into monounsaturated (one double bond) or polyunsaturated fats (two or more double bonds). Another classification is based on the length of the chain: short chain (<8 carbons), medium chain (8–14 carbons) or long chain (16 or more carbons), and even very long chain (20 or more carbons). With regard to the position of the double bond within the fatty acid chain, three families are typically distinguished: omega-3, omega-6 and omega-9 (also referred to as n-3, n-6 and n-9) (2,6).

Many fatty acids can be synthesized within the human body. Two very important FAs, however, must be administered, because they cannot be synthesized. For that reason linoleic acid (an 18 carbon omega-6 fatty acid) and alpha-linolenic acid (an 18-carbon omega-3 fatty acid) were called essential FAs.

The daily requirement of linoleic acid in health is 2-5g (or 1-2% of total energy), and perhaps about one fifth of that (or 0.2% of total energy) of alpha-linolenic acid. In ICU patients, 9–12 g/day of linoleic acid and 1–3 g/day of alpha-linolenic acid should be delivered on a daily basis (6).

Generally speaking, intravenous lipid emulsions (LCT, MCT or mixed emulsions) can be administered safely at a rate of 0.7 g/kg up to 1.5 g/kg over 12–24 h in ICU patients. (Grade B recommendation) (6).

PN admixtures should generally be administered as complete formulae to avoid essential FA deficiency. In patients with significant hypertriglyceridaemia (TG concentration above 4–5 mmol/l or 350–450 mg/dl), however, their use is contraindicated. When TG concentrations breach a threshold of 2.0–3.5 mmol/l or 190–260 mg/dl, smaller amounts of lipid emulsion should be administered (2).

The essential fatty acids are synthesized in plants and there is a high content in certain plant oils (e.g. corn, sunflower, soybean). Therefore intravenous emulsions were initially created using oil from these plants. Although the first clinically used intravenous lipid emulsion – based on cottonseed oil - was created in the United States of America (Lipomul), its administration was unsuccessful due to many side-effects, and it was withdrawn from the market in the mid-sixties. Until 1977 there was then no lipid emulsion commercially available in the USA (1). Meanwhile, Swedish researcher Arvid Wretlind constructed a lipid emulsion that was well tolerated as a source of energy and essential fatty acids. The emulsion was based on soybean oil emulsified with egg phosphatides (1,2). So, history began with the long-chain triglyceride (LCT) emulsions.

4.1. LCT Emulsions

LCT emulsions have been available for over 50 years and they still represent a valuable clinical option for PN. Nowadays, they are manufactured on a base of soya oil (e.g. Intralipid from Fresenius Kabi or Lipofundin N from BBraun), and are generally harmless
from the clinical perspective. To ensure safety, LCT emulsions should not be infused at a rate in excess of 0.1 g/kg/h, particularly in stressed or starved patients. Intravenous LCT emulsions are available in stock admixtures and separately with concentrations from 10% through 20% to 30%. Although useful in many patients, LCT emulsions are potentially harmful in those in whom the inflammatory response is marked. Overzealous production of inflammatory mediators can be damaging to tissues and may worsen the patient’s prognosis. Unfortunately the first generation LCT emulsions are highly pro-inflammatory. This has been a driver for the development of new formulations.

4.2. MCT/LCT Emulsions

Medium chain triglycerides (MCTs) are better tolerated by critically ill patients, not only because they do not serve as a source for synthesis of proinflammatory mediators, but also because they do not need carnitine for their transportation to mitochondria (in contrary to LCTs), so they can be effective even in carnitine-depleted patients (1). They should be administered at a rate equal to or lower than 0.15 g/kg/h (2). The use of MCT/LCT emulsions has helped to reduce the duration of mechanical ventilation in ICU patients, improved the condition of individuals with COPD, and improved albumin synthesis (11,12,13). In surgical patients a reduction of postoperative complications was observed, including a reduction of morbidity after hemihepatectomy (the latter represents the case of extended surgery) (14,15). These encouraging effects of MCT emulsions has resulted in the recommendation for their use in ICU patients (6).

Another approach and an alternative to physical mixture of LCTs and MCTs was the creation of mixed triglyceride molecules, named structured triglycerides (STG). In these, fatty acids of different chain lengths were esterified into one particle. In some in vitro and in vivo studies STGs showed beneficial effect on the metabolism of muscle, protein synthesis and nitrogen balance when compared to LCTs (3). Generally speaking, however, the clinical effects of STGs were similar to those obtained with MCTs/LCTs admixtures.

The inclination to change the fatty acid pattern (including the proportion of saturated, monounsaturated and polyunsaturated fats and the ratio between omega-6 and omega-3 essential fatty acids) and content of antioxidants (decrease of polyunsaturated FAs, increase in alpha-tocopherol) resulted not only in the creation of MCT-based emulsions, but also other emulsions, such as those based on olive oil or fish oil, and mixed formulae, with more than two emulsions (eg SMOF Lipid).

4.3. Omega-3-rich Emulsions

It is important to realize that when we discuss effects of the administration of emulsions containing omega-3-fatty acids or based on fish oil, we are de facto discussing the impact of eicosapentaenoic acid (EPA, 20 carbons and 5 double bonds) and docosahexaenoic acid (DHA, 22 carbons and 6 double bonds), and in some cases alpha linoleic acid (ALA, 18 carbons and 3 double bonds). Hence emphasis should be on the EPA and DHA content of feeds, and not simply the amount of fish oil without this information. Fish oils contain omega-3-polyunsaturated fatty acids (omega-3 PUFA), mainly as EPA and DHA. They can therefore generate potentially favourable immunomodulatory and perhaps anti-inflammatory effects (16,17,18). It is postulated that their administration leads to a more balanced immune response which may result in faster resolution of inflammation and recovery (17,18). Mechanisms of action of omega-3-FAs include:
- alterations in the physical properties of the cell membrane;
- effects on cell signalling pathways (transcription factors reported to be modified include nuclear factor kappa B (NFkB) and peroxisome proliferator activated receptor (PPAR)-alpha and gamma);
- alterations in the pattern of lipid mediators produced.
Omega-3-PUFAs have proven their clinical efficacy, and can now be recommended in many groups of patients on PN, such as:
- children with liver failure children (where they may help to reverse PN-associated cholestasis) (19);
- patients undergoing abdominal surgery (reduction of postoperative complications) (20);
- patients in ICU (ameliorated clinical course) (6).
A review of the effects of including fish oils in PN in ICU patients concluded that there is a significant reduction in the length of stay, but no differences in mortality were noted (6). The greatest influence was observed in patients with abdominal sepsis (6).
For those reasons ESPEN recommends its use in patients with acute respiratory distress syndrome (ARDS) (Grade A), mild sepsis (Grade B) and trauma patients (Grade A) (6, 21).
Canadian recommendations advocate the use of an enteral formula with fish oils, borage oils and antioxidants in patients with Acute Lung Injury (ALI) and ARDS (22).

4.4. Olive Oil

Some emulsions, such as Clinoleic (Baxter) and SMOF Lipid (Fresenius), contain MCT and olive oil. The latter was observed to decrease oxidation and improve lymphocyte function (3). Sala-Vila et al. have summarized the literature on olive oil-based emulsions and concluded that they are safe, well tolerated and present advantages in the liver function of burned patients (23). ESPEN guidelines also emphasize the safety of olive oil emulsions and recommend their use in ICU patients (6). These emulsions are also safe and possibly helpful in patients on home parenteral nutrition for intestinal failure (24).
All types of lipid emulsion are commercially available as separate bottles/bags or as a part (chamber) of three-chamber bags (such as SMOF Kabiven, Multimel, Nutriflex, etc.) To sum up, the creation and selection of the lipid emulsions have probably been the most difficult tasks in the composition of parenteral nutrition. The challenge has however been worth addressing, as correctly used they may improve the clinical outcome.

5. Micronutrients

Micronutrients (vitamins and trace elements) are essential parts of parenteral nutrition and should be administered right from its initiation. Adequate micronutrients are required for effective utilization of protein and energy substrates and, which is even more important, the patient’s micronutrient status at the time of commencing nutritional
support is not known. Micronutrients deficiencies can remain unknown for a long time before the development of clinical symptoms. During enteral nutrition achieving a proper dose of micronutrients is relatively easy, if only the infusion meets the energy requirements for the patient. This results from the European Union’s directive on dietary foods for special medical purposes FSMPs, which safeguards integral vitamin and trace element content. In PN, however, the administration of micronutrients, is completely dependent on additions to the regimen, which must therefore include the prescription of vitamins and trace elements. ESPEN recommends micronutrient supplementation of artificial nutrition at standard doses in all types of patients (6).

Commercially available vitamin preparations for PN include single vitamin products and multivitamins. The latter are typically composed of ascorbic acid, retinol, ergocalciferol, thiamin, riboflavin, pyridoxine, niacinamide, dexamethasone, DL-alpha-tocopheryl acetate, folic acid, cyanocobalamin, biotin and phylloquinone (Table 1).

**Table 1.**
Examples of vitamin products for PN which are commercially available in Europe

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Unit</th>
<th>Name of the PN supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (retinol)</td>
<td>μg</td>
<td>Vitalipid + Soluvit/Solivito¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cernevit²</td>
</tr>
<tr>
<td>D (cholecalciferol)</td>
<td>μg</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1000</td>
</tr>
<tr>
<td>E (alpha tocopherol)</td>
<td>mg</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.5</td>
</tr>
<tr>
<td>K</td>
<td>μg</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10.2</td>
</tr>
<tr>
<td>B₁ (thiamine)</td>
<td>mg</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.5</td>
</tr>
<tr>
<td>B₂ (ryboflavine)</td>
<td>mg</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.1</td>
</tr>
<tr>
<td>B₆ (pyridoxine)</td>
<td>mg</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.5</td>
</tr>
<tr>
<td>Niacin</td>
<td>mg</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>46</td>
</tr>
<tr>
<td>B₁₂</td>
<td>μg</td>
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<tr>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Folate</td>
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<td>400</td>
</tr>
<tr>
<td></td>
<td></td>
<td>414</td>
</tr>
<tr>
<td>Biotin</td>
<td>μg</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>69</td>
</tr>
<tr>
<td>C (ascorbic acid)</td>
<td>mg</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>125</td>
</tr>
</tbody>
</table>

¹Fresenius Kabi
²Baxter Healthcare

Commercially available trace element solutions for PN almost always include zinc, chromium, copper, selenium and manganese. They are generally multicomponent and there are neonatal, paediatric and adult versions to cater for different requirements. Some contain electrolytes, some also iron, molybdenum, fluoride and iodine. **Table 2** presents trace elements products available for PN (2).
### Table 2.
Examples of trace element products for PN commercially available in Europe

<table>
<thead>
<tr>
<th>Trace element</th>
<th>Unit</th>
<th>Name of the PN supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Additrace(^1)</td>
</tr>
<tr>
<td>Zinc</td>
<td>mg</td>
<td>6.5</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>100</td>
</tr>
<tr>
<td>Copper</td>
<td>mg</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>20</td>
</tr>
<tr>
<td>Iron</td>
<td>mg</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>20</td>
</tr>
<tr>
<td>Manganese</td>
<td>mg</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>5</td>
</tr>
<tr>
<td>Selenium</td>
<td>mg</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>0.4</td>
</tr>
<tr>
<td>Chromium</td>
<td>mg</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>0.2</td>
</tr>
<tr>
<td>Molybdenium</td>
<td>mg</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>0.2</td>
</tr>
<tr>
<td>Iodine</td>
<td>mg</td>
<td>131</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>1</td>
</tr>
<tr>
<td>Fluoride</td>
<td>mg</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>μg</td>
<td>50</td>
</tr>
</tbody>
</table>

\(^1\)Fresenius Kabi
\(^2\)French Co

Some patients, such as the critically ill, have increased requirements for most micronutrients (2). Large doses of zinc, copper and selenium may help severely burned patients to compensate for the losses through the skin and to reduce infection as well as to improve wound healing (25,26). For that reason trace elements should be supplemented in a higher than regular amount in burns patients (27). Additional selenium, according to some but not all researchers, should be administered to all critically ill patients (2). Trace elements excreted in bile (such as copper and manganese) will need to be given in restricted amounts in those with severe liver disease or biliary obstruction. Fixed dose combinations make such adjustments difficult.

### 6. Water and electrolytes

The administration of electrolytes during PN depends upon the patient’s requirements; the amounts must be considered clinically each day, and also modified according to laboratory tests. Typical values for adults are as follows:
- Sodium: 1-2 mEq or mmol/kg/d
- Potassium: 0.5 – 1 mEq or mmol/kg/d
- Calcium: 0.1 mEq/kg/d or 0.05 mmol/kg/d
- Magnesium: 0.1 mEq/kg/d or 0.05 mmol/kg/d
- Phosphate: 0.1 – 0.5 mEq/kg/d or 0.03 - 0.2 mmol/kg/d
- Chloride: as needed to maintain balance
- Acetate: as needed to maintain balance
In multichamber bags electrolytes are already included at standard doses in solution (amino acid chamber). If more than those included are needed, and when the PN is being prepared using separate substrates, it would be usual to commence with an isotonic saline solution to which is added high concentration solutions of the other salts, such as calcium gluconate, magnesium sulfate, and potassium chloride. Phosphates are available in both nonorganic and organic forms, the latter being better tolerated and safer from the pharmaceutical point of view (stability issue). Similarly to electrolytes, water provision should be adjusted to the clinical situation. In adults, however, the administration should very rarely be lower than 30 ml/kg/day. The standard range is 30-40 ml/kg/day, but is higher in the case of extrarenal or renal fluid losses, or fluid sequestration into extracellular or transcellular compartment (2). Therefore, in many patients, additional provision of water must be ensured as a part of PN (in the bag) or in the form of extra intravenous solutions. Some example solutions, commercially available for intravenous use, are presented in Table 3. It is of the utmost importance to notice the electrolyte content of these solutions.

**Table 3.** Commercially available solutions for intravenous administration

<table>
<thead>
<tr>
<th>Type of iv solution</th>
<th>mOsm/l</th>
<th>Sodium (mEq/l)</th>
<th>Potassium (mEq/l)</th>
<th>Chloride (mEq/l)</th>
<th>Calcium (mEq/l)</th>
<th>Magnesium (mEq/l)</th>
<th>Lactate (mEq/l)</th>
<th>Energy in 1000 ml (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% sodium chloride (saline)</td>
<td>308</td>
<td>154</td>
<td>-</td>
<td>154</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ringer’s solution</td>
<td>312</td>
<td>147</td>
<td>4</td>
<td>156</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lactated Ringer solution</td>
<td>277</td>
<td>130</td>
<td>4</td>
<td>109</td>
<td>3</td>
<td>-</td>
<td>28</td>
<td>-</td>
</tr>
<tr>
<td>Hartmann solution</td>
<td>275</td>
<td>131</td>
<td>5</td>
<td>111</td>
<td>2</td>
<td>-</td>
<td>28</td>
<td>-</td>
</tr>
<tr>
<td>Jonosteril</td>
<td>295</td>
<td>137</td>
<td>4</td>
<td>110</td>
<td>1.7</td>
<td>1.3</td>
<td>37</td>
<td>200</td>
</tr>
<tr>
<td>Glucose 5%</td>
<td>278</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>200</td>
</tr>
</tbody>
</table>

**7. Summary**

To ensure the proper function of the organism and its growth, PN must provide macronutrients (protein and energy) and micronutrients (electrolytes, trace elements, vitamins), together with water. Solutions of crystalline amino acids are used as the protein source during PN. These solutions always contain all essential amino acids, and the amount of non-essential amino acids varies depending on the admixture. Glucose is the only carbohydrate used in parenteral nutrition nowadays, while there is a wide
selection of lipid emulsions, including alone or in combination LCT emulsions, MCT, olive oil and fish oils. The choice depends on the clinical situation and is partially informed by trial data.

Trace elements, vitamins, electrolytes and water are indispensable components of every PN admixture and should be routinely used.

8. References


