Nutritional Therapy for Critically Ill COVID-19 Patients

Nurhayat Tugra OZER1, Kursat GUNDOGAN2

ABSTRACT
The world has experienced coronavirus disease 2019 (COVID-19) which is a pandemic and a public health crisis worldwide. It primarily affects the respiratory tract and associated with serious morbidity and mortality. There are currently no proven drug in COVID-19 patients. The main treatment of COVID-19 are supportive treatments. Nutrition therapy remains one of the cornerstone treatments for these patients. ASPEN (4) and ESPEN (5) nutrition guidelines for COVID-19 patients were compiled and this framework was created for the purpose of nutritional management in COVID-19. Considering that respiratory secretion of these patients poses a risk of contamination for healthcare professionals, recommendations have been prepared. These recommendations include effective nutritional management for COVID-19 patients, with the principle of entering the patient room as little as possible and intervening as little as possible.

Keywords: Nutrition, COVID-19, Critical care, Micronutrients

Introduction
The corona virus disease 2019 (COVID-19) pandemic caused by the SARS-CoV-2 virus causes poor clinical outcomes. Available data is pointed that elderly and polymorbid patients constitute the risk group in terms of poor clinical outcomes (1-3). Good supportive care is basic treatment of COVID-19. Acute respiratory complications due to COVID-19 requires intensive care unit (ICU) stay. ICU stay, especially long-term stay, pose a risk of severe malnutrition. Early diagnosis and treatment of malnutrition plays an important role in the prognosis of the disease. So, nutrition therapy is one of the cornerstone treatments for these patients. Even if there is lack of direct evidence about COVID-19, indirect evidence indicates that recommendations of nutritional therapy in COVID-19 patients is very similar to any other ICU patient with sepsis and acute respiratory distress syndrome.

Recommendations
1. When performing nutritional assessment of the patient, healthcare professionals should definitely use personal protective equipment.
2. MUST and NRS 2002 scoring systems should be used to evaluate the risk of malnutrition.
3. Indirect calorimetry is the gold standard in calculating of energy requirement. However, it can be calculated according to the patient’s weight or energy calculation equations can also be used.

If it is to be calculated by weight in patients at risk for COVID-19:
- 27 kcal/kg/day for polymorbid patients aged >65 years
- 30 kcal /kg/day for severely underweight polymorbid patients
- 30 kcal/kg/day (It should be adapted according to nutritional status, physical activity level, severity of disease and tolerance in the elder patients)
4. Protein requirement
- 1 g/kg/day for polymorbid inpatients (It should be adapted according to nutritional status, physical activity level, severity of disease and tolerance)
- 1.3 g / kg / day for intubated patients
- Fat and carbohydrate ratio should be 30:70 for patients without respiratory failure and 50:50 for intubated patients.
5. Patients should be provision of recommended daily vitamins, minerals and trace elements intake.
6. Because patients diagnosed with COVID-19 are generally elderly or polymorbid, nutrition should be started with slow infusion in these patients to avoid refeeding syndrome (gradually increasing gradually, starting from about 25% of the energy requirement). Serum phosphate, magnesium and potassium levels should be closely monitored.

7. It should be the aim to initiate early enteral nutrition (EN) on 24-36 hours after admission to the ICU or within 12 hours of intubation and mechanical ventilation.

8. Feeding tube should be attached to the patient during intubation (It may increased the risk of coughing and contamination during NG or OG tube insertion). Confirmation of the feeding tube with X-ray should be done simultaneously with other X-ray procedures to the patient.

9. It is recommended that the head of the bed should be raised to at least 10 to 25 degrees for purpose of continue to EN, prevention to aspiration, reduction facial edema and decrease to intraabdominal pressure in patients with prone position.

10. As the number of patients who need EN increases, problems of enteral pump may occur. Therefore, patients with small bowel feeding or signs of intolerance should be given priority to enteral pump delivery, and those who cannot receive pumps should try continuous gravity feeding.

11. Continuous EN should be preferred over intermittent or bolus EN in order to reduce contact with the patient.

12. These principles should be considered at enteral formula selection:
   - In the early acute stage of critical illness, standard high protein (containing> 20% protein of energy) polymeric isosmotic enteral formulas should be provisioned.
   - The addition of fiber should be considered as the patient’s clinical condition improves and vasoressor requirements decrease.
   - A fiber-free formula can be better tolerated if the patient has significant GI dysfunction. However, as soon as GI dysfunction recovers, a fiber-containing formula or supplement should be attempted to take advantage of the non-nutritional effects of the intestinal microbiota.

13. Enteral nutritional intolerance occurs frequently in the early and late acute stages of critical illness. Gastric residual volume monitoring is not reliable in determining the risk of delayed gastric emptying and aspiration. Patients should be monitored with a physical examination and confirmation of gas-stool output.

14. Patients undergoing extracorporeal membrane oxygenation should be closely monitored to avoid enteral feeding intolerance. In the first week of critical illness, trophic EN should be initiated.

15. PN may be considered when EN is contraindicated, especially in patients with severe septic shock or in patients who require high-pressure respiratory support, to minimize the risk of ischemic bowel.

16. Omega-3 fatty acids should be preferred due to severe inflammation in patients with the diagnosis of COVID-19 who need PN.

17. The amount lipid calories of propofol should be taken into account in nutritional requirements. Patients receiving propofol have a risk of severe hypertriglyceridemia. Serum triglyceride levels should be closely monitored in patients receiving propofol and / or intravenous lipid emulsions.

18. Patients in quarantine should exercise regularly (> 30 minutes every day or> 1 hour every two days) while taking the necessary precautions.

### Micronutrients

#### Vitamin C

There are publications showing that vitamin C has an antioxidant effect and improves the immune system. The studies with vitamin C in critically ill patients have not shown positive effects on mortality. The supplementation of vitamin C is not recommended for nutritional therapy of the critically ill patients. A study on the delivery of high doses of vitamin C (24 g / 7 days) to critically ill patients followed up in the ICU with the diagnosis of COVID-19 is ongoing (Identifier: NCT04264533). But, this study has not been concluded yet. According to our current knowledge, high-dose vitamin C treatment is not recommended for these patients.

#### Zinc

Zinc is a trace element for critically ill patients. Daily supplementation of zinc is not recommended in enterally fed patients while is recommended in patients fed parenterally. In experimental studies, zinc has been shown to inhibit the RNA polymerase of the corona virus causing COVID-19 disease. There is no clinical study on patients. In terms of the addition of zinc, patients with COVID-19 who are followed up in intensive care should be treated like current intensive care protocol.

#### Vitamin D

In addition to the metabolic effects of vitamin D, there is evidence that it strengthens the immune system against respiratory viruses. In studies conducted during previous influenza pandemic, vitamin D administration was showed to reduce the risk of influenza. The most recent studies reported that the supplementation of vitamin D in critically ill patients does not reduce mortality. Addition of vitamin D is not recommended in routine critically ill patient nutrition therapy. Also it is not recommended in patients hospitalized with COVID-19, as there are no adequate clinical trials.

#### Selenium

Selenium is a trace element for critically ill patients and important in terms of antioxidant effect. Routine addition of selenium to enteral nutritional solutions for critically ill patients without diagnosis of COVID-19 is not recommended. It is added to parenteral nutrition solutions as recommended by the ASPEN and ESPEN guidelines. There is no additional recommendation for critically ill patients with COVID-19. It should be treated like standard critically ill patients.

#### Thiamine (Vitamin B1)

Thiamine is a water-soluble vitamin that is a co-factor in many enzymatic steps in carbohydrate and protein catabolism. The replacement of thiamine is not recommended for critical patients received enteral nutrition in the recently published ASPEN and ESPEN guidelines. Daily replacement of nutritional solutions is recommended for patients received parenteral nutrition. In addition, high dose thiamine is recommended for patients with risk factors for thiamine deficiency. Patients who develop Wernicke’s encephalopathy are recommended 5x100 mg of thiamine for 3 days. There is no additional recommendation for critically ill patients with COVID-19. These patients should be treated with standard procedures applied in critically ill patients.
Conclusion

The delivery of effective nutritional therapy is considered to provide positive effects on the prognosis of the COVID-19 disease. Patients should be approached as general ICU patients with sepsis and acute respiratory distress syndrome. Patients should be performed for nutritional assessment and provided to sufficient energy, macronutrient and micronutrient requirement with a suitable feeding route. And, as stated in the guidelines, many studies on nutrition in COVID-19 disease are needed.

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