International Journal of Surgery 21 (2015) 70–74

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Immune enhancing nutrition in traumatic brain injury – A preliminary study

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HIGHLIGHTS

- We evaluated the effect of immune enhancing nutrition in patients with traumatic brain injury.
- IEN showed improvement in bacteremia rates compared to their standard feeding control.
- IEN formulas revealed a significant increase in prealbumin levels at week 2 and 3.
- Pneumonia and UTI rates were no different amongst groups.

ARTICLE INFO

Article history:
Received 2 February 2015
Received in revised form
6 May 2015
Accepted 13 July 2015
Available online 22 July 2015

Keywords:
Immune-enhancing nutrition
Infection rates
Pre-albumin
Traumatic brain injury

ABSTRACT

Traumatic brain injury (TBI) is a major cause of death and disability worldwide. Certain patients appear to benefit when they receive immune enhancing additives, such as glutamine, arginine, and omega-3 fatty acids. We hypothesized that TBI patients given enteral feedings containing these supplements may have improved nutrition measures and infection rates when compared to standard tube feedings.

This is a retrospective review of patients from a Level-One trauma center from July 2009 to July 2013. A total of 240 TBI patients received either an immune enhancing nutrition (IEN) formula (n = 126), or a standard formula (SF) (n = 114) based on the attending surgeon's preference. Data collected included demographic information, infection information and outcome measures.

Patients were similar in terms of age, ISS, head AIS, and initial prealbumin level. Patients receiving IEN were found to have lower rates of blood stream infections (10.3% vs 19.3%, $p < 0.05$), whereas pneumonia and UTI rates were similar between groups. In addition, both groups had similar rates of all-cause mortality and hospital length of stay, however IEN patients spent longer in the ICU and on ventilators. In TBI patients receiving IEN, prealbumin levels were higher at the second, third, and fourth week of admission (week 2 – 22.2 vs 17.4, $p = 0.006$; week 3 – 24.6 vs 20.1, $p = 0.04$; week 4 – 26.3 vs 22.1, $p = 0.19$; week 5 – 25.8 vs 20.3, $p = 0.21$).

This study suggests that patients with traumatic brain injury who receive IEN are more likely to have increased prealbumin levels perhaps reflecting improved nutrition throughout their hospital stay and may show some benefit in rates of infections, particularly in bacteremia.

1. Introduction

Traumatic brain injury (TBI) is a major cause of death and disability with an estimated incidence of 500,000 new cases per year in the United States. Approximately 10% of these patients will be classified as severe and will die at a rate of nearly 33% [1]. Patients with head injury require increased protein intake and undergo hypercatabolism, reflected in significant increases in energy expenditure and nitrogen loss. This change in metabolism results from the inflammatory response to injury, distinct from the catabolic state observed in simple starvation [2,3].

Protein loss varies in these individuals but is markedly elevated, resulting in nitrogen losses between 3 and 16 g per day, potentially several times higher than that observed in a healthy fasting individual (3–5 g of nitrogen/day) [4,5]. Weight loss, negative nitrogen

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http://dx.doi.org/10.1016/j.ijsu.2015.07.008
1743-9191/

balance and immune dysfunction constitute a characteristic response in both surgical and trauma patients. This condition facilitates the onset of acute malnutrition and infectious complications and, consequently, morbidity and mortality is increased [6]. TBI patients may also demonstrate this hypermetabolic state for weeks. Only about a quarter of these patients will be able to spontaneously consume the necessary calories and protein upon discharge [7].

In addition to the digestion process, the gastrointestinal tract is important in the immune response. Translocation of native bacteria or their products from the gut into the circulation, due to increased permeability of the intestinal mucosa, is a well-known feature of the metabolic response in trauma patients due to a relative state of immunosuppression. The persistence of these events may promote a continuous systemic inflammatory response syndrome that, in some cases, may result in multiple organ system dysfunction and eventually death [8].

Recently, it has been suggested that formulas containing elevated levels of nutrients associated with immune modulation might positively influence immune response to stress in adult surgical and trauma patients [9,10]. Promising results from the feeding of enteral diets with specific additives, such as glutamine, arginine, omega-3 fatty acids, probiotics, symbiotics and nucleotides has been reported recently, with various studies suggesting a decrease in septic complications, hospital cost or even mortality [11–13].

Homogenous populations have not been well studied, more specifically TBI patients without other significant organ related trauma. We hypothesize that a formula containing immune-enhancing ingredients would provide protection against infections in a homogenous group of patients with isolated traumatic brain injury.

2. Materials and methods

We conducted a retrospective analysis of patients with isolated traumatic brain injury admitted to a level one urban trauma center. The trauma registry was queried for any patients who received either a standard isonitrogenous formula (SF) or an immune enhancing nutrition formula (IEN) during hospitalization over a four year period from July 1, 2009 through July 1, 2013. For the purposes of our study, we considered Two-cal formula or similar formula our standard formula and Pivot-1.5 our IEN formula (Abbott Nutrition, Columbus OH, USA).

In order to be included in the study, patients must have been severely brain injured upon admission, defined as a head abbreviated-injury severity (AIS) score of at least 3 and/or Glasgow coma scale (GCS) ≤ 8, with computed tomography evidence of head injury. Patients must have been at least 18 years old at the time of injury and must have received enteral nutrition for at least four consecutive days during his or her hospitalization. In order to maintain homogeneity, patients who died within 48 h and those with other major injuries in other body regions (any other AIS greater than 3) were excluded from the analysis.

Table 1
Demographic information.

Characteristics on admission	IEN, Mean (SD)	SF, Mean (SD)	P value
Total n	126	114	
Age, years	43.7 (20.2)	46.7 (18.8)	0.19
Admit GCS	6 (4)	7 (5)	0.21
AIS-head	3.3 (0.8)	3.3 (0.6)	0.36
ISS	17.7 (7.6)	17.9 (7.5)	0.96

IEN: Immune-enhancing nutrition, SF: Standard formula, GCS: Glasgow Coma Scale, AIS: Abbreviated Injury Score, ISS: Injury Severity Score.

These patients' charts were then searched for demographic information, outcome variables and infectious data. Outcome measures included hospital and ICU length of stay (LOS), including days requiring mechanical ventilation and all-cause mortality. Infectious data included blood cultures, urine cultures, respiratory cultures, temperatures, white blood count (WBC) and chest x-ray (CXR) results. Pneumonia was defined as any opacity on CXR in the setting of temperature >38.3 °C and WBC >10,000 cells/μL with evidence of a pathogen on respiratory culture, which is similar to previous definitions [14]. Bacteremia and urinary tract infection were defined as positive culture in the setting of elevated temperature and WBC without evidence of common skin contaminants. Nutritional information was collected, including the type of nutrition received (IEN versus SF), the length of treatment, and nutritional measures (prealbumin, UUN and nitrogen balance). Statistical analysis was performed using SPSS version 12 (IBM Corp., Armonk, NY, USA). Groups were compared using a Chi square test for categorical variables and a Mann–Whitney U test for continuous variables. Data is reported as mean ± standard deviation (SD) and a p value of <0.05 was considered significant.

3. Results

From July 1, 2009 to July 1, 2013, a total of two-hundred forty patients met inclusion criteria and were included for analysis. Of these, 114 received standard formula and 126 received IEN formula. Both groups were similar in terms of age, initial hospital GCS score, injury-severity score (ISS), and AIS scores (Table 1). The two groups had similar duration of tube feeding and initial pre-albumin levels (week 1–13.1 vs 13.3, $p = 0.85$), however, they differed in each subsequent pre-albumin result (week 2–22.2 vs 17.4, $p = 0.006$; week 3–24.6 vs 20.1, $p = 0.04$; week 4–26.3 vs 22.1, $p = 0.19$; week 5–25.8 vs 20.3, $p = 0.21$; Fig. 1).

Both groups also had similar hospital LOS (24 vs 23 days), but differed in number of days spent in the ICU (11 vs 9 days) and on the ventilator (11 vs 7 days), with the IEN group having a longer duration in both cases (Table 2).

In addition IEN patients were less likely to experience bacteremia during their hospitalization (10.3% vs 19.3%, $p < 0.05$) although had similar rates of urinary tract infection (16.7% vs 20.2%, $p = 0.48$), pneumonia (57.9% vs 57.0%, $p = 0.89$) and *Clostridium difficile* infection (4.0% vs 5.3%, $p = 0.63$), see Fig. 2.

The results of positive cultures showed similar bacteria/fungi between the two groups (Tables 3–5). The bacteria/fungi are listed in alphabetical order and the incidence is separated by type of infection and type of enteral nutrition the patient received. The total number of bacteria isolated exceeds the number of total

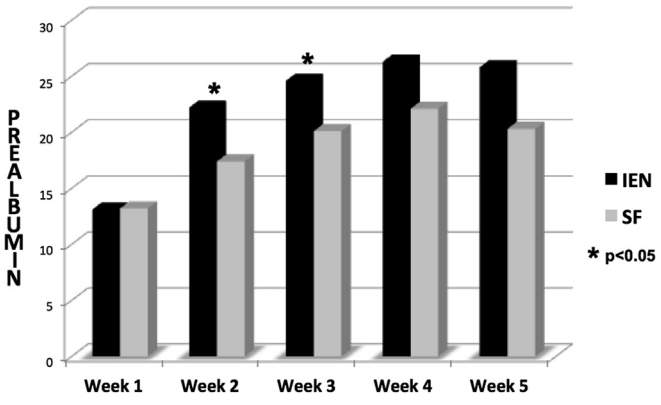

Fig. 1. Prealbumin levels by week.