Dietary supplements for patients after lung injury do not appear to improve outcomes; may be harmful

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In contrast to findings of previous studies, patients who experienced an acute lung injury, such as from pneumonia or sepsis, and received dietary supplements including omega-3 fatty acids and antioxidants had more days on a ventilator, more days in the intensive care unit (ICU), and a non-statistically significant increase in the rate of death, according to a study appearing in *JAMA*. The study is being published early online to coincide with its presentation at the European Society of Intensive Care Medicine meeting in Berlin.

"Patients at risk of developing acute lung injury (ALI) have omega-3 (n-3) levels approximately 25 percent of normal and those with established ALI have n-3 levels as low as 6 percent of normal, suggesting a potential role for n-3 dietary supplementation in patients with ALI," according to background information in the article. Preclinical data indicate that the n-6 γ-linolenic acid (GLA; a fatty acid), in conjunction with the n-3 fatty acid eicosapentaenoic acid (EPA), may also be beneficial in ALI. Three randomized controlled studies, conducted in patients with ALI or sepsis-induced respiratory failure, demonstrated an association between the administration of an enteral (oral) formula enriched in n-3 fatty acids, GLA, and antioxidants and improved outcomes on some measures. These supplements may modulate systemic inflammatory response and improve oxygenation and outcomes in patients with ALI. However, interpretation of these results is limited by the small sample sizes and as-treated analyses of only those patients who

tolerated full enteral nutrition.

Todd W. Rice, M.D., M.Sc., of the Vanderbilt University School of Medicine, Nashville, Tenn., and colleagues conducted a study to examine the effects of supplementation of n-3 fatty acids, GLA, and antioxidants on clinical outcomes in patients with ALI in a phase 3 trial. The researchers hypothesized that a twice-daily bolus (a large dosage) administration of these supplements would increase the ratio of n-3 to n-6 fatty acids, reduce inflammatory mediators, and improve certain clinical outcomes. The OMEGA study was a randomized, placebo-controlled, multicenter trial conducted from January 2008 through February 2009. Participants were 272 adults within 48 hours of developing ALI requiring mechanical ventilation whose physicians intended to start enteral nutrition at 44 hospitals in the National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. The intervention consisted of twice-daily enteral supplementation of n-3 fatty acids (docosahexaenoic acid [DHA] and EPA), GLA, and antioxidants compared with an isocaloric control. The primary measured outcome was the number of ventilator-free days to study day 28.

The study was stopped early for futility at the first interim analysis after 143 patients had been randomized to receive the n-3 supplement and 129 to receive the isocaloric control. All patients had complete follow-up to the earlier of hospital discharge or day 60.

The n-3 study supplement increased plasma EPA levels 8-fold on days 3, 6, and 12, whereas levels in control patients remained unchanged. The researchers found that the n-3 supplement group had fewer ventilator-free days to study day 28 compared with controls (14.0 vs. 17.2) and fewer ICU-free days (14.0 vs. 16.7). "In the n-3 group, 38 of the 143 patients (26.6 percent) died prior to day 60 or hospital discharge compared with 21 of the 129 (16.3 percent) in the control group. When adjusted for baseline variables previously shown to be associated with

mortality in ALI, the n-3 group had 25.1 percent 60-day mortality vs. 17.6 percent in the control group [not statistically significant]."

In addition, the n-3 supplement did not protect from hospital-acquired infections or improve nonpulmonary organ function. Patients receiving the n-3 supplement had more frequent instances of gastrointestinal intolerance.

"This study suggests that twice-daily enteral supplementation of n-3 fatty acids, GLA, and antioxidants change plasma levels of n-3 fatty acids but do not improve clinical outcomes or biomarkers of systemic inflammation in patients with ALI and in fact may be harmful," the authors conclude.

Deborah J. Cook, M.D., M.Sc., of McMaster University Health Sciences Center, Hamilton, Ontario, and Daren K. Heyland, M.D., M.Sc., of Queens University, Kingston, Ontario, Canada write in an accompanying editorial that more research is needed regarding the use of pharmaconutrition.

"Translational research as was used in the OMEGA trial will elucidate effects, or lack thereof, on inflammatory, immunologic, metabolic, and other processes. Clinical research will test whether modulating pathophysiology improves morbidity and mortality. Larger trials will help to inform practitioners regarding which interventions do more good than harm, which do more harm than good, and which truly have no effect. Interdisciplinary collaboration incorporating basic principles of nutrition will be needed to accelerate the generation of new knowledge. Currently, international audits of nutrition practice suggest that use of these and other pharmaconutrients is low. If and when the time is ripe, the fruits of these labors will be harvested in knowledge translation activities that drive quality improvement to help improve the care of critically ill patients around the world."

More information: JAMA. 2011;306[14]:1574-1581