Case Report

Therapeutic use of omega-3 fatty acids in severe head trauma

Abstract

Traumatic brain injury (TBI) has long been recognized as the leading cause of traumatic death and disability. Tremendous advances in surgical and intensive care unit management of the primary injury, including maintaining adequate oxygenation, controlling intracranial pressure, and ensuring proper cerebral perfusion pressure, have resulted in reduced mortality. However, the secondary injury phase of TBI is a prolonged pathogenic process characterized by neuroinflammation, excitatory amino acids, free radicals, and ion imbalance. There are no approved therapies to directly address these underlying processes. Here, we present a case that was intentionally treated with substantial amounts of omega-3 fatty acids (n-3FA) to provide the nutritional foundation for the brain to begin the healing process following severe TBI. Recent animal research supports the use of n-3FA, and clinical experience suggests that benefits may be possible from substantially and aggressively adding n-3FA to optimize the nutritional foundation of severe TBI patients and must be in place if the brain is to be given the opportunity to repair itself to the best possible extent. Administration early in the course of treatment, in the emergency department or sooner, has the potential to improve outcomes from this potentially devastating public health problem.

Traumatic brain injury (TBI) has long been recognized as a leading cause of traumatic death and disability [1-3]. Tremendous advances in surgical and intensive care unit management of the primary injury, including maintaining adequate oxygenation, controlling intracranial pressure, and ensuring proper cerebral perfusion, have resulted in reduced mortality [3,4]. However, the secondary injury phase of TBI is a prolonged pathogenic process characterized by neuroinflammation, excitatory amino acids, free radicals, and ion imbalance [5]. There are no approved therapies to directly address these underlying processes. Here we present a case that was intentionally treated with substantial amounts of omega-3 fatty acids (n-3FA) to provide the nutritional foundation for the brain to begin the healing process following severe TBI.

In March 2010, a teenager sustained a severe TBI in a motor vehicle accident. After prolonged extrication, he was resuscitated at the scene and flown to a Level I Trauma Center. His Glasgow Coma Scale score was 3. Computerized tomography revealed panhemispheric right subdural and small temporal epidural hematomas and a 3-mm midline shift (Fig. 1). The patient underwent emergency craniotomy and intracranial pressure monitor placement. The patient was rated at Rancho Los Amigos Cognitive Scale Level I, and the attending neurosurgeon’s impression was that the injury was likely lethal.

On hospital day 10, T2-weighted magnetic resonance imaging revealed right cerebral convexity subdural hemorrhage and abnormal fluid-attenuated inversion recovery signals consistent with diffuse axonal injury (Fig. 2). Believed to be in a permanent vegetative state, a tracheotomy and percutaneous endoscopic gastrostomy (PEG) tube were placed for custodial care; and enteral feedings were started (Promote; 80 mL/h; 1920 kcal/d). The following day, n-3FA were added to enteral feedings.

On day 10, it was recommended to the patient’s father to procure Nordic Naturals (Watsonville, CA) brand Ultimate Omega from a local retail store. With the cooperation of the attending neurosurgeon and hospital pharmacy, the patient began receiving 15 mL twice a day (30 mL/d), providing 9756 mg eicosapentaenoic acid, 6756 mg docosahexaenoic acid (DHA), and 19212 mg total n-3FA daily via his PEG. On day 21, he was weaned off the ventilator and transported to a specialized rehabilitation institute 3 days later. His level of functioning was measured at Rancho Los Amigos Level III. The patient began therapy that gradually led to cognitive and physical improvements. Notably, the patient was given permission and attended his high school graduation 3 months after the injury to receive his diploma. He was discharged to home 4 months after the injury. Over the following year, Nordic Naturals generously donated a steady supply of Pro Omega-D (the professional version of Ultimate Omega) that also provided vitamin D3 (6000 IU). The patient remained on this level of n-3FA for more than 1 year and experienced no adverse effects. Two years later, the patient is at Rancho Los Amigos Level VIII, but

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has speech and balance issues consistent with the location and size of the brain damage, and is walking with the aid of a cane because of significant left-sided weakness. Currently at home, he is working with an athletic trainer to strengthen his left leg and has started a small, part-time business as a disk jockey.

We are aware of only one report where n-3FA were used, that being the survivor of the Sago Mine accident in January 2006 suffering from hypoxia and exposure to toxic gases, dehydration, and rhabdomyolysis [6]. To our knowledge, this is the first report of specific use of substantial amounts of n-3FA following severe TBI.

It is well recognized that n-3FA are important for proper neurodevelopment and function [7,8]. However, average Western dietary intakes result in a deficiency of n-3FA and an overdominant intake of proinflammatory omega-6s (n-6FA). The ratio of n-3:n-6FA in the Western diet can be as low as 1:50. Such imbalance is reflected directly in the composition of neuron membrane phospholipids favoring inflammatory processes [9]. Arachidonic acid, the primary n-6FA in the brain, is metabolized by cyclooxygenase and lipoxygenase enzymes to proinflammatory eicosanoids that enhance vascular permeability, increase local blood flow, increase infiltration of leukocytes, and enhance production of proinflammatory cytokines [10]. Omega-3 fatty acids attenuate release of these proinflammatory cytokines, decrease cyclooxygenase activity, inhibit formation of proinflammatory eicosanoids and cytokines, and promote levels of anti-inflammatory docosanoids [10,11]. Docosahexaenoic acid, in particular, promotes neuronal survival [12-14], neurogenesis [15], neurite development [16,17], neuronal cell migration [18], synaptogenesis [17], and modulation of inflammatory cascade [19].

**Fig. 1** Computerized tomographic scan of the patient approximately 2 hours after the motor vehicle accident and before neurosurgery. Note the moderate-sized panhemispheric right subdural hematoma, a small right temporal epidural hematoma, subarachnoid hemorrhage, and 3-mm right to left shift of the midline.

**Fig. 2** T2-weighted magnetic resonance imaging on hospital day 10. Note the right cerebral convexity subdural hemorrhage, right postcentral gyrus and left temporal lobe parenchymal petechial hemorrhage, and small superior vermian subarachnoid hemorrhage in the image on the right. In addition, multiple zones of abnormal fluid-attenuated inversion recovery signals consistent with diffuse axonal injury are present on both images.
Laboratory animal research shows that n-3FA may help improve clinical outcomes when administered before or following TBI [20-22], spinal cord injury [23], and brain ischemia [24,25]. Omega-3 fatty acids [20], as well as DHA alone [21], significantly reduce the number of injured axons [20,21]. When DHA was given within an hour of spinal cord injury, neuromotor function was maintained; but the effect was lost when treatment was delayed for 4 hours [26]. These findings support the idea that treatment with n-3FA represents a promising therapeutic approach for neurotrauma that would be easy to translate to the emergency patient-care arena considering the well-documented safety and tolerability of these compounds [26].

Early nutritional intervention in TBI is underappreciated. Patients not fed within 5 and 7 days after TBI have a 2- and 4-fold increased likelihood of death, respectively; and decreasing amount of nutrition in the first 5 days is related to increased mortality rates [27]. Early enteral nutrition after brain injury can be accomplished by PEG [28] or nasogastric tube, even in the emergency department. Of the 49 total recommendations published by the America Society for Parenteral and Enteral Nutrition and the Society of Critical Care Medicine, only 2 warrant Grade A recommendations, both of which state that immune-enhancing enteral formulations with n-3FA should be used in critically ill surgical patients (including trauma) [29].

Although further research is needed to establish the true advantage of using n-3FA, our experience suggests that benefits may be possible from aggressively adding substantial amounts of n-3FA to optimize the nutritional foundation of severe TBI patients. An optimal nutritional foundation must be in place if the brain is to be given the best opportunity to repair itself. Administration earlier in the course of treatment, even in the emergency department setting, has the potential to improve outcomes from this potentially devastating public health problem.

References


Michael Lewis MD
Brain Health Education and Research Foundation
Arlington, VA
E-mail address: dr.michael.lewis@gmail.com

Parviz Ghassemi
Great Falls, VA 22066
E-mail address: peter@arctelcom.com

Joseph Hibben MD
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health, 3N-07
Rockville, MD 20852
E-mail address: Joseph.hibben@nih.gov

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