Effect of total parenteral nutrition upon intracranial pressure in severe head injury

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Animal investigations suggest that administration of hyperosmolar total parenteral nutrition (TPN) solutions may potentiate cerebral edema following head injury. Intravenous nutrition (TPN) is often required after head injury due to intolerance to enteral feeding (EN). This study evaluates the effect of TPN on intracranial pressure (ICP) measurements in severely brain-injured patients. Ninety-six severely brain-injured patients were randomly assigned to receive TPN or EN and were studied from hospital admission until 18 days postinjury. The TPN was started within 48 hours postinjury and the EN was started when tolerated. Peak daily ICP was not significantly different on admission and over time (overall mean ± standard error of the mean 32.01 ± 1.62 for TPN versus 32.5 ± 1.25 for EN). Intracranial pressure was greater than 20 mm Hg in 75% of TPN patients and 73% of EN patients. Conventional therapy failed to control elevated ICP in 36% of TPN patients and 38% of EN patients. Of these patients, subsequent barbiturate therapy failed to control ICP in 56% of TPN patients and 64% of EN patients. Serum osmolality was not significantly different between groups at admission or over the course of the study. The TPN group tended to have higher mean serum glucose levels for the first 13 days postinjury, while the EN group had a higher mean serum glucose content thereafter, but these differences were not statistically significant. This study shows that TPN can be given safely to the severely brain-injured patient without causing serum hyperosmolality or affecting ICP levels or ICP therapy.

KEY WORDS: head injury · intracranial pressure · parenteral nutrition

Clinical Material and Methods

Clinical Therapy

Ninety-six head-injured patients with an initial 24-hour peak Glasgow Coma Scale (GCS) score between 3 and 10 were randomly assigned to receive enteral or parenteral nutrition. There was a 1-year interval between collection of the first group (38 cases) and the second group (58 cases). In all patients the major injury was to the brain. Patients who were brain-dead on admission were not entered into the study. All patients were studied from hospital admission up to 18 days postinjury. Craniotomy was performed to debride the wounds, elevate skull fractures, or remove clots within the first 72 hours after injury. Patients requiring prolonged intubation had a tracheostomy performed by the 10th day of hospitalization, if required. A urinary catheter was routinely inserted. Mechanical ventilation.
was performed in every case. Twenty-six patients were treated with steroids; phenytoin was given only if seizures occurred. If the initial GCS score was less than 8, ICP was routinely monitored continuously until peak pressure was in the normal range (less than 20 mm Hg) or brain-death was documented. Patients who became brain-dead were included in the uncontrollable ICP group.

Intracranial pressure of over 20 mm Hg was treated by conventional means including intraventricular cerebrospinal fluid (CSF) drainage, hyperventilation, musculoskeletal blocking agents, or mannitol infusion. When conventional measures failed to maintain ICP below 25 mm Hg, barbiturate therapy was instituted. In two patients, decompressive lobectomy was performed when barbiturate therapy failed to control ICP.

**Nutritional Support**

The TPN group received full-rate nutritional support within 48 hours postinjury. Parenteral feedings consisted of sterile amino acid/dextrose solutions, multivitamins, trace elements, and intravenous lipid emulsions. Substrate administration was calculated daily, and patients were given no more than 7 gm glucose, 2.5 gm lipid, and 2.5 gm protein per kilogram body weight per day. Insulin was given if required to keep serum glucose levels less than 200 mg%. Patients in the parenteral group were weaned to enteral support as soon as bowel sounds were present and gastric residual volumes were less than 100 cc/2 hrs. Patients received TPN for a mean of 13 days postinjury. Polyvinyl chloride Salem sumps were inserted nasogastrically and a low wall suction was initiated. When low wall suction was no longer required, small-bore silicone feeding tubes were inserted.

Feedings were started for the enteral nutrition (EN) group when bowel function was present and after placement of the feeding tube in the stomach was proven. Patients were given either Traumacal, Ensure Plus, or Vital. Every attempt was made to feed patients into their small bowel in order to enhance tolerance to nutritional support. Eleven patients in the EN group were administered TPN on Day 7 postinjury. No patient had an enterostomy performed. A vigorous effort was made for patients in both groups to receive adequate calorie intake for weight maintenance and nitrogen balance. Calorie and protein intake was carefully recorded daily.

**Laboratory Studies**

Serum glucose, blood urea nitrogen (BUN), potassium, carbon dioxide, sodium, creatinine, and chloride levels were obtained every 6 hours while the patients were in the intensive care unit, and once each day when they were on the hospital ward. Peak daily levels were used in the analysis. Serum osmolality was calculated by the formula: 2(sodium) + BUN/2.8 + glucose/10.1

**Statistical Analysis**

Comparisons of continuous demographic data were performed between nutrition groups using t-tests, while categorical data were analyzed by chi-square tests. Continuous response data collected over time were analyzed by a repeated-measures analysis of variance (ANOVA). The model for this ANOVA can be expressed by the following equation: Y = M + G + P(G) + D + D(G) + E, where M = overall mean, G = nutrition group, P(G) = patient without the nutrition group, D = day, D(G) = day:nutrition group interaction, and E = random error. The test for a day:nutrition group interaction is particularly important as it tests whether the change in response over time is the same for both nutrition groups. Patients were grouped and analyzed over time according to their admission randomization group.

**Results**

Seventy-seven (80%) of all patients had ICP monitors placed (82% of all TPN patients and 78% of all EN patients). The mean age, sex, height, weight, and peak admission 24-hour GCS score were not significantly different between the TPN and EN groups (Table 1). Craniotomy was performed in 46% of TPN patients and 41% of EN patients; 29% of patients in the TPN group and 26% of patients in the EN group were given corticosteroids. The two groups had similar types of injuries (Table 2). Gunshot wounds to the head occurred in 15% of the TPN group and 19% of the EN group; 27% of the TPN group had intracranial hematomas versus 24% of the EN group; 12% of the TPN group had depressed skull fractures versus 10% of the
EN group; and diffuse brain injury occurred in 46% of the TPN group and 48% of the EN group. These characteristics were not significantly different between the two groups.

Peak daily ICP was not significantly different between groups on admission and over time (overall mean ± standard error of the mean 32.1 ± 1.62 for the TPN group versus 32.5 ± 1.25 for the EN group) (Fig. 1). All patients had ICP greater than 10 mm Hg (Table 3). The TPN group had ICP monitoring performed for a mean of 6.3 days versus 6.8 days for the EN group, and ICP was greater than 20 mm Hg in 75% of TPN patients and 73% of EN patients. Conventional therapy failed to control elevated ICP in 36% of TPN patients and in 38% of EN patients. Of these patients, subsequent barbiturate therapy failed to control ICP in 56% of TPN patients and 64% of EN patients. One patient in each group had a craniotomy and decompressive lobectomy performed to control ICP. This latter therapy controlled ICP in the TPN patients but not in the EN patients.

For the first 12 days the TPN group received more calories and protein than the EN group (p = 0.0001) (Fig. 2). After this period the two groups received almost identical caloric support. Total protein intake was significantly different (overall mean 85.3 ± 5.85 gm/day for the TPN group versus 51.7 ± 5.44 gm/day for the EN group, p = 0.002).

Serum osmolality was not significantly different between groups at admission or over the course of the study (Fig. 3). Although not statistically significant, the TPN group had a higher daily mean serum osmolality for the first 5 days postinjury. There was a significant day:nutrition group interaction seen in relation to serum glucose levels (p < 0.0001) (Fig. 4). The TPN group tended to have higher mean serum glucose levels for the first 13 days postinjury, while the EN group had higher mean serum glucose levels thereafter.

**Discussion**

Two mechanisms have been proposed to explain the potential detrimental effect of TPN on injured brain and vasogenic edema. Waters, *et al.*,21 suggested that the serum hyperosmolality associated with infusion of TPN sets into motion a cascade of events increasing experimental vasogenic cerebral edema. Serum hyperosmolality in areas of intact blood-brain barrier creates an osmotic gradient between blood and brain causing movement of water from tissue to blood. The resulting reduction in tissue pressure and hydraulic resistance in normal brain creates a gradient that increases bulk flow of water to normal brain from vasogenic edema areas. This series of events results in an increased area of brain edema. In that study ICP was not measured, but the authors raised the question of the effect of TPN on ICP in the presence of vasogenic edema.

Waters, *et al.*,21 showed that administration of 40.5% mannitol and TPN (35% dextrose and 3.5% amino acids) significantly increased serum osmolality and volume of Evans blue-stained white matter (vasogenic edema) when infused immediately after cold brain injury in cats. An important finding for clinical practice was that TPN (25% dextrose and 3.5% amino acids),

### TABLE 3

**Intracranial pressure (ICP) measurement and treatment**

<table>
<thead>
<tr>
<th>Factor</th>
<th>TPN Group</th>
<th>EN Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP &gt; 10 mm Hg</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>ICP &gt; 20 mm Hg</td>
<td>75%</td>
<td>73%</td>
</tr>
<tr>
<td>conventional therapy failure</td>
<td>36%</td>
<td>38%</td>
</tr>
<tr>
<td>barbiturate failure</td>
<td>56%</td>
<td>64%</td>
</tr>
</tbody>
</table>

*TPN = total parenteral nutrition; EN = enteral nutrition. Differences were not statistically significant.*
Parenteral nutrition and ICP in head injury

FIG. 3. Daily peak calculated serum osmolality in patients randomly assigned to receive total parenteral nutrition (TPN) or enteral nutrition (ENT). Values are means ± standard error of the means.

Fig. 4. Daily peak serum glucose levels in patients randomly assigned to receive total parenteral nutrition (TPN) or enteral nutrition (ENT). Values are means ± standard error of the means.

normal saline, and 5% dextrose did not significantly increase serum osmolality or the volume of edema. Attention should be drawn to their finding that specific-gravity measurements were not significantly different between control and individual TPN groups, despite the spread of Evans blue dye being significantly different. In addition, it is important to note that the cats they evaluated were given TPN immediately postinjury whereas patients are not given TPN immediately after injury.

In a report of three cases, Hipp, et al., showed that a caloric load (glucose) caused an immediate elevation of ICP in two patients fed with intravenous hyperosmolar nutrition formulas and in one patient fed with isotonic EN (unpublished data). They noted that CSF pyruvate and lactate levels were increased concomitantly with feeding.

There is extensive evidence that acute hyperglycemia can greatly enhance experimental cerebral ischemic damage. Clinical studies also suggest that hyperglycemia exacerbates such damage. Some studies have indicated that the osmotic load produced by acute hyperglycemia does not appear to account for increased damage in experimental ischemia. Pulsinelli, et al., demonstrated that injections of mannitol that mimicked the plasma osmolality changes produced by glucose did not increase neuronal damage. In the same model of cerebral ischemia in the rat, glucose-induced mortality was reversed by administering the glucose metabolic inhibitor, 2-deoxylucose, despite the fact that 2-deoxyglucose increased hyperglycemia further. Therefore, it seems likely that glucose does not enhance cerebral ischemic damage via its osmotic effects but rather via its metabolic effects. In the presence of ischemia, the brain begins to produce energy by anaerobic metabolism of glucose which results in increased tissue lactate levels in the brain. A number of studies have focused on the association between high lactate concentrations in the brain and the disruption of cerebral integrity with cerebral ischemia. There appears to be a threshold level above which lactic acid can damage cerebral tissue. This threshold likely is between 16 and 20 mmol/kg. How lactic acid harms tissue is not known. Intracellular pH changes or osmotic changes probably exacerbate a wide variety of pathological biochemical sequelae. Ischemia and traumatic lesions are not identical, but similar mechanisms may be responsible for lactic acid damage in both conditions.

In our study, the head-injured patients who were randomly assigned to receive TPN did not develop significant serum hyperosmolality in comparison to an enterally fed group, nor were there significant differences in ICP levels or required ICP therapy. Likewise, in the study by Waters, et al., solutions not significantly increasing serum osmolality did not increase vasogenic edema. Additionally, Reulen, et al., showed resolution of vasogenic edema by transventricular clearance into the CSF. Our patients underwent drainage of ventricular CSF as a measure to decrease ICP when the latter was above 20 mm Hg. What role drainage of CSF via a ventricular catheter may have had in decreasing cerebral edema in our patients is unknown.

We carefully monitored serum glucose levels and administered insulin to try to prevent hyperglycemia beyond 200 mg%. The highest glucose concentration infused was 25% glucose, and more commonly 2.5% glucose was administered with concentrated lipid emulsions, which provided almost 50% of the substrate intake. Intravenous lipid emulsions are isotonic, and their use combined with a lower concentration of dextrose will lower parenteral osmolality. We suggest use of intravenous lipid emulsions and close monitoring of blood glucose levels to prevent serum hyperosmolality and marked hyperglycemia in severely brain-injured patients.

Several investigations have documented the marked hypermetabolic hypercatabolic state following severe head injury. Early vigorous nutritional support is necessary to replace marked protein loss and to meet
high caloric requirements. Prolonged paralytic ileus and delayed gastric emptying often interfere with the initiation of enteral feedings early after injury. Based upon our previous studies showing a favorable effect of nutrition on outcome in severe head injury, we recommend initiating nutritional support with TPN. The patients should be switched to EN as soon as it can be tolerated. Other investigators recommend initiating enteral nutritional support in the acutely brain-injured patient, but we have not been able to achieve a sufficiently high success rate with this latter route.

Our results show that TPN can be given safely to the severely brain-injured patient without causing serum hyperosmolality or affecting ICP levels or ICP therapy. More investigation is needed to identify the relative role of hyperosmolality and glucose metabolism in the exacerbation of traumatic cerebral edema.

References


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