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INTRODUCTION PART TO THE ESPEN GUIDELINES ON ENTERAL NUTRITION

Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, Definitions and General Topics

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Summary The ESPEN guidelines on enteral nutrition are the first evidence-based European recommendations for enteral nutrition. They were established by European experts for a variety of disease groups. During guideline development it became evident that terms and definitions in clinical nutrition have been used inconsistently depending on medical disciplines as well as regional and personal preferences. Therefore, to increase explanatory accuracy it was necessary to unify them. In this chapter terms and definitions used throughout all guidelines are explained. Additionally answers to more general questions, which might be important in most indications are dealt with, i.e. use of fibre containing and diabetes formulae.

The full version of this article is available at www.espen.org.

Abbreviations: EN, Enteral nutrition; ONS, Oral nutritional supplements; MUFA, Mono-unsaturated fatty acids; LCHM, Low carbohydrate-high MUFA; HCLF, High carbohydrate low fat formulae

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Introduction

The aim of the ESPEN guidelines on enteral nutrition (EN) is to evaluate the evidence on EN in different indications and serve as orientation tools for distinct decisions in clinical practice. Therefore, the single chapters focus on specific questions relevant to the respective indication. More general questions, which might be important in all or several indications are dealt with in this introductory chapter to avoid repetition. Furthermore, the terminology and definitions used throughout these guidelines are also explained in this chapter.

Terminology

The following terms are used throughout the ESPEN guidelines for EN.

Enteral nutrition

The term EN is used to comprise all forms of nutritional support that imply the use of "dietary foods for special medical purposes" as defined in the European legal regulation of the commission directive 1999/21/EC of 25 March 1999,[1] independent of the route of application. It includes oral nutritional supplements (ONS) as well as tube feeding via nasogastric, nasoenteral or percutaneous tubes. This definition differs from definitions used in many other publications where "EN" is rather used for tube feeding only regardless if blenderized food or specific industrial products are used. This decision was based on the fact that many studies dealing with EN report on both ONS and tube feeding. Furthermore, prescription and reimbursement of EN is in many countries dependent of the use of industrial products rather than the route of application. EN is part of a qualified nutritional regimen in the in- and outpatient setting, and usually one of the tasks of professionals with special training in EN or the nutritional support team.

Enteral formulae

Any dietary food for special medical purposes designed for use in tube feeding or as an ONS. Enteral formulae can be (1) *nutritionally complete*, when given in the recommended amount, to be used as a sole source of nutrition or as a supplement to the patient's normal intake, or (2) *nutritionally incomplete*, to be used as a supplement only and not as a sole source of nutrition.

Oral nutritional supplements (ONS)

Supplementary oral intake of dietary food for special medical purposes in addition to the normal food. ONS are usually liquid but they are also available in other forms like powder, dessert-style or bars.

Synonyms used in literature: sip feeds.

Nutritional support

Nutritional support includes food fortification, ONS, tube feeding and parenteral nutrition as outlined in Fig. 1. It aims for increased intake of macro- and/or micronutrients. It is different from "special diets" which might be indicated in diseases like celiac disease.

Standard formulae

Standard formulae are enteral formulae with a composition, which reflects the reference values for macro- and micronutrients for a healthy population. Most standard formulae contain whole protein, lipid in the form of long-chain triglycerides (LCT), and fiber. However, non-fiber containing formulae with otherwise similar composition also exist.

Most standard formulae contain neither gluten nor lactose in clinically relevant amounts. The presence of gluten or lactose should clearly be mentioned on the label.

Disease-specific formulae

Disease-specific formulae include those with macro- and micronutrient compositions adapted

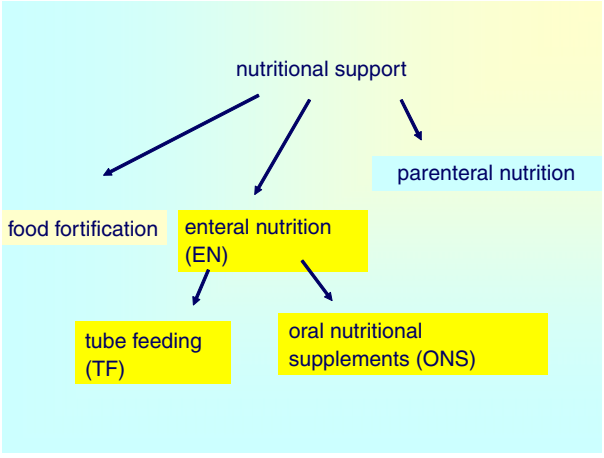

Figure 1 Nutritional support.

to the needs of a specific disease and/or digestive or metabolic disorder.

Immune modulating formulae

Immune modulating formulae contain substrates to modulate (enhance or attenuate) immune functions.

Synonyms used in literature: immunonutrition, immune-enhancing diets

Low, normal and high energy formulae

Normal energy formulae provide 0.9–1.2 kcal/ml, high energy formulae are anything above this, low energy formulae anything below.

High protein formulae

High protein formulae contain 20% or more of total energy from protein.

Whole protein formulae

Whole protein formulae contain intact proteins.

Synonyms used in the literature: polymeric, high molecular weight or nutrient defined formulae

Peptide-based formulae

Peptide-based formulae contain protein predominantly in peptide form (2–50 amino acid chains).

Synonyms used in the literature: oligomeric, low-molecular weight, chemically defined formulae.

Free amino acid formulae

Free amino acid formulae contain single amino acids as the protein source.

Synonyms used in the literature: elemental, monomeric, low molecular weight, chemically defined formulae.

High lipid formulae

High lipid formulae contain more than 40% of total energy from lipids.

High monounsaturated fatty acid (MUFA) formulae

High MUFA formulae contain 20% or more of total energy from MUFA.

Normal food

Normal diet of an individual as consumed at home/in a restaurant/etc. or as offered by the catering system of a hospital. This includes special diets e.g. gluten-free, lactose-free diets.

Fortified food

Normal food enriched with specific nutrients, in particular with energy and/or proteins, minerals, vitamins, trace elements.

Synonyms used in the literature: enriched food.

Nutritional counselling

Nutritional counselling of an individual or a group of persons by a nutritional expert, e.g. dietitian.

Synonyms used in the literature: dietary counselling, dietetic advice.

Definitions

The following definitions are used in the guidelines.

Malnutrition

Malnutrition is a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome.[2]

Undernutrition

Undernutrition is primarily used in the context of deficient energy or protein intake or absorption and is often described as protein energy malnutrition. It is frequently accompanied by multiple or single micronutrient and/or mineral deficiencies, although these may occur in the absence of macronutrient depletion and give rise to specific deficiency syndromes. Undernutrition may be due to a failure of food supply or intake, to deliberate fasting, or to disease and is characterized by weight loss and changes in body composition, which include loss of body fat, loss of lean mass (proportionately greater in disease compared to starvation alone) and a relative increase in extracellular fluid volume.

Severe nutritional risk

The term severe nutritional risk is used to describe the chances of a better or worse outcome from disease or surgery according to actual or potential nutritional and metabolic status.

Severe nutritional risk is defined as the presence of at least one of the following criteria:

- weight loss >10–15% within 6 months,
- BMI $<18.5\,kg/m^2$,
- SGA Grade C or NRS $\geqslant 3$,
- serum albumin $<30\,g/l$ (with no evidence of hepatic or renal dysfunction).

Cachexia

Cachexia is a term, which originates from the Greek words kakos, meaning bad and hexis, meaning condition ($=$ "bad condition") and, in general, describes severe wasting from any cause including starvation and disease. Many clinicians use it as a qualitative term to describe the patient's appearance of severe weight loss. Others have defined it quantitatively as a BMI $<18.5\,kg/m^2$. More recently, it has also been used more specifically to describe wasting in life-threatening diseases such as cancer, AIDS, chronic obstructive pulmonary disease, and advanced organ failure where it is defined by a documented non-intentional weight loss of more than 6% in the previous 6 months, accompanied by catabolic conditions and resistance to increased substrate intake. In the current guidelines this latter definition of cachexia has been adopted.

Wasting

Wasting is used to characterise involuntary loss of body weight (i.e. muscle mass, "muscle wasting") and decline of muscle strength. Wasting is not etiologically or pathologically different from undernutrition but has been used customarily in certain contexts. The term "wasting syndrome" is established in the AIDS terminology as involuntary weight loss of more than 10% and either chronic diarrhoea (>1 month) and/or fever.

Sarcopenia

Sarcopenia describes a state of loss of muscle mass specifically occurring in bedridden, immobile or elderly patients.

Nutritional screening

Nutritional screening is a rapid and simple process conducted by admitting staff or community health care teams.[3] The outcome of screening may lead to (1) the patient is not at-risk of malnutrition, but may need to be re-screened at specified intervals, e.g. weekly during hospital stay, (2) the patient is at-risk and a nutrition plan is worked out and implemented by the staff according to ordinary ward routines, or (3) the patient is at-risk, but metabolic or functional problems prevent a standard plan being carried out *or* there is doubt as whether the patient is at-risk.

In any of these cases, referral should be made to an expert for assessment.

Methods and application of nutritional screening have been described in a detailed ESPEN guideline (NRS).[3]

Nutritional assessment

Nutritional assessment is a detailed examination of metabolic, nutritional or functional variables by an expert clinician, dietitian or nutrition nurse.[3] It is a longer process than screening and it leads to an appropriate care plan considering indications, possible side effects, and, in some cases, special feeding techniques. It is based upon a full history, clinical examination and, where appropriate, laboratory investigations including muscle function and bioelectrical impedance analyses (BIA).[4] It will include the functional consequences of undernutrition, such as muscle weakness, fatigue and depression. It includes gastrointestinal assessment, including dentition, swallowing, bowel function, etc. It necessitates an understanding of the interpretation of laboratory tests, e.g. plasma albumin, magnesium, phosphate, zinc, calcium and micronutrients. Subjective global assessment (SGA) is a widely used method of assessment.[5]

General topics

The following paragraphs deal with the question if fiber containing fomulae or specific diabetes formulae have an advantage over standard formulae, since these formulae might be used in many different indications and these questions are not discussed in other chapters of the guidelines.

Fiber containing formulae

Traditionally, enteral formulae were fiber free because of the possible tube obstruction and the

concept that a bowel at rest has beneficial effects on outcome. The recognition of the positive biological actions of both fiber and its fermentation products (e.g. short chain fatty acids (SCFA)) and the possibility to incorporate different fibers into enteral formulae without increased risk of tube obstruction has changed the enteral feeding approach. Different types of fibers with different biological effects are known. According to the underlying disease, specific types of fiber are used today. However, the classification of fiber is still not uniform. The first definition was rather mechanistic and defined fiber as the components of plant polysaccharides and lignin, which are resistant to hydrolysis by digestive enzymes in man.[6] Later, due to known effects of fiber on glucose and lipid control, fiber was defined according to its solubility in water as soluble and non-soluble fiber. After the discovery of the biological effect of colonic fermentation in humans, fiber was defined as fermentable and non-fermentable.[7,8] Recently, the term prebiotics was introduced. Certain oligosaccharides (e.g. inulin, fructo- and galactooligosaccharides) have the capability to be selectively metabolized by gut bacteria resulting in improved gastrointestinal functions.[9] Up to now this concept is not studied adequately for EN. For clinical reasons, the classifications according to the physiological properties would be more useful but physiological effects are not always easy to measure.

Since a fiber intake of 15–30 g/day is recommended for normal food in healthy persons a similar intake is considered advisable also in patients on EN. The main purpose using fiber-containing formulae is feeding the gut to maintain gut physiology, improving gastrointestinal tolerance (e.g. prevention of diarrhoea and constipation) and for glycaemic and lipid control. Unfortunately, up to now, only few studies with small numbers of patients with divergent results are available. Although the fiber concept is fascinating there is a lack of good clinical data to give clear evidence-based recommendations.[10]

In acute illness, fermentable fiber is effective in reducing diarrhoea in patients after surgery and in critically ill patients. It was shown that guar gum (e.g. partially hydrolyzed guar gum) and pectin were superior to soy polysaccharides.[11–15] In non-ICU-patients or in patients requiring long-term EN the use of a mixture of bulking and fermentable fiber would appear to be the best approach. Soy polysaccharides, or soy polysaccharides combined with oat fiber were effective to increase daily stool weight and frequency during enteral feeding.[16–19] But the effect was studied only in a small group of patients during a short period. There is only a small study showing a beneficial effect of adding soy polysaccharides to control bowel habits in patients on long-term EN over 1 year.[20]

Although it is known that fermentable and viscous fibers (e.g. oat beta-glycan) are effective for glycaemic control, there are no short or long-term studies available using these fibers in enteral formulae.

For the future, we should identify the best type of fiber in enteral formulae for different conditions (e.g. short-term and long-term use in ICU patients and in non-ICU patients on long-term tube feeding with different gastrointestinal diseases, cerebrovascular dysphagia and diabetes). There is a clear need for larger trials using fiber-containing enteral formulae with clinical relevant primary endpoints; both in short-term EN in acute patients and in long-term conditions in chronically ill patients. Furthermore a combination of different fibers, prebiotics and probiotics should be studied because of synergistic effects in different diseases.

Which formula should be used in non-stressed diabetic patients?

The number of diabetics is rapidly increasing worldwide (from 171 million in 2000 to 366 million in 2030, WHO estimates), and with it the probability for a diabetic to undergo EN. As to the percentage of macronutrients, the American Diabetes Association and European Association for the Study of Diabetes recommend that 60–70% of energy be divided between carbohydrates and monounsaturated fat, with less than 10% from polyunsaturated fat, less than 10% from saturated fat and less than 15% from protein. Simple carbohydrates can be included but should constitute less than 10% of total energy.[21,22] Most diabetes-specific enteral formulae comply with this rule, however in two different ways: first "classic" diabetic formulae provide low amounts of lipids (30%), with a high supply of complex carbohydrates (55–60%), most of these being starch, possibly containing fructose. Newer formulae have replaced part of carbohydrates with mono-unsaturated fatty acids (MUFA) (up to 35% of total energy), and may include dietary fiber. It is difficult to assess the effects of an enteral formula on diabetes, as there is no consensus on the most relevant markers to be used: blood glucose, need for insulin, blood lipids, glycated haemoglobin, acute and chronic microvascular and macrovascular complications. Also, most studies report the effects of solid foods, not EN, whereas the latter induce more pronounced

insulin and glucose responses than the former.[23] Last, most are short-term studies (1-day ONS for breakfast). Taking into account published randomized controlled long-term (>7 days) studies of enteral formulae in diabetic patients, we try to answer the following questions:

- *Are there benefits of high carbohydrate—low fat formulae over standard formulae?*
  No long-term study of these enteral formulae in diabetic patients was found in the literature, which does not allow to draw conclusions on benefits of such formulae.
- *Are there benefits of low carbohydrate—high MUFA (LCHM) formulae over high carbohydrate—low fat formulae (HCLF) and standard formulae*?
  Glycaemic control: one study reports a better glycaemic control (glucose levels) with a LCHM formula compared to a standard formula.[24] Several studies of LCHM formulae report lower mean, fasting and/or post-prandial glucose levels,[25–29] with however only trends towards decreased HbA1c and fructosamine[25,27,29] and insulin requirements,[25,27,29] compared to HCLF formulae.
  Lipid profile: one study reports a better lipid profile (reduced plasma triglycerides and total cholesterol) with an LCHM formula compared to a standard formula.[24] Two studies of LCHM vs. HCLF formulae report decreased triglycerides and total cholesterol after 6–10 weeks,[24,26] whereas three other studies fail to do so.[25,27,29] Two of these five studies report a rise in HDL cholesterol levels.[25,26]
  Clinical outcome: it is only mentioned in two studies of LCHM vs. HCLF formulae, with a trend towards a reduction in infections and pressure ulcers in the LCHM group in one study,[25] and a trend towards a reduced length of hospital stay in the LCHM group in the other.[27]

In conclusion, LCHM formulae seem to improve cardio-vascular risk factors in diabetic patients, but fail (possibly due to the short duration of most studies) to show clinical benefits.

Which formula should be used for blood glucose control in ICU-patients?

In hospitalized patients with type 2 diabetes mellitus, LCHM (low carbohydrate, high MUFA) formulae have a more neutral effect on glycaemic control than standard formulae.[30] However, in the ICU setting where strict glycaemic control with the use of exogenous insulin is achieved relatively easily when standard or ICU-specific formulae are used,[31] there is no reason to believe that such formulae would be required.

Recently, a large randomized, controlled, clinical study of early fed patients in a surgical ICU, further referred to as ''the Leuven study'' provided relevant nutritional insights. The effect of strict maintenance of normoglycaemia (blood glucose between 80 and 110 mg/dl) with intensive insulin therapy during intensive care was compared with the conventional regimen, which recommended insulin only when glycaemia exceeded 215 mg/dl.[31] Although conventionally treated patients revealed only mild hyperglycaemia (mean blood glucose of 150–160 mg/dl), insulin titration to blood glucose levels below 110 mg/dl reduced hospital mortality by 34%.[31] The duration of mechanical ventilation and ICU stay, the incidence of bacteraemia, excessive inflammation, organ failure, and critical illness polyneuropathy were also significantly reduced.[31] The benefit of intensive insulin therapy was particularly pronounced among patients with prolonged critical illness, requiring intensive care for more than 5 days, with mortality reduced from 20.2% to 10.6%. The study showed that maintaining blood glucose below 110 mg/dl is crucial in order to obtain a maximum benefit,[32] disproving the notion that a threshold level of 144 mg/dl would suffice. In the Leuven study, best evidence nutrition protocols were applied: EN was attempted as early as possible and in order to achieve a preset target of total energy intake, parenteral supplements were given when needed, resulting in patients being fed equally in both study groups. Energy intake was increased from an average of 7 non-protein kcal/kg BW/d on day 1–23 kcal/kg BW/d on day 7, resulting in a mean intake of 19 kcal/kg BW/d. The average nitrogen intake ranged from 0.15 to 0.19 mg/kg BW/d. The improvements in outcome were entirely attributed to the tight glycaemic control with insulin, and the intervention was equally effective regardless of the amount and route of feeding.[32] This is in agreement with the knowledge that underfeeding by omitting lipids or by delivering hypocaloric parenteral nutrition neither prevents hyperglycaemia nor its infectious complications.[33] Exclusively parenterally fed patients required substantially more insulin in order to achieve normoglycaemia than those receiving EN.[32] This is explained by the effects of EN on incretin-mediated endogenous insulin release, and may indicate that some of the potential risks of parenteral nutrition are due to its higher hyperglycaemic potential. When insulin is titrated

to achieve normoglycaemia, this risk of parenteral nutrition disappears.[32]

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