Fundamental issues in **PARENTERAL NUTRITION**

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SECTION 1

Malnutrition in hospitalized patients and its negative impact

Understanding malnutrition and its ill-effects

Malnutrition is a significant public health problem which engenders considerable concern. It is a broad term which primarily indicates nutritional imbalance.[1] According to an acceptable definition "malnutrition is a state resulting from lack of uptake or intake of nutrition leading to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease."[2] Malnutrition can have multiple etiological causes; it can result from decrease in nutrient intake, increase in the body's caloric requirements secondary to a diseased state, inadequate or poor intestinal nutrient absorption (as in malabsorption syndromes), excessive nutrient losses, or a combination of them.[1]

Energy deficit and resultant malnutrition has emerged as a serious health problem among the hospitalized patients. The causes of malnutrition in hospitalized patients are similar to those seen in the community settings (Figure 1).[3] Nutritional risks are common in a diseased state and many patients are already malnourished secondary to their underlying disease at the time of admission to the hospital. Some of them have acute or chronic diseases which may be further complicated by pre-existing poor nutritional history. Hospitalization can worsen their nutritional status and predispose these patients to significant weight loss, slowing their recovery from the diseased states.[4] There is strong evidence base to show that malnutrition in hospitalized patients often remains unrecognized as the physicians' awareness of malnutrition is usually low.[5] Even when malnutrition is identified, seldom is the issue satisfactorily addressed until a dramatic deterioration in the patient's condition has occurred. Therefore, malnutrition in hospitalized patients remains an under-treated problem as well.[4-6]

Figure 1: Some important causes of malnutrition in hospitalized patients[3]

Reduced intake
Dysphagia
Nausea and vomiting
Old age
Pain
Obstruction

Increased nutrient requirements
Fever
Trauma
Surgery
Burns
Neoplasms

Increased nutrient losses
Malabsorption
Diarrhea
Protein losing enteropathy
Bleeding

Ensuring that critically ill patients receive adequate calorie and nutrient requirements should be a high priority for intensive care clinicians to enhance patients' recovery and improve their outcomes.

The prevalence of malnutrition in the hospital settings has been variably reported in literature and depends on several factors including clinical settings, patient population and the definition of malnutrition used for assessment; overall prevalence of malnutrition in the hospitalized patients is seen to vary between 20%-50%.[1] High rates of malnutrition among hospitalized patients have been reported in different studies from across the globe. Malnutrition prevalence among medical patients admitted in two hospitals in Berlin[7] was reported to be 24.2% and its prevalence in a tertiary hospital in India[8] was shown to be 39.6%; in a university hospital in Spain[9] 50.2% hospitalized patients were shown to be at nutritional risk and 11.9% were malnourished, and in the Middle East[6] malnutrition or risk of malnutrition is reported in between 6%-58% of hospitalized patients (Figure 2).

Take home points

- Malnutrition is widely prevalent in the hospitalized settings and is seen to vary between 20-50% among hospitalized patients
- Malnutrition in hospitalized patients often remains unrecognized as the physicians' awareness of malnutrition is usually low

Adverse impact of malnutrition in hospitalized patients

Malnutrition portends to several negative health consequences which primarily are a result of negative nitrogen and caloric balance. Virtually every organ of the body can get affected in malnutrition, although the heart, the lungs and the gastrointestinal tract are predominantly affected. Malnourished patients experience progressive weight loss and anergy; development of hypoalbuminemia is commonly seen. Malnutrition also has a significant impact on the immune response and several aspects of wound healing can get affected, including neovascularization, collagen synthesis and wound remodeling.[3] Immune-suppression as a result of malnutrition increases the risk of infections.[1] Untreated, malnourished patients can develop complications such as pneumonia and sepsis, and eventually deaths can occur.[3] In addition to compromising health outcomes and increasing the risk of complications, malnutrition in hospitalized patients prolongs hospital stay and increases morbidity and mortality rates.[1] Malnutrition also increases healthcare costs.[10] The significant economic impact of disease-related malnutrition could be seen in a study[10] which showed that estimated cost of treating hospitalized patients with malnutrition was 45% to 102% higher than the cost of treating non-malnourished patients. The different consequences of malnutrition in hospitalized patients are enumerated in Table 1. Early detection of nutritional risk in hospitalized patients and timely initiation of nutritional support should be a

Figure 2: Prevalence of malnutrition in hospitals across the globe[6-9]

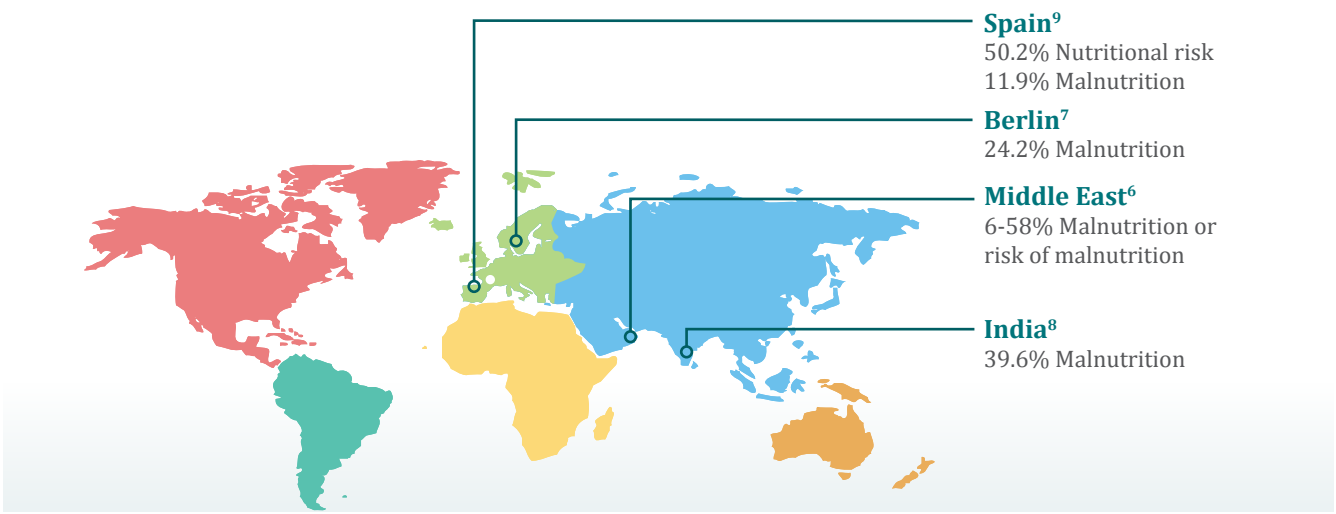

Table 1: Consequences of malnutrition in hospitalized patients[1,3,10]
Impaired wound healing[1,3]
Increased risk of infections[1]
Increased risk of complications[1]
Prolonged hospital stays[1]
Increased cost expenditure[10]
Overall increase in disease-related mortality and morbidity[1]

priority for most clinicians as it will likely improve the clinical outcomes of their patients and contain overall healthcare costs.

Parenteral nutrition in hospitalized patients

Nutritional support, whether through enteral or parenteral route, is essential in all critically ill patients to improve health outcomes. Enteral feeding is an acceptable and effective method for nutritional support in hospitalized patients however this form of nutritional feeding is associated with some complications, especially in critically ill patients:

- Enteral nutritional support can cause gastrointestinal intolerance and many patients on enteral feeds develop symptoms of nausea, bloating, and diarrhea[11]
- Enteral feeding, because of gastrointestinal intolerance, can result in under-feeding and thereby delay achievement of nutritional goals on enteral nutrition alone; many critically ill patients achieve their nutritional goals only after a week of initiation of enteral feeding[12]
- Large volume of enteral feed to the stomach using the nasogastric tube or through gastrostomy can promote reflux of gastric contents into the esophagus, which increases the risk of aspiration pneumonia, a potentially fatal event[11]
- Complications of hyperglycemia and electrolyte disturbances are not uncommon after enteral feeding[11]
- Some concerns have been raised regarding risk of bowel ischemia and its complications after administration of enteral feeds in serious patients with shock, ileus and gastric residual volumes.[13]

These disadvantages, especially the association of gastrointestinal intolerance with enteral feeds, can limit its efficacy in critically ill patients. Over the last few years, parenteral nutrition has emerged as an acceptable method for providing nutritional support in such patients, either alone or along with reduced volume of enteral nutrition.[14] Currently, parenteral nutrition – defined as administration of nutrients by the intravenous route – is established as a rational and acceptable method of nutritional support to hospitalized patients for preventing or minimizing the risk of malnutrition. It is usually administered through a dedicated central or peripheral venous line.[15]

Take home points

- Malnutrition has a significant impact on the immune response and several aspects of wound healing can get affected
- A study showed that estimated cost of treating hospitalized malnourished patients was 45% to 102% higher than the cost of treating non-malnourished patients
- There are some concerns regarding risk of bowel ischemia and its complications after administration of enteral feeds in serious patients with shock, ileus and gastric residual volumes
- Parenteral nutrition is established as a rational and acceptable method of nutritional support to hospitalized patients for preventing or minimizing the risk of malnutrition

Early vs. late introduction of parenteral nutrition

Nutritional support in critically ill patients admitted for serious illnesses is essential. It should be given through the parenteral route if the enteral feeds alone cannot compensate the caloric requirements or enteral feeding cannot be given for any reason.[14] However, the timing of initiation of parenteral nutrition in critically ill patients in whom calorie demands are not met by enteral nutrition alone remains a debatable issue. There is some evidence to support the fact that early interventional feeding in sick hospitalized patients, defined by experts as initiation of nutritional support within 24–48 hours of ICU admission or start of mechanical ventilation, can possibly improve the clinical outcomes especially when compared to no feeding.[13,16] One report[16] indicated that early initiation of parenteral nutrition reduced overall mortality

rates in critically ill patients (admitted in the ICU) in whom enteral nutrition could not be started within 24 hours of ICU admission. Benefits of early initiation of parenteral nutrition are also apparent in patients with short-term contraindications to early enteral therapy as it appears to be more cost-effective and reduces the total cost of hospital care.[17] Early initiation of parenteral feeding is therefore endorsed by the European Society of Parenteral and Enteral Nutrition (ESPEN) group which recommends initiation of parenteral nutrition within 24–48 hours of ICU admission if patients are not expected to be on normal nutrition within 3 days and enteral nutrition is either contraindicated or cannot be tolerated by the patient.[18] However, more recently, two studies – one performed in critically ill adults and the other in critically ill children[19,20] – showed that late initiation of parenteral nutrition (after 7-8 days of admission) was not always counterproductive and could in fact be superior to early initiation of feeding in terms of lesser infection rates, faster recovery, and shorter hospital stays. Therefore, although benefits with parenteral nutrition in critically ill patients have been unequivocally demonstrated, the timing of its initiation continues to remain controversial.

Indications and benefits of parenteral nutrition

Broadly total parenteral nutrition is indicated in the following clinical scenarios:[21]

- In patients in whom > 7 days nil-per-oral (NPO) status is anticipated (very sick patients, patients with inflammatory bowel disease, and those with acute exacerbation)
- In patients with paralyzed or dysfunctional gastrointestinal tract (such as small bowel obstruction)
- In newborns with an immature gut or in those with congenital malformations
- In patients suffering from chronic diarrhea and vomiting
- In patients in whom bowel anastomoses develops anastomotic leaks in the early postoperative period
- In patients who are extremely malnourished and require surgery or chemotherapy.

Several studies have emphasized benefits of parenteral nutrition in improving the nutritional status of critically ill patients. Its administration in severely malnourished patients reduces the rate of postoperative infection and hospital complications.[22] One report[23] suggested that preoperative parenteral nutrition given to malnourished patients undergoing surgery can reduce the risk of septic complications and serious sepsis. Another report[24] showed that perioperative parenteral nutrition in malnourished patients undergoing surgery reverses malnutrition, and facilitates rehabilitation. Therefore, parenteral nutrition has a widely proven efficacy in all hospitalized patients at nutritional risk, particularly in critically ill patients with severe malnutrition, in whom adequate nutritional delivery with enteral nutrition alone is either insufficient or difficult.[25]

Take home points

- One study showed that early initiation of parenteral nutrition reduced overall mortality rates in critically ill patients (admitted in the ICU) in whom enteral nutrition could not be started within 24 hours of ICU admission
- Benefits of early parenteral nutrition are also apparent in patients with short-term contraindications to early enteral nutrition as it appears to be more cost-effective and reduces the total cost of hospital care
- Preoperative parenteral nutrition given to malnourished patients undergoing surgery can reduce the risk of septic complications and serious sepsis

2016 Guidelines on nutritional support therapy in the critically ill adult patients: Selected excerpts from combined SCCM and A.S.P.E.N. recommendations

The 2016 guidelines provided jointly by the Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) on the provision and assessment of nutrition support therapy in the adult critically ill patients make certain pertinent recommendations on parenteral nutrition which are reproduced below:[26]

- Early initiation of exclusive parenteral nutrition as early as possible after ICU admission is recommended in severely malnourished patients

and in those determined to be at high nutrition risk when enteral nutrition is not feasible

- Parenteral nutrition is also recommended as a supplement to enteral nutrition in patients at either low or high nutrition risk after 7–10 days of initiating enteral feeding if the patients are unable to meet > 60% of energy and protein requirements on enteral route alone
- A hypocaloric parenteral nutrition (≤ 20 kcal/kg/day or 80% of estimated energy needs) with ≥1.2 gm protein/kg/day should be appropriate when initiating parenteral nutrition in the first week of ICU admission in patients at high risk of nutritional deficiency or in severely malnourished patients
- Soybean oil-based IV lipid emulsions should either be withheld or limited to a maximum of 100 gm/wk (often divided into 2 doses/wk) during the first week following initiation of parenteral nutrition in all critically ill patients if there is concern of essential fatty acid deficiency
- In critically ill adult patients on parenteral therapy, the amount of parenteral nutrition should be reduced as the tolerance to enteral nutrition improves, and parenteral nutrition should finally be discontinued when the patient is receiving > 60% of target energy requirements from enteral nutrition.

Advantages of using pre-mixed bags over manual compounding and single bottle nutrition

Parenteral nutrition can be administered in the form of individualized or pre-mixed standardized formulations. Pre-mixed formulations are sterile products which require minimal manipulation prior to administration. In contrast, individualized formulations need to be prepared either by automated or manual compounding in the hospital pharmacy. Compounding is a fundamental component of pharmacy practice and should be done by trained pharmacists. However, these norms are only seldom followed as in several parts of the world compounding is being done manually in the wards by the nurses without any pharmaceutical controls. This form of manual compounding can give rise to several problems including prescribing errors (omissions or excesses of nutrients), risk of infections due to frequent product manipulation and microbial contamination, and other stability issues. These errors can have detrimental consequences and may impair the patient's nutritional and metabolic status.[27] Commercially available parenteral pre-mixed bags can offset many of the shortcomings of manual compounding.[28-31] These pre-mixed parenteral formulations (compared to manual compounding):

- Are labor-saving and reduce nursing time[28,29]
- Are devoid of compounding errors[28]
- Are associated with reduced risk of blood stream infections[29-31]
- Have a prolonged shelf life and stability[29]
- Are more cost-effective.[28,29]

Providing parenteral nutrition through pre-mixed, all-in-one multichamber bags also has advantages over the use of single-bottle system. In the single-bottle system, macronutrients are usually provided in parallel through separate bottles and therefore require separate IV lines. Administering parenteral nutrition through bottles require frequent manipulations, is associated with administration errors, risk of infections and metabolic complications.[32] Multi-chamber premixed bags therefore are deemed more convenient and economical compared to the use of bottles. More manpower, infusion pumps and disposable infusion systems are required in single-bottle system. A study[33] showed all-in-one parenteral bags to be a useful alternative to single-bottle system in critically ill and metabolically stable surgical patients.

Conclusion

Malnutrition or imbalance in nutrition is widely prevalent in hospitalized patients. Many hospitalized patients, particularly the critically ill patients admitted in the ICU, are at nutritional risk. Malnutrition in hospitalized patients can be associated with several negative outcomes including high risk of infections, longer length of hospital stays, and overall increased morbidity and mortality. It also incurs additional economic burden on the healthcare system and the caregivers. Parenteral nutrition is an acceptable route for nutritional support in hospitalized patients who have severe malnutrition or are at a significant risk of malnutrition if nutritional requirements cannot be met through the enteral route. Parenteral nutrition, either alone or in combination with enteral nutrition, can improve nutrient delivery to critically ill patients. Parenteral nutrition can be administered either in

the form of individualized or pre-mixed standardized formulations. Pre-mixed parenteral bags are sterile products which require minimal manipulation prior to administration. Commercially available pre-mixed parenteral formulations offer several advantages over individualized formulations prepared through manual compounding, including reduced nursing time, no compounding errors, reduced risk of blood stream infections, prolonged shelf life and greater cost-effectiveness. Pre-mixed bags also appear superior to single bottle nutrition.

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SECTION 2

Selected issues related to parenteral nutrition

High protein; low glucose provision: Optimizing parenteral nutritional support in critically ill patients

Hospitalized patients are at an increased risk of malnutrition. Malnutrition can predispose them to several negative health consequences, and increase their risk of complications, morbidity and mortality. Parenteral nutrition is an established method of replenishing the high calorie demands of hospitalized patients by providing them a balance of nutrition including glucose, lipids, amino acids; along with microelements, electrolytes and water.[1]

Advantages of high protein provision in ICU patients

Protein is an important source of energy. Healthy adults require 0.8 – 1 gm of proteins/kg/day.[2] Any stressful state, such as that during critical illnesses, increases utilization of protein reserves in the body and create a negative nitrogen balance. The rational strategy to counteract the increased nitrogen demand and preserve the lean mass in critically ill patients is to provide sufficient protein content.[3] High protein intake, between 1.2–2 gm/kg/day, is recommended in critically ill ICU patients.[4] It has been shown that high protein intake (>1.2 gm/kg/day) is associated

Figure 1: Benefit of higher vs lower amino acid intake (1.2 gm/kg vs 0.8 gm/kg) in ICU patients receiving parenteral nutrition[4]

Benefits of higher amino acid intake over lower amino acid intake in ICU patients

- Greater improvement in grip strength (non-significant difference)
- Greater improvement in forearm muscle thickness on ultrasound
- Lesser fatigue

with reduced mortality rates.[3] An observational study[5] which evaluated mechanically ventilated patients provided with optimal nutrition including high proteins (at least 1.2 gm/kg) showed almost 50% reduction in 28-day mortality rates. Similar were the results of another observational study[6] in critically ill ICU patients which showed lower mortality rates with higher intake of proteins and amino acids. Recently a randomized study[4] was performed which evaluated outcomes in ICU patients who received parenteral therapy with either low amino acid concentration (0.8 gm/kg) or high amino acid concentration (1.2 gm/kg). The study results showed improvement in different clinical outcome parameters in ICU patients who received parenteral formulations with high amino acid concentration compared to low amino acid concentration (Figure 1). A good mix of essential amino acids (which cannot be prepared by the body) is important. Provision of branched-chain amino acids (leucine, isoleucine, and valine) can particularly enhance protein synthesis in patients with sepsis and injury.[2]

Optimal glucose provision and preventing hyperglycemia in ICU patients

Glucose is another source of energy, in fact, believed to be the primary source of energy to the body. Glucose should be provided in parenteral nutrition as a standard carbohydrate solution. It is recommended that carbohydrates should be provided in the parenteral formulations in combination with amino acids and lipid emulsions to improve nitrogen balance. Under normal circumstances, carbohydrate should provide 60% of non-protein energy requirements.[7] In critical illnesses maximum glucose utilization rate reaches 5-7 mg/kg/minute.[2] However, providing excess glucose through parenteral feeding can have counterproductive effects. Some previously used parenteral solutions provided high dextrose loads which predisposed to several complications including metabolic stress, excessive CO_2 production, and fatty liver. Administration of hypertonic solutions with excess carbohydrates also increases the risk of hyperglycemia.[8]

Parenteral nutrition is by itself a known risk factor for hyperglycemia. Several observational studies have shown that hyperglycemia can compromise patient outcomes and increase mortality risk in hospitalized patients, both in non-critically ill and the critically ill patients admitted in the ICU.[9,10] Hyperglycemia also increases the risk of nosocomial infections and can prolong hospital stay.[9] Hence, every effort should be made to prevent hyperglycemia during parenteral nutrition in critically ill patients. The concentration of glucose in parenteral nutrition should not be too high, and rather should be optimal. An initial low carbohydrate infusion rate of 1–2 gm/kg/day should be selected for critically ill patients in the ICU or other patients with a high risk of hyperglycemia (such as those with diabetes or sepsis). Glycemic monitoring is additionally necessary, particularly to monitor the rate of glucose infusion.[7]

Take home points

- Stressful state, such as critical illnesses, increase utilization of protein reserves in the body and create a negative nitrogen balance. To counteract the increased nitrogen demand and preserve the lean mass in critically ill patients, it is necessary to provide sufficient protein content
- High protein intake, between 1.2–2 gm/kg/day, is recommended in critically ill ICU patients
- Glucose should be provided in parenteral formulations in combination with amino acids and lipid emulsions to improve nitrogen balance
- Parenteral solutions with high dextrose loads can cause metabolic stress, excessive CO_2 production, and fatty liver. Administration of hypertonic solutions with excess carbohydrates also increases the risk of hyperglycemia

Advantages of olive oil-based lipid emulsions for parenteral nutrition

Intravenous lipid emulsions are an integral component of most currently used parenteral nutrition regimens. Lipids are a key source of energy and therefore are invaluable for correcting energy deficits and improving outcomes in critically ill patients. Their addition to the parenteral regimen reduces its fluid volume which is required to provide adequate caloric intake, thereby

facilitating safe administration of the parenteral formulation through the peripheral or central venous lines. Moreover, as lipids are energy dense, they also serve to reduce the dextrose load in parenteral solutions, thereby reducing the risk of hyperglycemia.[8]

The routine use of parenteral lipid emulsions in clinical practice began in 1961, with the development of soybean oil-based lipid emulsions.[11] Since then, the practice of using soybean oil-based lipid emulsions in parenteral formulations for critically ill patients has been in vogue. Soybean oils are rich in long-chain triglyceride (LCT). The LCT-based lipid emulsions provide essential fatty acids such as linoleic (ω-6 PUFA) and α-linolenic acid (ω-3 PUFA). However, as the use of soybean oil-based lipid emulsions increased several problems related to high intake of ω-6 PUFA came to the fore.[12]

Studies showed that lipid emulsions rich in ω-6 PUFA could:

- Induce endothelial dysfunction[13]
- Augment inflammatory response due to increased synthesis of pro-inflammatory mediators[12,13]
- Induce immune-suppression by impairing the functions of neutrophils, lymphocytes and macrophages, as well as that of the reticuloendothelial system; thereby increasing risk of infections[12,13]
- Promote increase in oxidative stress due to the interaction of excess reactive oxygen species (formed during critical illnesses) with multiple double bonds in ω-6 and ω-3 PUFA.[8]

The 2016 joint guidelines by the SCCM and A.S.P.E.N[14] therefore recommend withholding soybean oil–based lipid emulsion in the first week following the initiation of parenteral nutrition in critically ill patients and limiting it to a maximum of 100 gm/wk if there is concern of essential fatty acid deficiency.

Over the last few years, several new lipid emulsions have been formulated for parenteral nutrition which have partially replaced soybean oil with other oils, including medium chain triglycerides (MCT), olive oil, or fish oil, in order to reduce the adverse effects of excess ω-6 PUFA. In one such parenteral lipid emulsion now available, olive oil has replaced a significant proportion of soybean oil (80% olive oil + 20% soybean oil).[12]

Lipid emulsions which are predominantly olive oil-based have several advantages:

- They have a neutral immunological effect (in contrast to soybean oil) and therefore do not seem to impair immune response; it may be safe to use them in critically ill patients at risk of immune-suppression[12]
- They demonstrate better liver tolerance compared to MCT/LCT-based emulsions[12]
- They can mitigate abnormal glucose metabolism that occurs with soybean oil-based lipid emulsions[15]
- They are much less susceptible to lipid peroxidation (free radical damage) and its adverse consequences[8]
- The lower PUFA and high antioxidant content of olive oil improves vitamin E status and is effective in countering disease states associated with oxidative stress, particularly in preterm infants[16]
- They can reduce mechanical ventilation time and the length of ICU stay compared to soybean oil-based emulsions and improve overall clinical outcomes in critically ill ICU patients[17]
- They provide a balanced intake of the different classes of fatty acids and thereby maintain a normal essential fatty acid status[18]
- They can provide nutritional support in several groups of patients including preterm infants, patients with trauma, burns, those on hemodialysis and may also be suitable for home parenteral nutrition.[15]

Can excess immune-suppression caused by fish oil-based lipid emulsions be counterproductive?

Both olive oil- and fish oil-based lipid emulsions are an advancement over the previously used soybean oil-based lipid emulsions, particularly in view of their favorable immune and inflammatory responses.[12] However, olive oil-based lipid emulsions, which are rich in monounsaturated fatty acids (MUFA), are believed to have less immune-suppressive effects compared to fish oil-based lipid emulsions, which are rich in ω-3 PUFA.[19] Its significance remains debatable. For many years there have been concerns over the fact that significant immune-suppression caused by

dietary lipids can impair the host's natural response to infections, although the same has not been clearly established in human studies.[20] Some studies have evaluated the effects of dietary lipids on immune functions – the majority of them being experimental – and have demonstrated greater immune-suppression by ω-3 PUFA (fish oil) compared to MUFA (olive oil).

An experimental study[21] performed on a murine model showed that diet rich in ω-3 PUFA (such as that obtained from fish oil) could significantly affect host resistance to infection by the bacteria *Listeria monocytogenes*. The ω-3 PUFA rich diet seemed to reduce survival rates after infection with *Listeria monocytogenes* and impair the body's ability to clear the microorganism. These results were in line with those of another similar experimental study[22] which also showed low survival rates of mice fed on fish oil-based lipid emulsions after being injected with a lethal dose of the pathogenic bacterium *Listeria monocytogenes*. In contrast to the marked immune-suppressive effects of fish oil, olive oil appears to have a more moderate immune-suppressive effect. In fact, diets containing predominantly MUFA (such as olive oils) do not appear to impair host resistance to infection.[19] In murine models, olive oil-rich diet lead to higher survival rates and greater bactericidal activity after infection with Listeria compared to fish oil-rich diet, suggesting the possible adverse effects of significantly strong immune-suppression by fish oil-containing diets compared to olive oil-containing diets.[22] Since the dietary effects of lipids on the immune system is largely derived from experimental data, further validation of these results are required in well-designed human trials, however, safety issues related to excess immune-suppression caused by fish oil-based lipid emulsions should be taken into account when using them in critically ill patients with severe sepsis.

Take home points

- Lipid emulsions rich in ω-6 PUFA (such as soybean oil-based emulsions) can induce endothelial dysfunction, augment inflammation, cause immune-suppression, and promote increase in oxidative stress
- Olive oil-based lipid emulsions have a neutral immunological effect, are much less susceptible to lipid peroxidation, and provide a balanced intake of different classes of fatty acids thereby maintaining a normal essential fatty acid status
- Fish oil-containing diet is believed to induce a significantly stronger immune-suppression compared to olive oil-containing diets

Incompatibility issues between vitamins and trace elements in the same parenteral formulation

Micronutrients, which include both vitamins and trace elements, have an instrumental role to play in many metabolic processes and therefore should be supplemented for enhancing recovery and improving survival in critical illnesses. For their supplementation the enteral route is preferred, however when not available, these essential nutrients should be provided by the parenteral route to prevent their nutritional deficiencies in critically ill patients.[23] Several incompatibility issues arise when both vitamins and trace elements are mixed in the same parenteral admixture.[24] Vitamins, in particular are highly reactive by nature and can undergo different chemical reactions including photodegradation, oxidation and interactions with storage constituents which can affect their stability in the admixture.[25] In fact, vitamins are amongst the least stable ingredients in the parenteral nutrition admixtures.[26]

A study[27] showed stability of vitamins B1, B2, B6 for only up to 72 hours when added to a parenteral formulation stored at temperatures between 4^0C and 25^0C; vitamin C was seen to be stable for only up to 48 hours in the formulation stored at 25^0C. Therefore, significant losses of vitamins, particularly that of vitamin C (ascorbic acid), can be expected upon prolonged storage of the parenteral formulations which can have serious clinical consequences. This leads to chances of reduced vitamin bioavailability if the parenteral bag is used a long time after its reconstitution.

Due to their reactive nature, prolonged storage after addition of vitamins to the parenteral admixture should be strongly discouraged as significant vitamin

losses can occur in these cases which can be associated with detrimental clinical outcomes.[28] They may be added shortly before administration of the parenteral formulation.[29] Another suitable way is to provide them in the form of a piggy-back infusion over 15-30 minutes or a slow 5 minutes bolus either at the end or the beginning of the daily parenteral nutrition administration.[30]

Conclusion

Parenteral nutrition, either alone or in combination with enteral nutrition, can improve outcomes in critically ill patients. Many critically ill patients have protein loss and a negative nitrogen balance thereby requiring increased protein and amino acid intake. The protein requirement in healthy adults is 0.8 – 1 gm/kg/day, however critically ill patients should be administered 1.2-2 gm/kg/day of proteins to replenish their high protein requirements, prevent cachexia and enhance recovery. Parenteral nutrition is a known risk factor for hyperglycemia which can compromise patient outcomes and increase mortality risk in both non-critically ill hospitalized patients as well as critically ill patients admitted in the ICUs. Efforts should be made to prevent hyperglycemia during parenteral nutrition in critically ill patients. The concentration of glucose in parenteral nutrition should be optimal and an initial low carbohydrate infusion rate of 1–2 gm/kg/day should be selected for critically ill patients in the ICU. Also excessive intake of PUFA (as in soybean oil-based lipid emulsions) should be avoided in parenteral formulations because of their known immune-suppressive effect and the potential to augment inflammation and increase oxidative stress, all factors which can have detrimental effects in critically ill hospitalized patients. Olive oil–based lipid emulsions have favorable immune-inflammatory effects and can beneficially modify the lipid profile thereby improving the patient prognosis. Vitamins can be added to the formulation just before the initiation of parenteral nutrition or can be separately provided in the form of aqueous solutions as a (piggy bag) infusion.

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