Parenteral Nutrition

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Grand Rounds
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Objectives

• Quick Basic Nutrition Review
• Parenteral Nutrition vs. No Nutrition
• Enteral vs. Parenteral Nutrition
• Causes of Infections in Patients on Parenteral Nutrition
## Basic Substrates

<table>
<thead>
<tr>
<th></th>
<th>VO₂ (L/g)</th>
<th>VCO₂ (L/g)</th>
<th>RQ</th>
<th>Energy (kcal/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid</td>
<td>2.0</td>
<td>1.4</td>
<td>0.7</td>
<td>9.1</td>
</tr>
<tr>
<td>Protein</td>
<td>0.96</td>
<td>0.78</td>
<td>0.8</td>
<td>4.0</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>0.74</td>
<td>0.74</td>
<td>1.0</td>
<td>3.7</td>
</tr>
</tbody>
</table>

VO₂ = Oxygen required; VCO₂ = Carbon dioxide produced; RQ = Respiratory quotient
Daily Energy Needs

- Harris-Benedict: Basal energy expenditure (BEE) calculates energy needs in kcal/day.
- Men: $66.5 + (13.8 \times \text{wt}) + (5 \times \text{ht}) - (6.8 \times \text{age})$
- Women: $655 + (9.6 \times \text{wt}) + (1.7 \times \text{ht}) - (4.7 \times \text{age})$
- wt = ideal body weight (kg)
- ht = height (cm)
Daily Energy Needs

- Activity factors

- Multiply the BEE to adjust energy requirements based on patients overall status ($\text{BEE} \times \alpha$)

- Fever: $\alpha = 1.1$ for each degree above $37^\circ$

- Mild stress (long bone fracture, mild trauma): $\alpha = 1.25$

- Severe stress (multi-organ trauma): $\alpha = 1.6$

- Burns $>40\%$ TBSA: $\alpha = 2.0$
Protein Requirements

- 1 g protein/kg/day = 0.16 N/kg/day
- Hypercatabolic state
  - Up to 2 g protein/kg/day
  - Burns, major trauma with sepsis
- Goal: positive nitrogen balance
  - Measure urinary urea nitrogen (UUN)
- Nitrogen balance = Nitrogen intake – UUN - 4
Mix and Match

• **NPC = non-protein calories**
  • Carbohydrates: 60-70% of total calories
    • Primary fuel for CNS, RBC, WBC, renal medulla
    • High RQ (1.0 vs 0.7 for lipids)
    • Can lead to metabolic acidosis and need for increased minute ventilation
  • Lipids: 10-25% of total calories
  • Protein: <20% of total calories
Introduction

• Late 1960’s parenteral nutrition (TPN) established as a form of management.

• Small controlled trials suggested TPN as being harmful.

• Enteral nutrition became the preferred route.
Introduction

• Incidence of obese patients in the ICU increased.
• Leading to insulin resistance and hyperglycemia.
• Increasing the risk of infection and sepsis.
Parenteral Nutrition vs No Nutrition
Meta-Analysis

- 26 controlled clinical trials comparing TPN and no nutrition.
- 2,211 patients
- No reduction in mortality or incidence of major complications between groups.
- Malnourished patients only: significant reduction in incidence of complications.

Meta-Analysis

• Early studies included a large number of non-obese patients and the reduction of complications was larger.

• More recent studies included a large number of obese patients and the reduction of complications was smaller.

• Obese patients received TPN and were significantly overfed.

Controlled Study

• 395 VA surgical patients.

• Received either perioperative TPN or no nutritional support.

• Patients receiving TPN had more infections.

• Subgroup of malnourished patients: the incidence of infections was not increased.

• Non-infectious complications fell from 40% to 20%.

Controlled Study

• Note: Patients on TPN received 1,000 calories more than their metabolic needs.

• Overfeeding increases the risk of infectious complications in non-malnourished patients.

Randomized Study

- 124 patients undergoing hepatectomy.
- Average weight 50 kg, triceps skin-fold thickness only 10 mm.
- Randomly assigned to perioperative TPN or no nutritional support.
- TPN significantly reduced the incidence of complications, infections and the use of diuretics.

Meta-Analysis

- 7 out of 27 randomized studies.
- 798 malnourished patients.
- Compared TPN with no nutritional support.
- TPN significantly reduced the incidence of mortality compared to no nutrition.
- Trend to reduce complications and infections when compared to no nutritional support.

Parenteral Nutrition vs No Nutrition

• TPN can greatly benefit patients who are malnourished when compared to no nutritional support.

• Excessive calorie intake via TPN given to well-nourished patients can increase the risk of infectious complications.
Parenteral Nutrition vs Enteral Nutrition
Meta-Analysis

• 30 controlled trials.

• Compared early enteral nutrition vs TPN.

• No difference in mortality between patients in either group.

Meta-Analysis

- 12 controlled trials.
- Compared enteral nutrition vs TPN in ICU patients only.
- Total 748 patients in ICU.
- No difference in mortality between patients in either group.

Intensive Care Medicine: Meta-Analysis

- 9 controlled trials.
- Compared enteral nutrition vs TPN in ICU patients.
- Included only studies in which 95% of patients had complete follow up.
- Intention to treat analysis conducted.

Intensive Care Medicine: Meta-Analysis

• Patients receiving TPN had a significant reduction of mortality compared to those who received enteral nutrition started after 24 hours.

• Benefit lost if enteral feeds were started immediately at admission.

Intensive Care Medicine: Meta-Analysis

- Benefit of reduced mortality in the group receiving TPN was robust.
- Persisted after the inclusion of two further studies with at least 90% completed follow up in the intention to treat analysis.

TPN vs Enteral Meta-Analyses

- Incidence of infectious complications all statistically higher in patients receiving TPN.

- Recommendations:
  - Enteral nutrition more favorable than TPN.
  - Further good-quality studies are required.
  - Infectious complications are more apparent than real because they were caused by controllable factors (hyperglycemia).
TPN vs Enteral Meta-Analyses

- Only 6 compared the incidence of infections.
- In 3 out of these 6 studies there was no difference in the incidence of infections.
- In the other 3 trials there was an increased incidence of infections in patients receiving TPN.
- Significant hyperglycemia in patients receiving TPN compared to those receiving enteral nutrition.

TPN vs Enteral Meta-Analyses

- In 2 of those 3 studies:
  - No difference between groups:
    - Antibiotics
    - Ventilatory support
    - Need for dialysis
  - Unclear if there was any clinical harm from the reported infections in the TPN groups.


Parenteral Nutrition vs Enteral Nutrition

• TPN does not alter mortality when compared with enteral nutrition.

• TPN is beneficial when enteral nutrition cannot be started within 24 hours of admission.

• TPN is beneficial for non-obese malnourished patients.
Parenteral Nutrition vs Enteral Nutrition

• TPN is associated with hyperglycemia.

• No differences in antibiotic use, need for ventilatory support or for dialysis among groups.

• Intention to treat analysis: no differences in the duration or cost of patients’ hospital stay.
Euglycemia

- Two controlled clinical trials of 2,658 medical and surgical critically ill patients.
- Maintenance of euglycemia has profound effect on outcome.
- Euglycemia reduced mortality and complications in surgical patients and reduced complications in medical patients.

Parenteral Nutrition
Special Issues
Glutamine

- Primary fuel for bowel mucosa: supplementation may improve integrity
- Conditionally essential amino acid: rapidly mobilized during stress
Meta-Analysis

- World J Gastro
- 9 RCT with 373 surgical patients.
- Various abdominal surgeries.
- Randomized to TPN supplemented with or without glutamine.
- TPN with glutamine: decreased the rate of infections, reduced length of hospital stay, improved nitrogen balance.

Omega-3 Fatty Acids

• Found in fish and canola oil

• Decreases pro-inflammatory transcription factor.

• Non-randomized prospective trial: 661 patients receiving TPN supplemented with fish oil.

• Reduced mortality, lowered antibiotic use and hospital stay.

• RCT are required to verify findings.

Causes of infections in Patients on Parenteral Nutrition
Translocation Theory

• Observational study in animals.
• Intestinal atrophy in animals receiving TPN.
• Intestine does not receive food enters a resting state.
• Atrophy promotes bacterial translocation leading to infection and sepsis.

### Translocation Theory

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>Nutritional Support</th>
<th>Intestinal atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guedon et al</td>
<td>7</td>
<td>NPO</td>
<td>No atrophy after 21 days</td>
</tr>
<tr>
<td>Rossi et al</td>
<td>7</td>
<td>NPO</td>
<td>Atrophy after 9 months</td>
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<tr>
<td>Pironi et al</td>
<td>2</td>
<td>TPN</td>
<td>Atrophy after 2-3 months</td>
</tr>
<tr>
<td>Sedman et al</td>
<td>203</td>
<td>TPN</td>
<td>No atrophy after &gt;10 days</td>
</tr>
</tbody>
</table>


Translocation Theory

- Bacterial translocation:
  - Culture bacteria from:
    - Bowel lumen
    - Mesenteric lymph nodes
    - Blood
Translocation Theory

- 132 patients underwent laparotomy with mesenteric lymph node biopsies and blood cultures.
- 73% of blood cultures grew gram-positive bacteria.
- Only 2 patients had the same bacteria cultured from the intestine, mesenteric lymph node and blood.

Lipid Theory

- Lipids in TPN promote bacterial growth.
- Perhaps by altering or blocking the reticuloendothelial system.
Lipid Theory

• Controlled clinical trial

• 253 bone marrow transplant patients received 30% energy intake as TPN fat.

• 259 patients received 6% energy intake as TPN fat.

• Energy calculations were based on their resting metabolic rate.

• Tight glycemic control with insulin.

Lipid Theory

• No difference in the incidence of bacteremia or fungal infections between groups.

• No difference in the time to any infection over 60 days between groups.

• Some patients in the low fat intake group developed essential fatty acid deficiency.

Summary

• TPN can be life-saving for patients who cannot eat or absorb nutrients.

• The use of TPN does not increase mortality.

• TPN is likely to cause hyperglycemia in obese, insulin-resistant patients.

• Hyperglycemia increases the rate of infectious and non-infectious complications.
Summary

• Enteral nutrition is safer on obese patients or those with insulin resistance.

• Route of nutritional support does not alter the risk of infection through either bacterial translocation or the use of IV lipids.

• Selection of enteral nutrition vs. TPN should depend on the availability of the GI tract.
Summary

• Remember that NG tubes can cause fluid aspiration and pneumonia.
• Avoid hyperglycemia.
• Avoid overfeeding obese patients.
• Future Focus:
  • Metabolic effects of nutrients.
  • Role of reduced energy intake in obese patients.
  • Role of anti-oxidants.