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

Michael Lewis, MD[1,*], **Parviz Ghassemi, MS**[2], and **Joseph Hibbeln, MD**[3]

Parviz Ghassemi: peter@arctelcom.com; Joseph Hibbeln: Joseph.hibbeln@nih.gov

[1]Brain Health Education and Research Foundation Arlington, VA

[2]10150 Akhtamar Drive, Great Falls, VA 22066, (703) 926-8010

[3]National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, 5625 Fishers Lane, 3N-07, Rockville, MD 20852

Keywords

Omega-3; Fish Oil; Traumatic Brain Injury (TBI); Essential Fatty Acids

Introduction

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 (ICU) management of the primary injury, including maintaining adequate oxygenation, controlling intracranial pressure (ICP), and ensuring proper cerebral perfusion, have resulted in reduced mortality[3–4]. However, the secondary injury phase of TBI is a prolonged pathogenic process is 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.

Case History

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 three. Computerized tomography (CT) revealed panhemispheric right subdural and small temporal epidural hematomas and a three millimeter midline shift (figure one). The patient underwent emergency craniotomy and ICP 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 ten, T2 weighted magnetic resonance imaging (MRI) revealed right cerebral convexity subdural hemorrhage and abnormal FLAIR signals consistent with diffuse axonal injury (figure two). 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; 80ml/hour; 1920 kcal per day). The following day, omega-3 fatty acids were added to enteral feedings.

[*]Address for Correspondence: 10004 Weatherwood Court, Potomac, MD 20854, (240) 481-2989, dr.michael.lewis@gmail.com.

Use of omega-3 fatty acids

Day ten, it was recommended to the patient's father to procure Nordic Natural brand UltimateOmega 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/day) providing 9,756 mg Eicosapentaenoic Acid (EPA), 6,756 mg Docosahexaenoic Acid (DHA), and 19,212 mg total n-3FA daily via his PEG. On day 21, he was weaned off the ventilator and transported to a specialized rehabilitation institute three days later. His level of functioning was measured at Rancho Los Amigos Level III. The patient began therapy which gradually led to cognitive and physical improvements. Notably, the patient was given permission and attended his high school graduation three months after the injury to receive his diploma. He was discharged to home four months after the injury. Over the following year, Nordic Naturals generously donated a steady supply of ProOmega-D (the professional version of UltimateOmega) which also provided Vitamin D3 (6000 International Units). The patient remained on this level of n-3FA for over one year and experienced no side effects. Two years later, the patient is at Rancho Los Amigos Level VIII, but has speech and balance issues consistent with the location and size of the brain damage, and is walking with the aid of a cane due to 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.

Discussion

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 over-dominant 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 (COX) and lipoxygenase (LOX) enzymes to pro-inflammatory eicosanoids that enhance vascular permeability, increase local blood flow, increase infiltration of leukocytes, and enhance production of proinflammatory cytokines[10]. N-3FA attenuate release of these proinflammatory cytokines, decrease COX activity, inhibit formation of proinflammatory eicosanoids and cytokines, and promote levels of anti-inflammatory decosanoids [10–11]. DHA, 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].

Laboratory animal research shows that n-3FA may help improve clinical outcomes when administered prior to or following TBI[20–22], spinal cord injury (SCI)[23], and brain ischemia[24–25]. N-3FA[26], as well as DHA alone[21], significantly reduces the number of injured axons[20–21]. When DHA was given within an hour of SCI, neuromotor function was maintained but the effect was lost when treatment was delayed four hours [27]. These findings support the idea that treatment with n-3FA represent a promising therapeutic approach for neurotrauma which would be easy to translate to the emergency patient-care arena considering the well-documented safety and tolerability of these compounds [27].

Early nutritional intervention in TBI is underappreciated. Patients not fed within five and seven days after TBI have a two- and four-fold increased likelihood of death, respectively, and decreasing amount of nutrition in the first five days is related to increased mortality rates [28]. Early enteral nutrition after brain injury can be accomplished by PEG[29] or nasogastric tube, even in the Emergency Department. The American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM), published guidelines and only two Grade A recommendations among 49 total recommendations both state that immune enhancing enteral formulations with n-3FA should be used in critically ill surgical patients (including trauma)[30].

Conclusion

While further research is needed to establish the true advantage to 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.

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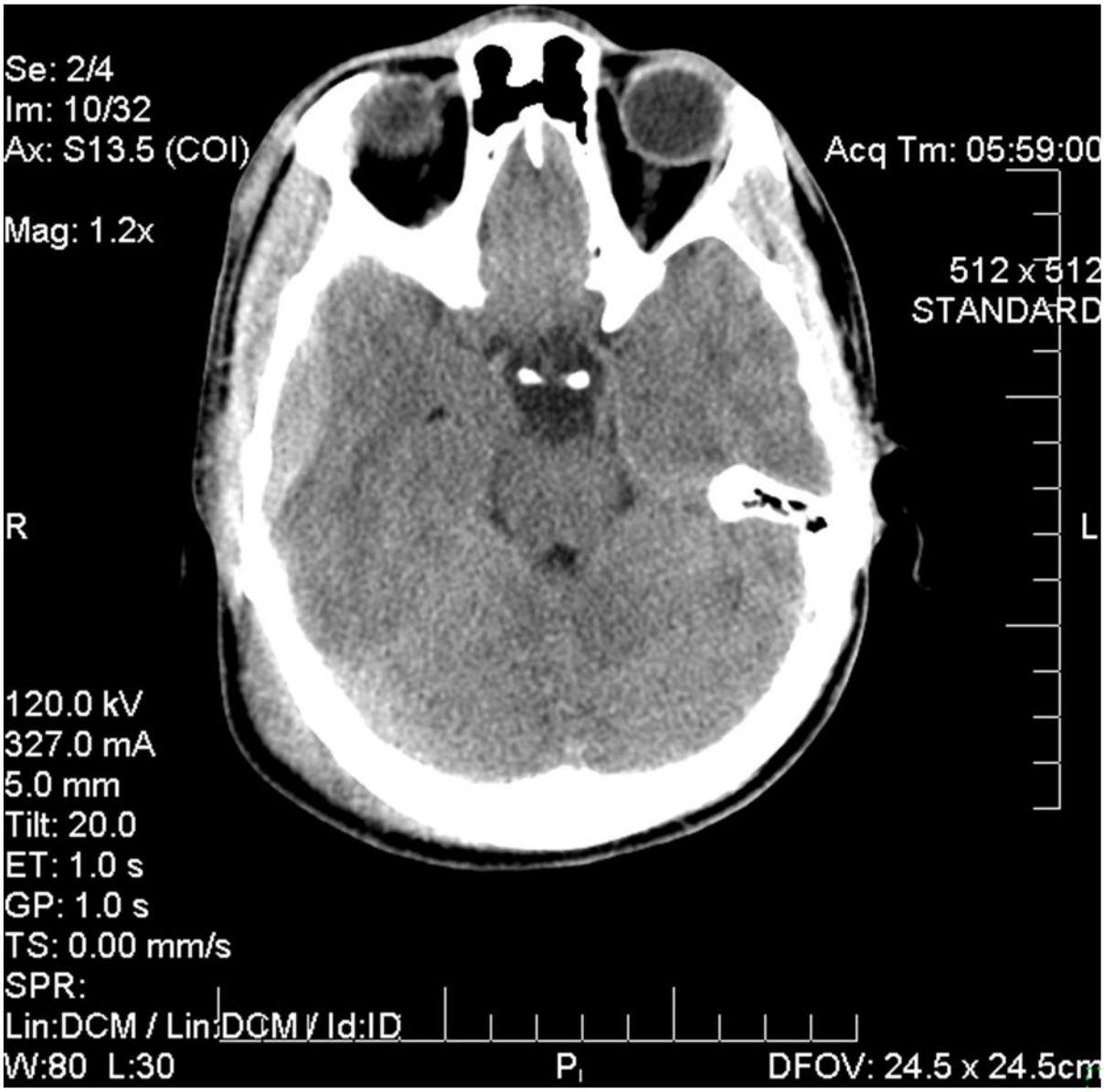

Figure One.
Computerized tomography scan of the patient approximately two hours after the motor vehicle accident and prior to neurosurgery. Note the moderate sized panhemispheric right subdural hematoma, a small right temporal epidural hematoma, subarachnoid hemorrhage, and three millimeter right to left shift of the midline.

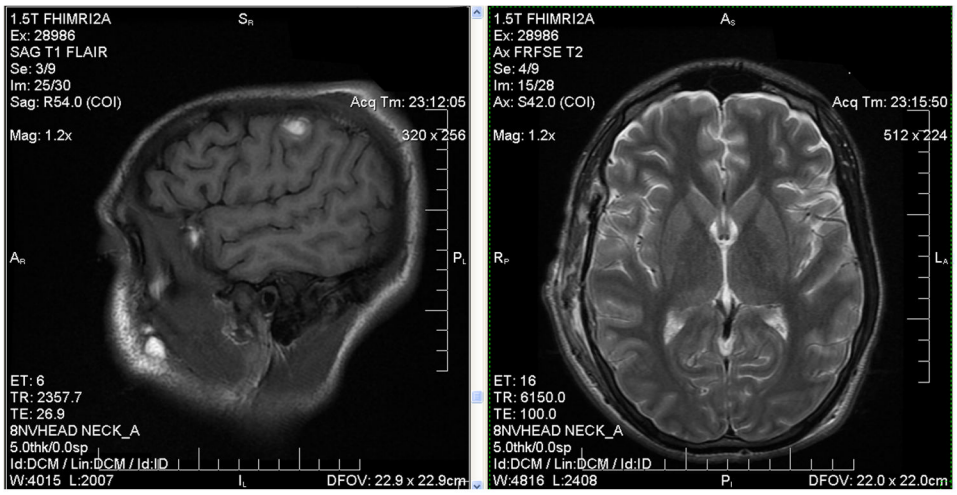

Figure Two.

T2-weighted magnetic resonance imaging on hospital day ten. 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. Additionally, multiple zones of abnormal FLAIR signal consistent with diffuse axonal injury are present on both images.