The Perspective of a R.D. Working with Civilian Traumatic Brain Injury

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INTRODUCTION

Traumatic brain injury (TBI) causes a very serious assault to the body, not only due to the primary or secondary injuries, but also by the effects it has on all of the body’s systems. Brain injury results in a significant increase in metabolism and catabolism that, if left unchecked, can lead to malnutrition. It has been shown that adequate nutrition support can attenuate these metabolic changes that result in muscle loss and therefore positively affect outcomes. This paper will review the current nutrition support standards of care in the moderate to severely brain-injured population, potential routes of nutrient administration, benefit of specific nutrients, and drug-nutrient interactions of concern.

RATIONALE FOR NUTRITION SUPPORT IN TBI

In the initial acute phase following a traumatic brain injury, the patient is in a hypermetabolic and catabolic state. The literature indicates energy expenditure ranges between 100-200% of resting metabolic rate, and this increased energy expenditure can last anywhere from one week to one year following the injury (Deutschman et al., 1986; Loan, 1999; Moore et al., 1989). During the initial acute stage of injury, Glycogen stores are quickly depleted. This results in a need to use muscle proteins as a source of required glucose energy, leading to significant lean body mass catabolism (Berg et al., 2006). Non-stressed individuals lose approximately 200-300 grams of muscle per day, whereas TBI patients lose up to 1000 grams of lean body mass per day (Loan, 1999). The major cause of this highly catabolic state is a post-injury increase in chemical messengers. These messengers include cortisol, glucagon, catecholamines, and cytokines, all of which contribute to breakdown of muscle rather than fat for energy (Table 1) (Darbar, 2001; Loan, 1999; Moore et al., 1989; Young et al., 1988). In addition to an increase in catabolic chemical messengers post-injury, there is a decrease in anabolic hormones, such as human growth hormone (Demling, 2009). The increase in metabolic rate and resulting muscle catabolism can lead to malnutrition if not attenuated by provision of adequate nutrition support.

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Table 1 Chemical messengers effects on inflammatory response

<table>
<thead>
<tr>
<th>Messenger</th>
<th>Function</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>Cortisol</td>
<td>gluconeogenesis</td>
<td>↑rate of muscle catabolism</td>
</tr>
<tr>
<td></td>
<td>proteolysis</td>
<td></td>
</tr>
<tr>
<td>Glucagon</td>
<td>gluconeogenesis</td>
<td>↑rate of muscle catabolism</td>
</tr>
<tr>
<td>Catecholamines (epinephrine, norepinephrine)</td>
<td>Insulin resistance</td>
<td>↑rate of muscle catabolism</td>
</tr>
<tr>
<td>Cytokines (IL-1, IL-6, TNF)</td>
<td>Activates immune response</td>
<td>↑rate of muscle catabolism</td>
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Inadequate nutrition support post-injury can lead to significant malnutrition. This can include significant weight loss resulting in poor outcomes including increased mortality, increased length of hospitalization and rehabilitation. If the TBI patient is fed inadequately for one week, this may lead to a 10% loss of lean body mass. If nutrition needs are not met for two weeks, this may lead to a 30% loss of LBM, and increased mortality (Darbar, 2001). Malnourished TBI patients (BMI <15) entering rehabilitation have a length of stay approximately 28 days longer than those who are not malnourished (Dénes, 2004).

STANDARDS OF CARE

The major principles driving the nutrition care of TBI patients include early nutrition support, provision of adequate calories (Kcals) and protein, preference for enteral nutrition, use of nutrition protocols, and ongoing assessment of efficacy of nutrition support.

Evidence for early nutrition support (within the first 24-72 hours post-injury) is limited in the TBI population; however, there is growing evidence that this practice is beneficial. In one study, early nutrition support (within 5 days after trauma) was shown to be one of the few therapies that could positively affect two-week mortality in TBI patients (Hartl et al., 2008). Benefits of early nutrition support in other critically ill populations include lower risk of infection, decreased activation and release of inflammatory cytokines, decreased hospital and ICU length of stay, and attenuation of catabolism of skeletal muscle (McClave et al., 2009).

Determining calorie requirements is difficult in this population as many factors influence the rate of metabolism. Calorie needs may be decreased with barbiturate coma, propofol infusions, and other sedatives (Frankenfield, 2006; McCall et al., 2003; Moore et al., 1989; Rajpal, 2009). Infection, fever, posturing, storming, and presence of other injuries may increase caloric needs (Clifton et al., 1986; Frankenfield, 2006; Moore et al., 1989; Rajpal, 2009). Typically the energy needs are calculated by prediction formulas which predict basal energy expenditure (BEE), such as the Harris-Benedict formula, which also includes an injury factor (Cook et al., 2008). The Brain Trauma Foundation (BTF) recommends a calorie provision of 140% of BEE (Bratton et al., 2007). It has been shown that prediction formulas often under or over-predict calories, and if able, it is desirable to measure energy expenditure via indirect calorimetry. This
measurement is considered the “gold standard” in determining calorie needs (Felipez and Sentongo, 2009; McClave et al., 2009; Pepe and Barba, 1999).

Protein needs are elevated in the TBI population, and the BTF Guidelines suggest needs that range from 1.5 – 2.0 g per kg (Bratton et al., 2007). Several studies have shown variable beneficial results in delivering greater than 2 grams per kilogram. One study showed that when given 2.2 g of protein per kg, TBI patients corrected their negative nitrogen balance at a faster rate than those who were given less protein, however, they had increased urinary nitrogen excretion (Twyman et al., 1985).

Enteral delivered nutrition support is the preferred route of nutrient delivery if the patient’s gastrointestinal (GI) tract is functioning and accessible. Benefits of enteral nutrition include the following (Artinian et al., 2006; McClave et al., 2009; Taylor et al., 1999):

- gut barrier maintenance,
- modulation of stress and immune response,
- lower risk of infection when compared to parenteral nutrition administration,
- reduction in hospital length of stay,
- lower cost of nutrition support,
- quicker return of cognitive function in neurosurgery patients.

While enteral nutrition support is less risky than parenteral nutrition support, there are still some risks associated with it. If enteral feeds are started prior to adequate resuscitation, or if GI perfusion is poor, there is an increased risk of GI tract ischemia. High infusion rates of pressors and/or sedatives, anesthetics, as well as abdominal injuries influence blood perfusion to the GI tract. Additionally, enteral feeding intolerance, such as abdominal pain, nausea, and vomiting have been described in critically ill patients, negatively affecting the rate at which patients achieve their nutritional goals.

Parenteral nutrition (PN) is another potential route of nutrition support delivery; however, its use can result in more complications than enteral nutrition, and therefore, is not the preferred option. Risks of PN include increased risk of infection, increased cost, and increased risk of mortality (McClave et al., 2009). In the TBI population, however, it has been shown that patients on PN have fewer interruptions in feeding and their nutrition goals are reached more quickly (Bratton et al., 2007; Young et al., 1987). One study showed that for those with head trauma, EN and PN were equally effective in meeting nutrition goals with similar infection rates and similar cost (Borzotta et al., 1994).

An assessment by a registered dietitian (RD) early in the TBI patient’s admission is essential in determining nutrition goals and the nutrition plan of the TBI patient. It has been shown that implementing the RD’s recommendations is correlated with decreased length of stay, higher serum albumin, and increased weight gains (Braga et al., 2006). In addition to the RD assessment, use of nutrition protocols is useful in enhancing nutrition delivery. In one study, use of the nutrition protocol increased the percentage of calories provided, and was identified as the factor having the greatest impact on successful delivery of enteral nutrition in the first week of neurocritical illness (Zarbock et al., 2008).

Assessing efficacy of nutrition support is a difficult task in the ICU setting due to the confounding effects of critical illness and treatment on typical nutrition assessment parameters. Patient weights are strongly influenced by clinically induced fluid gains and losses, and are not immediately useful, though may be more helpful in the later stages of healing. Nutrition labora-
tory tests are highly inaccurate in the setting of critical illness as the acute-phase response results in re-direction of the synthesis of visceral proteins towards wound healing and the immune response (McClave et al., 2009; Moore et al., 1989; Young et al., 1988; Young et al., 1985). It is recommended that if albumin or transthyretin (prealbumin) are being used to assess nutrition status, always check C-reactive protein (CRP) as well, to determine the patient’s level of inflammatory response. When CRP is elevated, this is an indication that albumin and prealbumin will be decreased, and their use as a tool for assessment of nutrition status will not be useful. If using visceral proteins to monitor nutrition status, trends in laboratory values are more helpful compared to isolated measurements of these laboratory tests. Other indicators of adequacy of nutrition include wound healing, ability to wean from mechanical ventilation, as well as ability to participate in rehabilitative therapies.

Standards of care regarding nutrition therapy in the TBI patient are based on guidelines from various organizations including The American Dietetic Association, American Society of Parenteral and Enteral Nutrition (ASPEN), Society of Critical Care Medicine (SCCM), and the Brain Trauma Foundation (BTF). The most comprehensive nutrition guidelines come from the combined efforts of ASPEN and SCCM, however, these guidelines are not specific to the TBI population. The BTF has published nutrition guidelines as well, though, due to the lack of nutrition studies in the TBI population, these guidelines are not specific. Table 3 is a comparison of the nutrition guidelines from ASPEN/SCCM and the brain trauma foundation for moderate to severe brain injury, and may be helpful in identifying areas where more research is needed in the TBI patient population.

**Table 2** Comparison of ASPEN/SCCM guidelines and BTF guidelines

<table>
<thead>
<tr>
<th>Guidelines pertaining to…</th>
<th>ASPEN/SCCM</th>
<th>BTF</th>
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<tbody>
<tr>
<td>Calories</td>
<td>No specific guidelines in TBI; Met cart gold standard</td>
<td>100-140% replacement of resting metabolism</td>
</tr>
<tr>
<td>Protein</td>
<td>1.2 – 2.0 g/kg in critical illness</td>
<td>15-20% of kcals</td>
</tr>
<tr>
<td>Timing of initiating feed</td>
<td>24-48 hours following admission</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Dosing of EN</td>
<td>50-65% of goal by day 7</td>
<td>100% of goal by day 7</td>
</tr>
<tr>
<td>EN vs. PN</td>
<td>EN preferred, PN only when necessary</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Nutrition protocols</td>
<td>Should be implemented</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>

It should be noted that currently there are no published nutrition guidelines for those with mild TBI and/or concussions.

**SPECIFIC DIETS OR NUTRIENTS OF CONCERN**

Specific diets or nutrients to be avoided in the TBI population are unknown, though there is some question regarding the safety of the use of the amino acid glutamine during the acute phases of TBI. During critical illness, glutamine becomes conditionally essential, and administration of exogenous glutamine in this patient population has shown some promise (McClave et
Benefits include glutamine’s anabolic/anticatabolic properties, use as an antioxidant, and its use as a fuel for dividing cells. However, in the TBI population, it has been hypothesized that increased glutamine in the diet leads to increased glutamate in the interstitial fluid. Increased glutamate has been linked to high intracranial pressures and increased cerebral swelling (Cook et al., 2008; Enriquez and Bullock, 2004). Several studies have shown that feeding patients additional glutamine does increase glutamate levels in the interstitial fluid, however, more studies are needed to determine the benefit of this practice in the brain-injured population (Berg et al., 2006).

**IMPORTANCE OF NUTRITIONAL FORMULATIONS**

The use of immune-enhancing formulas in the critically ill population is of growing interest, and studies have shown better outcomes with the use of these formulas. Immune-modulating formulas may include higher ratio of omega-3 vs. omega-6 fatty acids, and/or increased provision of antioxidants including vitamins E and C, zinc, and selenium. ASPEN and SCCM recommend the use of immune-enhancing formulas in surgical and medical ICU patients, but suggest using standard formulas in populations in which there is little evidence that use of enhanced formulas improve outcomes (McClave et al., 2009). In the TBI population, evidence is lacking that these formulas provide additional benefit compared to those receiving standard formulas (Martindale et al., 2009). One study looked at early nutrition along with using an immune-enhancing formula in head injury patients, and no additional benefit was found (Minard et al., 2000). Another small study (n=13) looked at feeding an immune-enhancing enteral formula to trauma patients, and this did not affect outcomes or levels of pro-inflammatory cytokines (Jeevanandam et al., 1999). Due to the positive results seen in other populations, larger, randomized control trials are warranted in the TBI population.

**DRUG AND NUTRIENT INTERACTIONS**

When devising a nutrition plan, drug-nutrient interactions should be taken into account. It is possible that calorie needs will be lower with certain medications, such as propofol, which provides 1.1 kcals of fat with each milliliter infused, in addition to decreasing metabolic rate. Other medications may cause increased need for nutrients, such as vitamin D and folic acid for those on seizure prophylaxis (Félipez and Sentongo, 2009). The effect that any drug has on the GI tract should also be considered. For instance, vasopressors decrease gut perfusion, therefore, one should be cautious about aggressive nutrition regimens. Table 3 shows a list of common drug-nutrient interactions in the TBI population. This is not a comprehensive list of all interactions; however, these are most common in the neurocritical care unit.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Nutrient interaction</th>
</tr>
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<tbody>
<tr>
<td>Barbiturates</td>
<td>Decreased metabolic rate</td>
</tr>
<tr>
<td>Propofol</td>
<td>$\beta$ fat kcal (Omega-6; pro-inflammatory)</td>
</tr>
<tr>
<td></td>
<td>$\beta$ Increased urinary excretion of zinc, iron</td>
</tr>
<tr>
<td>Seizure prophylaxis</td>
<td>Increased need for vitamin D, folic acid</td>
</tr>
<tr>
<td>Dilantin</td>
<td>Carbohydrates interfere with absorption</td>
</tr>
<tr>
<td>Vasopressors</td>
<td>Decreased gut perfusion</td>
</tr>
</tbody>
</table>
CONCLUSION

Traumatic brain injury can cause a very dramatic increase in metabolism and catabolism resulting in extensive loss of lean body mass if adequate nutrition support is not provided. It has been shown that adequate and timely nutrition therapy can lead to positive outcomes for those with brain injury. Standards of care for nutrition support of TBI patients include early enteral nutrition if possible, measurement using indirect calorimetry rather than prediction of calories to be provided, and the use of nutrition protocols to deliver support. Because of the need for nutrition research in this population, the benefit of specific nutrients is unknown.
REFERENCES


