REVIEW

Yoğun Bakım Derg 2019
https://doi.org/10.33381/dcbybd.2019.1972

Approach to Nutritional Therapy in Patients Who Require Vasopressors General Information and Protocol Proposal

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Cite this article as: Öcal S, Topeli A, Akıncı SB, Halil MG, Abbasoğlu O. Approach to Nutritional Therapy in Patients Who Require Vasopressors General Information and Protocol Proposal. Yoğun Bakım Derg 2019

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Received: 06.03.2019
Accepted: 06.03.2019
Available online: 11.03.2019

ABSTRACT

Studies of enteral nutrition (EN) therapy in patients who require vasopressors are limited. Unfortunately, hemodynamically unstable patients or patients receiving vasopressors were mostly excluded from the large randomized controlled trials in nutrition. We aimed to present the protocol by Hacettepe University Adult Hospital Nutrition Support Team as different approaches to EN of these patients.

Key words: enteral nutrition, nutrition, vasopressor, shock

Introduction

Patients in shock, with or without hypotension are frequently evaluated and treated in intensive care units. In patients with shock, tissue hypoperfusion can cause organ and system dysfunctions, such as brain, kidney, heart and gastro-intestinal (GI) tract.The viewpoint in this group of patients is against EN therapy, regarding the risk of intestinal perfusion deficit and reperfusion injury.In animal studies, ≥50% reduction in GI blood flow is documented to cause ischemic injury to the bowel wall (1).In patients with shock, however, it is not possible to determine whether local perfusion deficit occurs in GI tract or the severity of blood flow reduction. Unfortunately, in large-scale randomized controlled trials, patients with hemodynamic instability or in need of vasopressors are often excluded. Regarding the lack of studies and guidelines on nutritional treatment approach, variation in practice is encountered. In this article, as Hacettepe University Adult Hospital Nutrition Support Team, we present the EN protocol on patients with vasopressor requirement.

Overview

In literature, the initial studies for nutritional support in shock consist cardiogenic shock patients.In a prospective study in 2001, *Revelly et al.* documented increase in cardiac index and decrease in systemic vascular resistance with thermodilution, 3 hours after the onset of EN therapy in cardiogenic shock patients with inotropic and/or vasopressor requirement (2).Similarly, *Berger et al.*prospectively evaluated 70 patients, undergoing coronary by-pass surgery, requiring more than 5 days of surgical intensive-care unit (ICU)admission, vasopressor treatment and invasive mechanical ventilation. 63 patients received epinephrine or norepinephrine and 67 received dobutamine or dopamine.The authors documented that 1326 kcal/day of EN therapy is well tolerated and does not cause sever GI tract complications in cardiogenic shock patients, requiring vasopressor support.However, they also noted that shock patients should be monitored closely for abdominal signs and symptoms (3).

Following cardiogenic shock studies, retrospective studies, regarding EN therapy in septic shock patients were published.In 2010, *Rai et al.* published a retrospective study of 43 septic patients. In this study, mean enteral nutrition start time was 1.3 days,the mean doses of norepinephrine and epinephrine were 8.1 and 1.4 mg/day, respectively. Norepinephrine was the most frequently used vasopressor. In

this group of patients, EN therapy was well tolerated, despite high gastric residual volume and delayed gastric emptying (4).In a retrospective study in 2016, patients were divided into 3 groups: receiving less than 600 kcal/day ENtherapy (trophic nutrition), more than 600 kcal/day EN therapy and not receiving EN. In septic shock patients, norepinephrine was the most frequently used vasopressor and patients in not receiving EN group were treated with more than one vasopressor. In septic shock patients, receiving trophic nutrition in the first 48 hours, mechanical ventilation times and hospital length of stay was significantly shorter ($p<0.001$) (5).

In their large-scale prospective cohort trial, *Khalid et al.* documented that early EN therapy (within first 48 hours of therapy) after hemodynamic stabilization (fluid resuscitation, followed by treatment with one or more vasopressors) lowers hospital mortality.In early EN therapy and late EN therapy groups, mortality rateswere 22.5% and 28.3%, respectively ($p=0.03$) (6). Due to a secondary retrospective evaluation of a sepsis study, in 353 patients with severe sepsis, requiring stable or decreasing doses of vasopressors, regarding 90-day mortality rate, EN therapy alone was reported to be significantly superior to parenteral nutrition (PN) therapy alone and EN + PN therapy group. In EN therapy group septic patients, mean calorie and protein intakes per day were 918 kcal and 33.6 g, respectively, thus nutritional support was not considered aggressive (7).

In single center, randomized EAT-ICU study in 2017, *Allingstrup et al.* compared early goal directed EN therapy vs standard EN therapy in ICU patients with 47% severe sepsis (8). In early goal-directed EN and standard EN therapy groups, daily median calorie intakes (25-75 percentiles) were1877 (1567-2254) and 1061 (745-1470) kcal and daily mean protein intakes were 1.47 (1.31-1.69) and 0.50 (0.29-0.69) g/kg, respectively. Between study groups, no statistically significant difference was documented in aspect of 6-month quality of life, new-onset organ insufficiency, severe complications, and ICU and hospital length of stay.However detailed information of septic patients; vasopressor requirement rates or doses were not reported (8). *Rice at al.* conducted two randomized control studies about EN therapy in patients with acute respiratory distress. These studies included patients with vasopressor requirements. However, in severe and refractory shock were excluded from the study. High doses of dopamine and dobutamine were identified as >15 µg/kg/min, and of epinephrine and norepinephrine as >30 µg/kg/min.In patients with acute respiratory distress and vasopressor requirement, when compared trophic with full EN therapy, there was no statistically significant difference in mechanical ventilator free days or mortality (9, 10).

In NUTRIREA-2 study (randomized controlled, multi-centered), shock patients (61% septic and 19% cardiogenic) requiring norepinephrine, epinephrine and dobutamine were evaluated (11). In the first 24 hours following intubation or ICU admission, patients were randomized to EN or PN therapy groups and started on nutrition support.In shock patients, median (25%-75% percentiles) norepinephrine doses for EN and PN therapy groups were 0.56 (0.30-1.20) and 0.50 (0.25-1.03) µg/kg/min respectively. Also, median lactate levels for EN and PN therapy groups were 3.8 (3-5) and 3.9 (3-5) mEq/L, respectively. In EN therapy group, daily calorie and protein intake was lower; GI complication (nausea, vomiting, diarrhea, bowel ischemia, acute colonic pseudo-obstruction) frequency was higher.Although 28-day mortality was reported as 37% for EN and 35% for PN therapy groups, it seems difficult have a grasp of these results, due to lack of a control group (i.e. not receiving EN or PN therapy) (11).

In the event of uncontrolled shock (norepinephrine requirement >1 µg/kg/min) or inadequate tissue perfusion (hyperlactatemia >2mmol/L), European Association of Intensive Care Medicine (ESICM) guide recommends against the onset of EN therapy. However, in case of fluid responsiveness and hemodynamic stability is achieved with fixed or decreasing vasopressor doses, low dose EN therapy can be started (12).

Conclusion

In ICU patients with uncontrolled shock, EN therapy is not a priority.However, in case of prolonged vasopressor requirement or malnutrition due to co-morbidities, EN therapy can be planned.In the light of this information, the treatment protocol we formed in our hospital is presented below.

Hacettepe University Adult Hospital Nutrition Support TeamNutrition Support Therapy Protocol for Patients with Vasopressor Requirement

- Nutritional support therapy in shock patients with or without hypotension is not a priority.
- In shock patients EN therapy should not be started in the following conditions:
  1. High dose norepinephrine (>0.5 µg/kg/min), dopamine (>10 µg/kg/min) or epinephrine (>0.2 µg/kg/min) requirement
  2. Lactate levelabove 4 mmol/L
  3. In case of organ failure (encephalopathy, oliguria, skin perfusion insufficiency, etc.) decision should be made individually. Organ failure can be evaluated with a SOFA score ≥2 points or rise ≥2 points above the basal level (13).
- Until hemodynamic stability is achieved, EN support should be trophic (maximum dose 20 ml/h) rather full support.
- In the following group of patients, with careful monitorization, EN therapy should be started and increased to full dose within 5 to 7 days:
  - Lactate below <4 mmol/L or decreasing
  - Improvement in perfusion deficit or organ failure
- In absence of perfusion deficit or multi-organ failure and existence of chronic vasopressor requirement (more than 7 days), trophic EN can be started and increased, regarding patient tolerance. Norepinephrine, dopamine and epinephrine doses should be below 1, 20 and 0.5 µg/kg/min, respectively.When nutritional target cannot be achieved with EN, PN therapy with or without EN should be considered.
- Patients on EN support and requiring vasopressor infusion should be monitored carefully for development of abdominal symptoms.
  - Gastric residual volume should be assessed 3 times a day and when ≥400 mL, EN therapy should be suspended.
  - In addition to residual volume, EN therapy should be re-evaluated in existence of symptoms, suggesting a motility disorder, such as abdominal distension, vomiting and abdominal pain.
- Patients on vasopressors without severe malnutrition (NUTRIC score <5 points (Table 1) and weight loss <10%), PN support should not be started until days 5 to 7.

Table 1. NUTRIC scoring system(14)

Variable	Range	Points
Age	<50	0
	50 - <75	1
	≥ 75	2
APACHE II	<15	0
	15 - <20	1
	20 - 28	2
	≥ 28	3
SOFA	< 6	0
	6 - <10	1
	≥ 10	2
Number of comorbidities	0-1	0
	≥ 2	1
Hospital length of stay until ICU admission	0 - <1	0
	≥ 1	1

Total Points	Risk	Explanation
5 - 9	High risk	• Associated with worse clinical outcomes (mortality, ventilation). • These patients are the most likely to benefit from aggressivenutrition therapy.
0-4	Low risk	• These patients have a low malnutrition risk.

AUTHOR CONTRIBUTIONS:

Concept: OA; **Design:** SÖ, AT; **Supervision:** AT, SBA, MHG; **Literature Search:** SÖ; **Writing Manuscript:** SÖ; **Critical Review:** AT, OA; **Other:** SBA, MHG.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Acknowledgement: I would like to thank Hacettepe University Adult Hospital Nutrition Support Unit.

References

1. Kles KA, Wallig MA, Tappenden KA. Luminal nutrients exacerbate intestinal hypoxia in the hypoperfused jejunum. J Parenter Enteral Nutr 2001;25(5):246-252. [CrossRef]
2. Revelly JP, Tappy L, Berger MM, et al. Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. Intensive Care Med 2001;27(3):540-547. [CrossRef]
3. Berger MM, Revelly JP, Cayeux MC, et al. Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. Clin Nutr 2005;24(1):124-132. [CrossRef]
4. Rai SS, O'Connor SN, Lange K, Rivett J, et al. Enteral nutrition for patients in septic shock: a retrospective cohort study. Crit Care Resusc 2010;12(3):177-181.
5. Patel JJ, Kozeniecki M, Biesboer A, et al. Early Trophic Enteral Nutrition is Associated with Improved Outcomes in Mechanically Ventilated Patients With Septic Shock: A Retrospective Review. J Intensive Care Medicine 2016;3(7):471-77. [CrossRef]
6. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. Am J Crit Care 2010;19(3):261-268. [CrossRef]
7. Elke G, Kuhnt E, Ragaller M, et al. Enteral nutrition is associated with improved outcome in patients with severe sepsis: a secondary analysis of the VISEP trial. Med Klin Intensivmed Notfmed 2013;108(3):223-233. [CrossRef]
8. Allingstrup MJ, Kondrup J, Wiis J, et al. Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial. Intensive Care Med 2017; 43:1637–1647. [CrossRef]
9. Rice TW, Mogan S, Hays MA, et al. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med. 2011;39(5):967-974. [CrossRef]
10. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA. 2012;307(8):795-803. [CrossRef]
11. Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). Lancet 2018; 391: 133–43. [CrossRef]
12. Blaser AR, Starkopf J, Alhazzani W, et al. Early Enteral Nutrition in Critically Ill Patients: ESICM Clinical Pratice Guidelines. Intensive Care Med 2017:43:380-398. [CrossRef]
13. Vincent R, Moreno J, Takala S, et al. The SOFA (Sepsis related Organ Failure Assessment) score to describe organ dysfunction/failure . On behalf of the Working Group on Sepsis Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707-71. [CrossRef]
14. Heyland DK, Dhaliwal R, Jiang X, et al. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Critical Care 2011;15(6): 268-279. [CrossRef]