

Original Article

Enteral nutrition with omega-3 fatty acids in critically ill septic patients: A randomized double-blinded study

ABSTRACT

Purpose: The present study was done to investigate the effect of the enteral omega-3 fatty acids on critically ill septic patients.

Methods: A total of 110 critically ill septic patients were divided into two groups, 55 patients in each. Group A received enteral nutrition with 1000 mg omega-3 three times daily and Group B received enteral nutrition without omega-3. Demographic data, sepsis characteristics, number of patients required invasive ventilation, ventilation days, Intensive Care Unit (ICU) sequential organ failure assessment (SOFA) score, organ failure-free days, hemodynamic failure-free days, ICU stay, ICU, and hospital outcome were recorded.

Results: Leukocytic count and C-reactive protein were higher in Group B during ICU stay ($P = 0.010$ and 0.003 , respectively). The number of organ and hemodynamic failure-free days was higher in Group A ($P < 0.05$). Overall, ICU SOFA score was higher in Group B ($P = 0.03$). There was no difference in the number of patients requiring mechanical ventilation ($P = 0.41$). ICU stay was longer in Group B ($P = 0.019$); however, post-ICU hospital stay was similar in both groups. There were no differences regarding ICU and hospital survivors ($P > 0.05$).

Conclusions: Enteral nutrition with omega-3 can improve organ function and decrease ICU stay in septic patients. Omega-3 fatty acids do not affect ICU mortality or decrease the post-ICU hospital stay.

Key words: Critical illness; omega-3 fatty acid; sepsis

Introduction

Sepsis is a common problem in critically ill patients. Sepsis is the systemic response to infection manifested by two or more conditions that can occur during the systemic inflammatory response syndrome (SIRS).^[1] SIRS characterized by body temperature $>38.5^{\circ}\text{C}$ or $<35^{\circ}\text{C}$, heart rate >90 beats/min, white blood cells $>12,000$ cells/ mm^3 , tachypnea, and hypocapnia.^[2] Mortality associated with sepsis can reach 40% and can rise to 70% in septic shock.^[3] Inflammatory response due to severe sepsis may lead to multiorgan failure.^[4] The management of sepsis in the critically ill

patients is a challenge. Fluid resuscitation, inotropes, and supportive care are essential to prevent organ dysfunction and complications.^[5,6]


Nutrition support in Intensive Care Unit (ICU) may help support the immune system to deal with sepsis.^[1] It has been shown that enteral nutrition for critically ill patients may reduce the length of ICU stay, infection, and mortality rate.^[7] It has been shown that omega-3 has an immune-enhancing effect by boosting neutrophil activity and reduced inflammation;^[1,6] however, it is unclear if this effect can support the immune

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ibrahim ES. Enteral nutrition with omega-3 fatty acids in critically ill septic patients: A randomized double-blinded study. Saudi J Anaesth 2018;12:529-34.

Access this article online

Website: www.saudija.org	Quick Response Code 
DOI: 10.4103/sja.SJA_50_18	

EZZELDIN SALEH IBRAHIM

Department of Anaesthesia and Intensive Care, Faculty of Medicine, Menoufia University, Shebeen El-Kom, Egypt

Address for correspondence: Dr. Ezzeldin Saleh Ibrahim, Department of Anaesthesia and Intensive Care, Faculty of Medicine, Menoufia University, Shebeen El-Kom, Egypt. E-mail: ezzeldin7@yahoo.com

system in the critically ill patients. Some studies showed that immunonutrition can reduce the overall therapeutic interventions.^[2,6]

In the literature review, few investigated the role of parenteral fatty acid-enriched formulae on the systemic inflammatory response. There are not enough studies to show the effect of enteral omega-3 fatty acid in critically ill patients.

This study was carried out to assess the effect of immune-enhanced enteral diet with omega-3 fatty acid on critically ill septic patients.

Methods

After receiving the approval of the Ethics Committee of Menoufia University Hospital and the written assent from the patients' first of kin, this randomized double-blinded study was conducted on 110 critically ill septic adult patients (age > 18 years) from both genders.

Sepsis was diagnosed clinically and with laboratory tests. Sepsis was defined clinically if the patient had two or more signs of sepsis. Clinical signs of sepsis were body temperature $\geq 38.3^{\circ}\text{C}$ or $\leq 36^{\circ}\text{C}$, heart rate > 90 beats/min, respiratory rate > 20 /min, or $\text{PaCO}_2 < 32$ mmHg. Laboratory signs of sepsis were high C-reactive protein (CRP), white blood cell count $> 12,000/\text{m}^3$ or $< 4000/\text{m}^3$, and positive microbiological cultures such as blood, sputum, and urine.

All septic patients who could receive enteral nutrition were included in the study. Patients with end-stage liver or renal disease, hemodynamic instability, immunosuppression, patients on steroids, gastrointestinal comorbidity, and allergic to omega-3, received omega-3 a week before ICU admission, patients who expected to live < 24 h, and patients who were mechanically ventilated on ICU admission were excluded from the study.

Sepsis characteristics such as the type and the source of the infection were identified at the time of ICU admission.

Study design

The study was a randomized double-blind study. Independent pharmacists prepared the enteral nutrition bags. Patients were randomized into two groups, 55 in each using a computerized computer program (Group A and Group B). Patients, ICU nurses, investigator, and ICU physicians were blinded to the study. All patients received the conventional treatment for sepsis and the enteral nutrition according to our unit protocol. Group A received enteral nutrition supplemented with 3000 mg omega-3 in three divided daily doses. Omega-3

fatty acid supplement consisted of docosahexaenoic acid and eicosapentaenoic acid (DHA + EPA) in fish oil. Omega-3 fatty acid formula used in the study was high strength omega-3 from simply supplements (www.simplysupplements.co.uk), and the formula contained 1000 mg fish oil with 180 mg EPA and 120 mg DHA. Group B received the same enteral nutrition formula as Group A without adding the omega-3 supplement. The diet of Group A was enriched with DHA and EPA; however, it remained isocaloric and isonitrogenous as Group B diet. The energy content of the enteral nutrition formula was 1.5 kcal/ml and contained 10 g protein/ml.

The enteral feeding started within 6 h of patients meeting the enrollment criteria. The feeding was given at a constant rate of 50–150 ml/h through nasogastric tube. The feeding used to stop for 8 h during the night to rest the bowel. The aim was to achieve a minimum of 50% basal energy expenditure (BEE) $\times 1.3$ in the first 24 h. When the enteral feeding was tolerated, the rate was increased to achieve 75% of BEE $\times 1.3$ within 72 h.^[8]

Omega-3 supplementation was given until the patients were discharged from ICU. During ICU stay, the body temperature was recorded according to our unit's protocol. CRP and leukocytic count were requested every other day during ICU stay according to our unit's protocol. The mean values for leukocytic count and CRP count during ICU stay were compared for Group A and Group B.

The number of patients requiring mechanical ventilation and mechanical ventilation days was recorded. Complications of sepsis such as the development of any organ failure were monitored by changes in sequential organ failure assessment (SOFA) score. Hemodynamic failure (cardiovascular SOFA score 2 or more) was considered if the patient was on dopamine dose > 5 ug/kg/min, norepinephrine, or epinephrine.^[9] SOFA score > 1 and 2 defined organ dysfunction and organ failure, respectively.^[10]

Hemodynamic failure-free days were defined as the number of days between ICU admission and discharge when the cardiovascular SOFA scores of patients were < 2 . Organ failure-free days were defined as the number of days between ICU admission and discharge without any organ failure. For both groups, we recorded hemodynamic failure, organ dysfunction, and organ failure-free days. ICU stay, the number of ICU survivors, post-ICU hospital stay, and the hospital survivors were recorded.

Statistical analysis

The sample size was calculated using GraphPad InStat statistics version 3 (GraphPad Software, La Jolla, California, USA). Based

on previous studies, omega-3 would reduce severe sepsis in critically ill patients with acute gastrointestinal injury. At the level of significance 0.05 and power of 90%, the calculated sample size was 78 patients divided into two groups.^[9] The total number of patients randomized in the present study was 110 to ensure reliable results.

Statistical analysis was done using SPSS 19 (SPSS Inc., an IBM company, Chicago, IL, USA). Continuous variables were analyzed using independent *t*-test to compare between the two groups. All proportions of both groups were compared using Chi-square test. *P* < 0.05 was considered to be statistically significant.

Results

In the present study, a total of 894 patients were admitted to our ICU unit over a year. A total number of 156 patients were identified as septic critically ill patients. One hundred and ten patients met the inclusion criteria and were randomized for the study. Fifty-five patients were included in each group. Group A had omega-3 in their enteral diet and Group B had omega-3-free enteral diet. The flowchart [Figure 1] shows the study groups. There was no statistically significant difference between the two studied groups regarding their demographic data [Table 1].

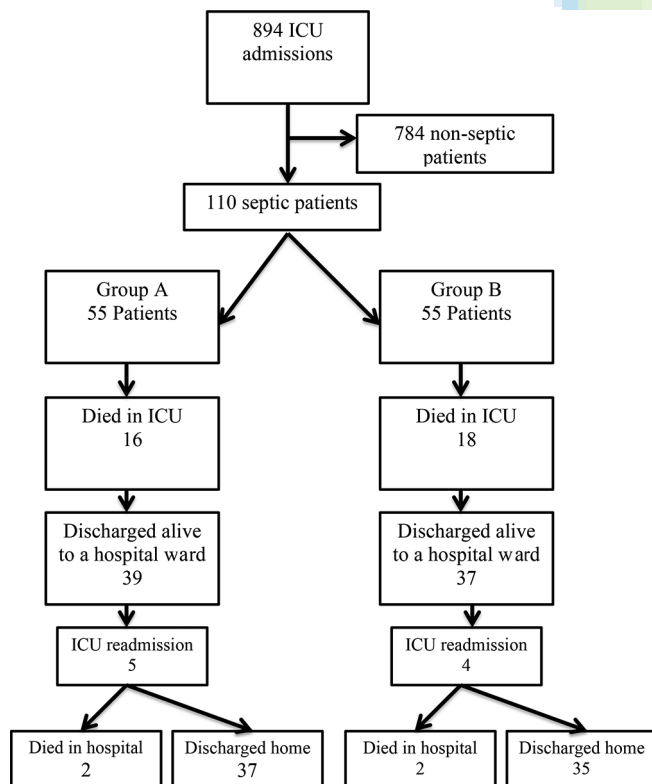


Figure 1: The study groups

Both groups showed no statistical significant regarding the source or type of infection. Admission body temperature, CRP, and leukocytic count were comparable in both groups (*P* > 0.05). Group A showed lower leukocytic count [Figure 2] and CRP level [Figure 3] compared to Group B during ICU stay (*P* < 0.05). There was no difference in body temperature during ICU stay. Table 2 shows infection characteristics during ICU stay.

There was no difference in admission SOFA score for both groups. SOFA score was significantly lower in Group A during ICU stay (*P* = 0.03). Group A patients had significantly more organ and hemodynamic failure-free days during ICU stay compared to Group B (*P* < 0.05). The number of patients requiring mechanical ventilation and the number of mechanical ventilation days were comparable in both groups (*P* > 0.05). Patients in Group B had longer ICU length of stay compared to Group A (*P* = 0.019). There was no statistical difference in the number of ICU and hospital survivors in both groups. There was no statistical difference in post-ICU hospital stay (*P* = 0.34). Table 3 shows organ failure characteristics and patients' outcome.

Discussion

Some clinical trials have focused on drugs to block the inflammatory cascade in sepsis and on immune modulators.^[7,11] Omega-3 fatty acid has been used as immune nutrient to reduce the inflammatory response.

Table 1: Patients' demographic data

Variables	Group A (n=55)	Group B (n=55)	<i>P</i> (t-test or Chi-square test)
Age (years)	61.20±7.63	62.35±8.15	0.65
Weight (kg)	75.54±7.76	78.49±6.26	0.11
Height (cm)	165.15±4.34	164.87±5.35	0.30
BMI (kg/m ²)	27.70±2.96	28.90±2.28	0.27
Gender (male/female)	29/26	28/27	0.66
APACHE II score	15.45±3.13	15.24±3.96	0.42
Admission SOFA score	5.10±1.6	5.25±1.4	0.32

BMI: Body mass index; SD: Standard deviation; SOFA: Sequential organ failure assessment; APACHE: Acute physiology and chronic health evaluation

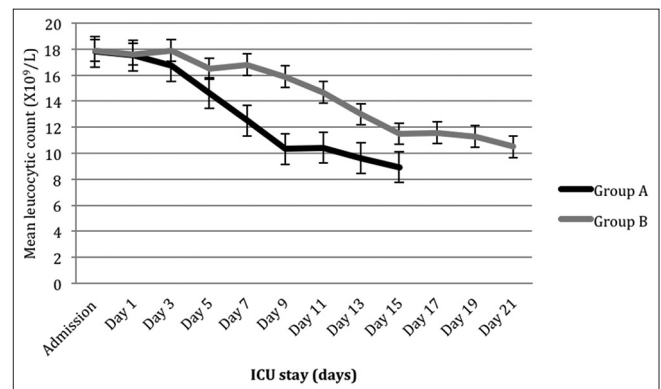


Figure 2: Mean Intensive Care Unit stay leukocytic count

Table 2: Sepsis characteristics

Infection characteristic	Group A (n=55)	Group B (n=55)	P
Infection site, n (%)			
Urinary tract	24 (43.6)	23 (41.8)	0.82
Respiratory system	11 (20)	13 (23.6)	
Blood	9 (16.4)	10 (18.2)	
Others	11 (20)	9 (16.4)	
Type of infection, n (%)			
Community acquired	19 (34.5)	21 (38.2)	0.73
Hospital acquired	36 (65.5)	34 (61.8)	
Admission body temperature, °C (mean±SD)	38.52±0.10	38.63±0.33	0.33
ICU stay body temperature, °C (mean±SD)	37.02±0.90	37.10±0.83	0.20
Admission leukocytic count, ×10 ⁹ /L (mean±SD)	17.79±1.63	17.93±1.56	0.41
ICU leukocytic count, ×10 ⁹ /L (mean±SD)	16.58±1.57	18.24±1.73	0.010*
Admission CRP, mg/L (mean±SD)	71.5±16.70	72.1±15.76	0.36
ICU CRP, mg/L (mean±SD)	65.26±13.32	70.28±16.74	0.003*

*Statistical significance. SD: Standard deviation; ICU: Intensive Care Unit; CRP: C-reactive protein

Table 3: Organ failure characteristics and patients' outcome

Variables	Group A (n=55)	Group B (n=55)	P
ICU stay SOFA score	6.10±1.6	8.89±1.8	0.03*
Organ failure-free days, median (IQ)	11 (4-11)	4 (0-10)	0.002*
Organ dysfunction-free days, median (IQ)	9 (1-11)	2 (0-8)	0.001*
Hemodynamic failure-free days, median (IQ)	12 (8-13)	8 (5-10)	0.002*
Number of patients required mechanical ventilation, n (%)	5 (9.1)	6 (10.9)	0.41
Mechanical ventilation days (mean±SD days)	5.32±1.66	6.37±2.36	0.31
Number of patients died during ICU stay, n (%)	16 (29.1)	18 (32.7)	0.27
ICU stay (days)	12.36±2.34	16.56±4.90	0.019*
Hospital stay (post-ICU days)	13.44±2.46	14.73±3.45	0.34
ICU survivors, n (%)	39 (70.9)	37 (67.3)	0.32
Hospital survivors, n (%)	37 (67.3)	35 (63.6)	0.24

*Statistical significance. ICU: Intensive Care Unit; SOFA: Sequential organ failure assessment; SD: Standard deviation; IQ: Interquartile range

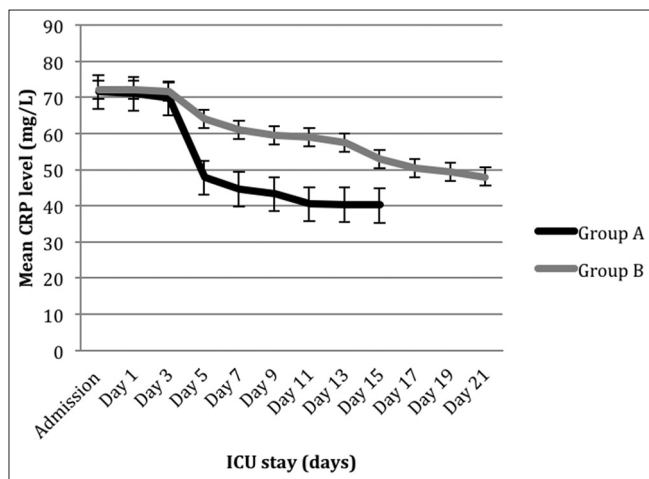


Figure 3: ICU stay CRP levels

In the present study, we investigated the effect of omega-3-enriched diet on a group of septic critically ill patients. The study showed that patients who received omega-3-enriched diet had lower sepsis indices such as CRP and leukocytic count. Patients who received omega-3 had

lower ICU SOFA score with better organ functions. ICU stay was shorter in this group of patients; however, there were no differences in ICU and hospital outcomes when compared to the group of patients who received omega-3-free diet.

Studies have investigated the role of using different parenteral nutrition formulae enriched with omega-3 fatty acids in the critical care setting.^[12-14]

Chen *et al.* studied the role of parenteral fish oil in reducing mortality in patients with advanced acute gastrointestinal injury.^[15] The authors focused on a single group of patients in the critical care setting and found that omega-3 can improve the mortality rate. Our study was a case-mix study with different causes of sepsis. Our case-mix study showed improvement to ICU morbidity, which was monitored by SOFA score and organ failure-free days. There was no reduction in mortality rate in the present study, which might be due to the difference in the causes of sepsis compared to Chen *et al.*'s group of patients.^[15]

A systematic review and a meta-analysis by Mo *et al.* were conducted to show the effect of parenteral omega-3 nutrition on patients with sepsis.^[16] The authors concluded that parenteral omega-3 could improve the outcome in this group of patients. The authors did not question the safety of injecting such formula; however, they acknowledged the low quality of the studies they reviewed. In our study, we used a common and safe route of administering omega-3 to avoid any complications that might arise from intravenous injection.

Barbosa *et al.* studied the effect of parenteral fish oil on inflammatory mediators and outcome in septic patients.^[12] The authors found that fish oil modified the inflammatory cytokines and shortness of the hospital stay. In the present study, we measured only CRP as an inflammatory response mediator. CRP is a routine investigation in our ICU unit. We did not measure any other inflammatory mediators, which could be a weak point in our study. Barbosa *et al.* found that parenteral fish oil did not affect patients' ICU length of stay; however, it decreased the duration of hospital stay.^[12] Our group of patients who received enteral omega-3 had shorter ICU stay with no difference in hospital stay. Barbosa *et al.*'s group of patients who received parenteral nutrition were sicker than our patients according to SOFA score, and they needed more ICU care.

Pradelli *et al.* did a meta-analysis to evaluate parenteral n-3 polyunsaturated fatty acid (PUFA) in surgical and ICU patients.^[13] The authors concluded that n-3 PUFA is safe and can reduce the total duration of hospital stay and reducing the rate of infection. Our enteral omega-3 diet reduced ICU stay but not hospital stay. It is unclear if the parenteral route is more effective and can have a longer duration of action that can cover the period of hospital stay.

Nowadays, enteral route is a preferable route; however, very few studies have investigated the enteral regimen in humans. Some experimental studies which used enteral diet supplemented with omega-3 and omega-9 showed that fatty acids could decrease metabolic dysfunction and improve outcome in sepsis.^[17,18]

Farzaneh-Far *et al.* studied the effect of omega-3 on some inflammatory mediators including CRP in patients with stable coronary artery disease.^[19] The authors found an independent and inverse association between omega-3 and CRP.

Tayyebi-Khosroshahi *et al.* found that omega-3 did not affect CRP levels in hemodialysis patients.^[20] Our results agree with Farzaneh-Far *et al.*; however, it does not agree with

Tayyebi-Khosroshahi *et al.* results.^[19,20] The differences in findings may be due to the differences in the pathophysiology of sepsis and renal insufficiency. Both diseases are different in the inflammatory cascade and response.

Rice *et al.* studied the effect of a mixed formula of enteral nutrition on patients with acute pulmonary injury.^[21] The authors used the same total daily dose as the doses used in the present study, but they prescribed it twice daily. Rice *et al.* found that omega-3 did not improve the ventilation-free days or patients' outcome. The authors showed an increased number of days with diarrhea.^[21] The authors concluded that enteral supplements might harm patients with acute lung injury. Our study did not agree with Rice *et al.* results regarding ventilation-free days and nonpulmonary organ dysfunction. In the present study, the number of days with diarrhea was not recorded, which can be a weak point of our study since omega-3 was given enterally.

Stapleton *et al.* did a study to show the effect of enteral omega-3 fatty acids on mechanically ventilated patients with acute lung injury.^[22] The authors found that omega-3 fatty acid did not improve patients' outcome regarding biomarkers of pulmonary or systemic inflammation, ventilator-free days, ICU stay, organ failure, or mortality.^[22] The results of Stapleton *et al.* did not agree with the present study regarding the effect on organ failure and ICU stay. The present study agreed with Stapleton *et al.* results regarding the effect of omega-3 fatty acids on the mechanical ventilation and the mortality rate.

Pontes-Arruda *et al.* studied the effect of enteral nutrition with EPA, γ -linolenic acid, and antioxidants in the early treatment of sepsis.^[23] The authors showed fewer patients in the study group who developed multiorgan failure compared to the control group. The authors also showed lower incidence of respiratory failure in the same group of patients.^[23] Our results agree with Pontes-Arruda *et al.*; however, in the present study, we did not find any differences between the two groups regarding the need of invasive respiratory support and the duration of mechanical ventilation. It is unclear if the difference in the diet composition with the additive of antioxidants could be beneficial to the respiratory system.

Gadek *et al.* did two different studies to show the effect of two different enteral immune nutrient diets on patients with acute lung injury.^[24] The authors found that diet supplementation improved the patients' outcome and gas exchange.^[24] Our study did not show an advantage of omega-3 in decreasing the respiratory support in septic patients. The results were different maybe because ARDS patients primarily showed alveolar capillary affection which is different to septic patients.

In the present study, enteral omega-3 did not affect the ventilation characteristics. It is unclear if the administration route of omega-3 fatty acids plays a role in improving the alveolar–capillary membrane.

Conclusions

Enteral omega-3 fatty acid improves organ functions in critically ill septic patients. Omega-3-enriched enteral diet can reduce the ICU length of stay; however, it does not affect patients' outcome regarding ICU and hospital mortality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Annane D, Bellissant E, Cavaillon JM. Septic shock. *Lancet* 2005;365:63-78.
- Bone RC, Fisher CJ Jr, Clemmer TP, Slotman GJ, Metz CA, Balk RA, *et al*. Sepsis syndrome: A valid clinical entity. Methylprednisolone severe sepsis study group. *Crit Care Med* 1989;17:389-93.
- Hoffmann JN, Werdan K, Hartl WH, Jochum M, Faist E, Inthorn D, *et al*. Hemofiltrate from patients with severe sepsis and depressed left ventricular contractility contains cardiotoxic compounds. *Shock* 1999;12:174-80.
- Linkermann A, Stockwell BR, Krautwald S, Anders HJ. Regulated cell death and inflammation: An auto-amplification loop causes organ failure. *Nat Rev Immunol* 2014;14:759-67.
- Andrews B, Semler MW, Muchemwa L, Kelly P, Lakhi S, Heimbarger DC, *et al*. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: A randomized clinical trial. *JAMA* 2017;318:1233-40.
- Sessler CN, Shepherd W. New concepts in sepsis. *Curr Opin Crit Care* 2002;8:465-72.
- Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. *N Engl J Med* 2003;348:138-50.
- Pontes-Arruda A, Aragão AM, Albuquerque JD. Effects of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in mechanically ventilated patients with severe sepsis and septic shock. *Crit Care Med* 2006;34:2325-33.
- Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, *et al*. Use of the SOFA score to assess the incidence of organ dysfunction/failure in Intensive Care Units: Results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;26:1793-800.
- Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, *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;22:707-10.
- Minnecci PC, Deans KJ, Banks SM, Eichacker PQ, Natanson C. Meta-analysis: The effect of steroids on survival and shock during sepsis depends on the dose. *Ann Intern Med* 2004;141:47-56.
- Barbosa VM, Miles EA, Calhau C, Lafuente E, Calder PC. Effects of a fish oil containing lipid emulsion on plasma phospholipid fatty acids, inflammatory markers, and clinical outcomes in septic patients: A randomized, controlled clinical trial. *Crit Care* 2010;14:R5.
- Pradelli L, Mayer K, Muscaritoli M, Heller AR. n-3 fatty acid-enriched parenteral nutrition regimens in elective surgical and ICU patients: A meta-analysis. *Crit Care* 2012;16:R184. Erratum in: *Crit Care* 2012;17:405.
- Palmer AJ, Ho CK, Ajibola O, Avenell A. The role of ω -3 fatty acid supplemented parenteral nutrition in critical illness in adults: A systematic review and meta-analysis. *Crit Care Med* 2013;41:307-16.
- Chen H, Wang W, Hong C, Zhang M, Hong Y, Wang S, *et al*. Omega-3 fish oil reduces mortality due to severe sepsis with acute gastrointestinal injury grade III. *Pharmacogn Mag* 2017;13:407-12.
- Mo Y, Hu X, Chang L, Ma P. The effect of ω -3 fatty acid supplementation in parenteral nutrition on the outcome of patients with sepsis: A systematic review and meta-analysis. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2014;26:142-7.
- Svahn SL, Ulleryd MA, Grahne L, Ståhlman M, Borén J, Nilsson S, *et al*. Dietary omega-3 fatty acids increase survival and decrease bacterial load in mice subjected to *Staphylococcus aureus*-induced sepsis. *Infect Immun* 2016;84:1205-13.
- Tsou SS, Chiu WC, Yeh CL, Hou YC, Yeh SL. Effects of omega-3 fatty acids on inflammatory mediators and splenocyte cytokine mRNA expressions in rats with polymicrobial sepsis. *Nutrition* 2008;24:484-91.
- Farzaneh-Far R, Harris WS, Garg S, Na B, Whooley MA. Inverse association of erythrocyte n-3 fatty acid levels with inflammatory biomarkers in patients with stable coronary artery disease: The heart and soul study. *Atherosclerosis* 2009;205:538-43.
- Tayyebi-Khosroshahi H, Houshyar J, Dehghan-Hesari R, Alikhah H, Vatankhah AM, Safaeian AR, *et al*. Effect of treatment with omega-3 fatty acids on C-reactive protein and tumor necrosis factor- α in hemodialysis patients. *Saudi J Kidney Dis Transpl* 2012;23:500-6.
- Rice TW, Wheeler AP, Thompson BT, deBoisblanc BP, Steingrub J, Rock P, *et al*. Enteral omega-3 fatty acid, gamma-linolenic acid, and antioxidant supplementation in acute lung injury. *JAMA* 2011;306:1574-81.
- Stapleton RD, Martin TR, Weiss NS, Crowley JJ, Gundel SJ, Nathens AB, *et al*. A phase II randomized placebo-controlled trial of omega-3 fatty acids for the treatment of acute lung injury. *Crit Care Med* 2011;39:1655-62.
- Pontes-Arruda A, Martins LF, de Lima SM, Isola AM, Toledo D, Rezende E, *et al*. Enteral nutrition with eicosapentaenoic acid, γ -linolenic acid and antioxidants in the early treatment of sepsis: Results from a multicenter, prospective, randomized, double-blinded, controlled study: The INTERSEPT study. *Crit Care* 2011;15:R144.
- Gadek JE, DeMichele SJ, Karlstad MD, Pacht ER, Donahoe M, Albertson TE, *et al*. Effect of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in patients with acute respiratory distress syndrome. Enteral nutrition in ARDS study group. *Crit Care Med* 1999;27:1409-20.

Copyright of Saudi Journal of Anaesthesia is the property of Wolters Kluwer India Pvt Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.