Nutritional Considerations in Clinical Treatment:
The Perspective of a Neurosurgeon

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INTRODUCTION

Traumatic brain injury (TBI) remains a highly lethal injury with mortality ranging from 20-50 percent (Bulger et al., 2002; Demetriades et al., 2004; Jiang et al., 2002). Approximately 52,000 patients die from TBI each year (Sosin et al., 1995; Thurman et al., 1999) with approximately 85 percent of the deaths occurring within the first two weeks (Roberts et al., 2004). TBI pharmaceutical trials have failed to demonstrate any efficacy in reducing deaths (Narayan et al., 2002). Proper trauma transport systems and maintenance of cerebral perfusion and oxygenation by avoidance of hypoxemia, arterial hypotension and intracranial hypertension reduces mortality and improves outcome (Brain Trauma Foundation, 2000; Chesnut et al., 1993; Härtl et al., 2006; Sampalis et al., 1999; Smith et al., 1990).

Currently, the metabolic status and nutritional needs of TBI patients are less of a priority than maintaining cerebral perfusion. However, TBI results in a hypermetabolic and catabolic state that increases systemic and cerebral energy requirements (Clifton et al., 1986; Deutschman et al., 1986; Hovda et al., 1995; Weekes and Elia, 1996). A recent review from the Cochrane Collaboration states that early feeding may be associated with a trend towards better outcomes after TBI (Perel et al., 2006). The “Guidelines for the Management of Severe Traumatic Brain Injury” recommend that the patient’s feeding requirements should be met by the end of the first week after TBI (Brain Trauma Foundation, 2000). These recommendations were based on two small, randomized trials (Rapp et al., 1983; Taylor et al., 1999). There are no studies on the relationship of mortality to the amount and frequency of feeding in TBI patients. In the few studies done, none controlled for factors known to affect mortality from TBI, such as hypotension, age, pupillary status, and CT scan findings.

The Brain Trauma Foundation (BTF) prospectively collects data on pre- and inhospital TBI management in 20 Level I and 2 Level II trauma centers in New York State as part of a TBI quality improvement program. An analysis was conducted examining the effect of timing and quantity of nutritional support on early mortality. Early onset of nutritional support and amount of nutritional support was hypothesized to be associated with a reduced mortality at two weeks. In addition, a feeding compliance implementation program was undertaken at one of the participating hospitals to increase the net caloric intake of patients.

METHODS

The BTF designed and implemented a quality improvement initiative in New York State to improve severe TBI acute care and outcome. The program is funded by the New York State Department of Health, Division of Healthcare Financing and Acute and Primary Care Reimbursement. This program tracks pre- and inhospital severe TBI data through an online internet

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database called TBI-trac®. The database consists of clinical information from the prehospital environment, emergency department, the first 10 days of ICU care, and two-week mortality. When the study began in 2000, enrollment was limited to five Level I trauma centers and this number increased to a total of 24 trauma centers in 2005, 22 of which were Level I trauma centers and two were Level II centers. This report is based on patients treated at these trauma centers between June 6, 2000 and December 31, 2005.

RESULTS

Data for 1,818 patients were entered in the database from June 6, 2000 through December 31, 2005. Patients were excluded if they had a GCS score greater than or equal to 9 on day 1 (92 patients), or a GCS motor score of 6 on day 1 (16 patients). Patients were also excluded if they had a GCS score of 3 with pupils bilaterally fixed and dilated and were not pharmacologically paralyzed (152 patients). In addition, patients were excluded for a GCS greater than or equal to 4 with pupils bilaterally fixed and dilated or missing pupillary information (93 patients), or with missing outcome assessment (51 patients). Because nutritional requirements for pediatric and adult patients are different, 153 pediatric patients less than 16 years of age were excluded. After these exclusion criteria were applied, a total of 1,261 patients were eligible for analysis.

In order to examine the effect of nutritional support within the first week after admission, only patients who had at least 7 days of inpatient data (were alive for at least 7 days) were analyzed. A total of 464 patients had less than 7 days of data resulting in a final sample of 797 patients. Patients who had less than 7 days of data were older (41.9 vs. 39.0 years, p<0.01) and were more likely to be hypotensive on day 1 (17.6% vs. 13.3% p<0.04) than patients with greater than 7 days of data. A greater proportion of their CT scans were abnormal (84.3%) compared to those with greater than 7 days of follow up (74.4%, p <0.001). Two-week mortality was also significantly higher when compared to those with 7 or more days of records (42.0% vs. 9.9%, p <0.0001).

Administration of feeding began in 61% of patients during days 1 through 3; however, 5% of patients were not fed over the 7-day period and the majority (62%) of patients never reached 25 kcal/kg/day within 7 days. No differences were found in patient characteristics or severity of illness by nutrition level achieved within the first 5 days of treatment. Two-week mortality by nutrition status was significantly higher among patients never fed within 5 (p=0.0008) or 7 (p<0.0001) days. Mortality significantly decreased with increasing nutritional level such that the rate was 6.3% and 7.6% among patients fed more than 25 kcal/kg/day within 5 and 7 days, respectively. Older age and having a high ICP were also significantly associated with two-week mortality while CT scan status was marginally related. The lack of correlation between hypotension and pupillary status and mortality may be explained by the specific exclusion criteria in this study; patients with bilaterally fixed and dilated pupils and GCS scores of 3 were excluded, as were patients who were not alive by day 7.

Nutrition level continued to predict two-week mortality after controlling for age, hypotension, pupillary status, initial GCS, and CT scan status. Patients not fed within 5 days had 2.1 times the risk of two-week mortality, while those not fed within 7 days had 4.1 times the risk of two-week mortality. The amount of nutritional support given within 5 and 7 days also contributed significantly to mortality risk. Every 10 kcal/kg decrease in nutritional support administered within 5 and 7 days resulted in 30%-40% increased risk of mortality (Figure 1).
Further analysis of the relationship between ICP monitoring and early nutrition reveals that nutrition had a significant impact in patients with elevated ICP. In the first 5 days, patients with high ICP and without nutritional support, had a significantly increased mortality when compared to patients with intracranial hypertension who were fed (25.7% vs. 12.9%, respectively, p=0.04). In patients who did not undergo ICP monitoring the lack of early nutritional support had an even more pronounced impact on mortality (25.8% vs. 6.3% mortality, p=0.0004).

**DISCUSSION**

**Current findings**

The present study adds several significant findings to the existing literature. It is the largest database that has used prospectively collected data to address the relationship between nutrition and early mortality after TBI. The main findings can be summarized as follows: First, any nutrition within the first 5 days after TBI is associated with reduced mortality. Second, there is a significant relationship between the maximum level of nutrition reached and mortality; every 10 kcal/kg decrease in caloric intake is associated with a 30-40% increase in mortality. Third, early nutrition within 5 days after TBI emerges as an independent factor affecting mortality even after controlling for known predictors of mortality such as arterial hypotension, age, CT diagnosis, GCS and pupillary status. Patients who were not fed within 5 or 7 days after TBI had a 2- and 4-
fold increased likelihood of mortality, respectively. In addition, patients with elevated ICPs or patients who did not undergo ICP monitoring had a significantly increased mortality if they were not fed within 5 days after trauma when compared to patients who received nutrition. These findings demonstrate that feeding is as significant an intervention as avoidance of early arterial hypotension and hypoxia in reducing mortality from severe TBI.

**How does feeding affect mortality?**

Generally, nutritional support has emerged as a significant factor in improving the outcome of critically ill patients. Early initiation of enteral nutrition is associated with a lower incidence of infections, reduced length of hospital stay and possibly improved outcome in critically ill patients in surgical and medical ICUs (Marik and Zaloga, 2001). However, the mechanism by which nutrition affects outcome is unclear. One possibility is that it may provide important nutrients during a critical time period when demand exceeds available resources.

Studies have shown a rise in energy expenditure after TBI, even in paralyzed patients (Clifton et al., 1986). This hypermetabolic state after TBI may be due to systemic factors such as infection and a post-traumatic stress response, but there appears to be a cerebral component as well. There is an increase in cerebral metabolic rate for glucose in TBI possibly as a result of mitochondrial dysfunction (Merenda and Bullock, 2006). Studies in humans indicate that this increase in glucose utilization may last up to 5-7 days after TBI (Bergsneider et al., 1997) (Hovda et al., 1995). The significance of this cerebral hypermetabolic state is illustrated by the therapeutic effect of interventions that suppress cerebral metabolism such as barbiturate coma, hypothermia and interventions that improve blood flow and supply of nutrients such as cerebral perfusion pressure management. One of the beneficial effects of early aggressive nutritional support may be the steady supply of glucose when the brain depends on increased glucose metabolism to maintain metabolic energy balance.

Another effect of early nutrition may be its attenuation of the post-traumatic stress response and improvement of early immunological function (Bastian et al., 1998; Rovlias and Kotsou, 2000). This could result in an indirect effect on outcome mediated by a lower infection rate. A meta-analysis that compared early (within 36h) to delayed initiation of enteral nutrition in critically ill patients (not only TBI) demonstrated a 55% reduction in infection rate in patients who received early nutritional support (Marik and Zaloga, 2001). As infection rate was not collected as part of the TBI-trac® database, this relationship could not be examined. It is unlikely, however, that infection rate would have such a significant impact on two-week mortality.

Nutrition could also have an impact on the post-traumatic stress response which is associated with adverse outcome from TBI (Rovlias and Kotsou, 2000). The post-traumatic stress response is characterized by increased blood levels of glucose, lactate, catecholamines and cortisol. In the blunt trauma population, however, early feeding within 24 hours after injury had no effect on the metabolic stress response (Eyer et al., 1993).

Arterial hypotension doubles mortality from TBI (Chesnut et al., 1993). The relationship between nutritional support and hypotension was examined based on the hypothesis that the fluid volume given with nutrition improves the patient's hemodynamic status and prevents arterial hypotension. There was, however, no relationship between arterial hypotension and nutritional support within the first 5 days after TBI.

Another finding in this study was that early nutritional support may have a protective effect in patients with intracranial hypertension. Results indicate that patients with high ICPs who are fed have a significantly lower mortality when compared to patients who do not receive nutri-
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Nutritional support (12.9% vs. 25.7%, respectively). Nutritional support may protect the brain by providing large amounts of energy substrates, during a critical time period when hyperglycolysis and hyperemia are present, in an effort to maintain energy balance and cerebral ionic hemostasis (Bergsneider et al., 1997).

**Why were patients not fed?**

Our analysis showed that the lack of nutritional support was not related to the severity of the injury or other factors associated with outcome from TBI. Beyond this, it is difficult to determine what affected the decision not to feed patients early on. Possibilities include that patients did not tolerate enteral nutrition early after TBI and that early nutritional support may not have been given a priority by the treating physicians. Other factors that interfere with feeding and that were not registered in this database include patient transport within the hospital and enteral administration of phenytoin.

**Program in Participating Trauma Center to improve compliance**

Achieving adequate nutritional intake in this patient population is difficult and nutritional therapy in many ICUs is suboptimal (Cahill et al., 2010). Despite best intentions many Trauma Centers fail to achieve adequate caloric intake. One Level 1 Trauma Center was consistently well below the goal of 25 Kcal/kg/day, and a Quality Improvement (QI) initiative was undertaken. Their process and results are described below.

**Methods**

Nurse registars collect Kcal/kg per patient per day into an online data base (TBI-trac®) as part of a quality initiative through the Brain Trauma Foundation. Quarterly data review demonstrated that the mean Kcal/Kg/day was well below goal. The QI team reviewed patient records, developed protocols, obtained Attending physician consensus, monitored compliance and revised the nutrition protocol as needed. The Nutrition Protocol was revised several times as results were analyzed. The current protocol calls for enteral feeding over 20 hours of the day, with a 4 hour time period built in for “catch up.”

**Results**

The percent of patients receiving nutrition by Day 2 increased from 29% in 2007 to 50% in 2010. Average Kcal/kg on hospital day 5 increased from a mean of 14.4 in 2007 to 28.8 in 2010 (p=0.006, Figure 2). The percent of patients who received at least 25 Kcal/kg on Day 5 increased from 19.4% in 2007 to 75% in 2010 (p=0.018). The percentage of patients who achieved 25 Kcal/kg/day on any day within the first 5 days post injury increased from 25.8% in 2007 to 91.7% in 2010 (p=0.001).

**Findings**

A successful feeding protocol must address the unique needs of the TBI patient. Our ICU found success by building into the protocol time each day to make up or catch up if feeds were held for any reason. With this protocol we have been successful in achieving adequate nutritional intake in the severe TBI patient.
CONCLUSIONS

In this severe TBI prospective database, nutritional support initiated within 5 days after trauma is associated with a significant reduction in two-week mortality. Furthermore, the amount of nutrition is related to mortality. These results held after controlling for other parameters known to affect mortality such as arterial hypotension, age, pupillary status, initial GCS and CT scan findings. Thus, nutrition may be an independent predictor of mortality. A prospective, randomized trial would be necessary to confirm this finding to generate class I evidence. It is doubtful, however, that such a trial comparing nutrition vs. no nutrition will be done given the ethical implications. Together with arterial hypotension, hypoxia and intracranial hypertension early nutritional support is one of the few therapeutic interventions that can directly affect outcome.


**Figure 2** Average kcal/kg received by patients in a Level I trauma center on hospital day 5 significantly increases from 2007 to 2010.

**SOURCE:** Ghajar presentation (June 24, 2010).
REFERENCES


