

CLINICAL SUMMARY

Use of an enteral formula with EPA/GLA and antioxidants (Oxepa®) in critically ill patients with early sepsis without organ failure was associated with less development of severe sepsis and/or septic shock. Results from the INTERSEPT* Study.

This study provides evidence that use of an enteral formula with EPA/GLA and elevated antioxidants in patients with early stages of sepsis without any organ failure can slow the progression of the disease to severe sepsis and/or septic shock.

Critical care nutrition support guidelines recommend an enteral formula containing an anti-inflammatory lipid profile (ω -3 fatty acids, borage oil, and antioxidants) in patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).^{7,8}

Eicosapentaenoic acid (EPA), a fatty acid from fish oil, and gamma-linolenic acid (GLA), a fatty acid from borage oil, help modulate the inflammatory response by producing eicosanoids that are less proinflammatory compared with those produced by arachidonic acid.

Previous studies have demonstrated the anti-inflammatory benefits of feeding a formula with EPA/GLA and antioxidants (Oxepa) in improving oxygenation,¹⁻⁶ reducing pulmonary inflammation,² reducing time in the ICU,^{1,3-5} reducing time on the ventilator,^{1,3,4} reducing new organ failures,^{1,4,5} and reducing mortality^{3,4} in patients with acute lung injury.

This prospective, multicenter, randomized, double-blinded, controlled trial was conducted to evaluate the effect of feeding an enteral formula with EPA, GLA, and elevated antioxidants (Oxepa) versus an isonitrogenous, isocaloric control formula (Ensure Plus HN®) in delaying the progression of the disease to severe sepsis and/or septic shock in patients with early sepsis without organ failure. Patients were randomized to receive one of the 2 formulas for 7 days via continuous tube feeding at a minimum of 75% of basal energy expenditure x 1.3.

This is the first study to feed this type of formula to critically ill patients with early sepsis without organ failure.

*INTERSEPT = Investigating Nutritional Therapy with EPA, GLA, and Antioxidants Role in Sepsis Treatment

Pontes-Arruda A, et al. Enteral nutrition with eicosapentaenoic acid, g-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(3):R144.

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One hundred fifteen patients were enrolled. Based on the intent-to-treat analysis, compared to patients fed the control product, patients fed Oxepa® developed:

- less severe sepsis (sepsis associated with at least one organ failure) or septic shock (sepsis associated with hypotension despite adequate fluid resuscitation)
- fewer cardiovascular and respiratory failures

Patients fed Oxepa also experienced more ICU- and hospital-free days and fewer required mechanical ventilation than patients fed the control product.

No difference in 28-day all-cause mortality was observed between the groups. See table below for a listing of study results.

Patients received a median 1538 and 1523 kcals (Oxepa vs control) and a mean 63.4 ± 22.8 and 62.6 ± 24.3 g protein/day (Oxepa vs control), which provided approximately 25-26 kcals/kg and 1.0-1.1 g protein/kg.

Pontes-Arruda A, et al. *Crit Care*. 2011;15:R144. [Epub ahead of print]

Table: Average values in a subgroup analysis of 18 patients prescribed full volume feeds vs the 'before' group.

Outcome	EPA/GLA (n=57)	Control (n=58)	P value
Severe sepsis and/or septic shock	26.3%	50%	0.0259
Cardiovascular failure	21.0%	36.2%	0.0381
Respiratory failure	24.6%	39.6%	0.0362
ICU-free days, mean	21.1 ± 4.7	14.7 ± 5.1	< 0.001
Hospital-free days, mean	19.5 ± 7.8	10.3 ± 8.6	< 0.001
Mechanical ventilation	17.5%	34.5%	0.295
28-day all-cause mortality	26.2%	27.6%	0.72

NUTRITION CONCLUSIONS

Patients with early sepsis who received Oxepa experienced improved clinical outcomes compared with patients fed the control formula. These results demonstrate that use of Oxepa in patients in the early stages of sepsis without organ failure is associated with less development of severe sepsis and/or septic shock, primarily as a result of the development of fewer cardiovascular and respiratory failures.

References: 1. Gadek JE, DeMichele SJ, Karlstad MD, et al. Effect of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in patients with acute respiratory distress syndrome. *Crit Care Med*. 1999;27:1409-1420. 2. Pacht ER, DeMichele SJ, Nelson JL, et al. Enteral nutrition with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants reduces alveolar inflammatory mediators and protein influx in patients with acute respiratory distress syndrome. *Crit Care Med*. 2003;31:491-500. 3. Singer P, Theilla M, Fisher H, et al. Benefit of an enteral diet enriched with eicosapentaenoic acid and gamma-linolenic acid in ventilated patients with acute lung injury. *Crit Care Med*. 2006;34:1033-1038. 4. Pontes-Arruda A, Aragao 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;34:2325-2333. 5. Elamin EM, Hughes LF, Drew D. Effect of enteral nutrition with eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA), and antioxidants reduces alveolar inflammatory mediators and protein influx in patients with acute respiratory distress syndrome (ARDS). *Chest*. 2005;128:225S. 6. Mayes T, Gottschlich MM, Kagan RJ. An evaluation of the safety and efficacy of an anti-inflammatory, pulmonary enteral formula in the treatment of pediatric burn patients with respiratory failure. *J Burn Care Res*. 2008;29(1):82-88. 7. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *JPEN J Parenter Enteral Nutr*. 2009;33:277-316. 8. Canadian Clinical Practice Guidelines: Summary of Recommendations. www.criticalcarenutrition.com/docs/cpg/srrev.pdf. Accessed October 5, 2011.