Sweet’N Low et. Al
Hyperglycemia’N Nutrition Support
Food Feud: Clinical Pearls for 2004

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New Orleans, LA
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50 CENTS  66th year  No. 347

Metro Edit

21 TIGERS 14 SOONERS

LSU No. 1
SUGAR BOWL VICTORY GIVES TIGERS FIRST TITLE SINCE 1958
Objectives

- List the benefits of euglycemia (and risks of hyperglycemia)
- Develop an algorithm for the monitoring, prevention and management of hyper- and hypo- glycemia.
- (Laissez Les Bons Temps Rouler!!)
Starvation Vs. Stress
<table>
<thead>
<tr>
<th>Hormone</th>
<th>Acute Starvation</th>
<th>Chronic Starvation</th>
<th>Trauma/Sepsis I</th>
<th>Sepsis II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Glucagon</td>
<td>+</td>
<td>N</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Growth Hormone</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Catecholamines</td>
<td>+</td>
<td>N</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>
Stress Hyperglycemia

- a. k. a. “diabetes of stress” or “pseudo-diabetes”
- Associated with increased morbidity and mortality
- Potential enhancement by TPN
- Insulin resistance (peripheral & hepatic)
- Elderly at higher risk
When Sweet Turns “Sour”

- Increased mortality and disability in non-diabetic patients.
- Increased CVC infection rates in diabetic patients. (McMahon)
- Increased mortality from AMI in diabetic patient (Malmberg et. al.)
- Impaired immunologic response to infection (Rayfield et. al.)
- Impaired gastrointestinal motility (Oster-Jorgensen et.al)
- Increased cardiovascular tone (Guigliano et. al.)
Other Potential Detrimental Effects of Hyperglycemia

- Increased incidence of mediastinitis in diabetic patients undergoing CABG
- Hyperosmolarity
  - \((2\text{Na}+\text{Gluc}/18+\text{Bun}/2.8)\)
- Osmotic diuresis
- Electrolyte imbalance
- Glycation (glycosylation) of immunoglobulins (Hennessey et. al.)
Hyperglycemia – In Vitro Abnormalities

- Granulocyte adhesion
- Chemotaxis
- Phagocytosis
- Respiratory burst
- Intracellular killing
- Complement function
- Predisposing environment for Candida albicans infection
Hyperglycemia - How sweet it is!

How sweet is sweet?

- 220 mg/dL?
- 200 mg/dL?
- 180 mg/dL?
- 150 mg/dL?
- 145 mg/dL?
- 130 mg/dL?
- 120 mg/dL?
- 110 mg/dL?
Hyperglycemia Contributing Factors

Rule of Ds

- Dextrose – PB, TPN, EN, PO liquids
- Diabetes
- Disease (Stress, Insulin resistance)
- Drugs (Steroids, Propofol, vasopressors, et. al.)
- Dialysis – CAPD, CAVHD
- Decreased intravascular volume
- Decreasing youth (aging)
- Doctors et. al.
- Da family, Doughnuts et. al.
Intensive Insulin Therapy In Critically Ill Patients
Van den Berghe et. al. 2001 & 2003

Conventional - >215 (180-200) (N=783)
Intensive - >110 (80-110 mg/dL) (N=755)

Septicemia Overall ICU Mortality > 5 Days ICU Mortality Hospital Mortality CI Polyneuropathy

% Reduction
Glucose Control And Mortality in Critically Ill Patients. Finney et. al. JAMA 290, 2003

- End point- ICU mortality
- Six bands (ranges) of glycemic control
- Proportion of admission time spent by individual patient in each band was measured

Conclusions:
- Increased insulin administration positively associated with ICU death regardless of glucose level
- Control of glucose level appear to account for mortality benefit
- Speculative glucose upper limit of 145 mg/dL
Management of Hyperglycemia

- Reduce CHO & Insulin resistance -
  - TPN: <25 kcal/kg/d (total calories) - “permissive underfeeding”
  - Protein 1.2 – 1.5 gm/kg/d
  - Parenteral Willett, Atkins formulas?

- Set goal range (mg/dL)
  - 80-110  Van den Berghe et. al.
  - 80-120  (100-150 if medically stable ) McMahon
  - <145  Finney et. al.

- Goal rate
  - <4 mg/kg/min. Begin @ 3mg/kg/min (actual/usual wt.) If > 10% above ideal, use ideal wt. (Rosmarin et. al.)
Management of Hyperglycemia

- Remember: The lower the maximum goal level, the greater the risk of hypoglycemia.
- Infuse low and slow and increase according to monitored glucose levels.
- Minnie (Sweet) Pearls (@ Glucose):
  - 1 mmol = 180 mg
  - To convert mmol/L to mg/dl, multiply by 18
  - To convert mg/dL to mmol/L, multiply by 0.05551
## Sliding - Sliding Scales

<table>
<thead>
<tr>
<th>Glucose</th>
<th>Ins</th>
<th>Ins</th>
<th>Glucose</th>
<th>Ins</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150</td>
<td>0</td>
<td></td>
<td>&lt;100</td>
<td>0</td>
</tr>
<tr>
<td>150-200</td>
<td>5</td>
<td></td>
<td>100-150</td>
<td>2</td>
</tr>
<tr>
<td>201-250</td>
<td>10</td>
<td>5</td>
<td>151-200</td>
<td>4</td>
</tr>
<tr>
<td>251-300</td>
<td>15</td>
<td>10</td>
<td>201-250</td>
<td>6</td>
</tr>
<tr>
<td>301-350</td>
<td>20</td>
<td>15</td>
<td>251-300</td>
<td>8</td>
</tr>
<tr>
<td>351-400</td>
<td>25</td>
<td>MD</td>
<td>&gt;300</td>
<td>10</td>
</tr>
<tr>
<td>401-450</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;451</td>
<td>MD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Insulin in TPN Solution

- Plasma glucose level reasonably controlled < 200 mg/dL
- Influencing factors controlled
- Dose not requiring change < 24 hr.
- Administration dose:
  - 0.1 IU/gm CHO/L
  - Increase by 0.05 IU/gm CHO/L until glucose controlled.
Insulin Infusions
Multiple Protocols

- 1 IU/ml in NaCl
- Limited to ICU or closely monitored units
- Frequent glucose determinations & rate adjustment – q. 1 hr. initially
- 1-2 IU/hr. initially, titrated according to established protocols and ranges of glucose levels
Insulin Infusions
Multiple Protocols

- **Mirtallo** –
  - 2 IU/hr. Initiate @>180mg/dL Adjusted until <200 mg/dL, limit <15 IU/hr.

- **Van den Berghe et. al.** -
  - “Strict algorithm”. Initiate @>110mg/dL, limit 50 IU/hr.

- **Mizock - Brown & Dodek** -
  - 3 IU bolus + 2 IU/hr. @>207 mg/dL
  - Comprehensive nomogram – no limit

- **Monitor, monitor, monitor**
Brown G and Dodeck P, Intravenous insulin nomogram improves blood glucose control in critically ill patients, Critical Care Medicine, 2001; 29:1714-1719.


### INSULIN INFUSION PROTOCOL - Regular Human Insulin Only (ICU only)

**GOAL:**
The goal is to maintain serum glucose between 7 and 11.5 mmol/L.

**MONITORING:** Check glucose q1h (either capillary or blood) until stable (3 values in desired range). Checks can be reduced to q2h x 4 hours → q4h if blood glucose remains in desired range. Restart q1h checking if any change in insulin infusion rate occurs. If glucose is changing rapidly (even if in the desired range) OR if in a critical range (<3.5 or >20mmol/L) q30minute checks may be needed. However, blood glucose will not change significantly in <30 minutes with any change in insulin.

### Initiating Insulin Infusion

<table>
<thead>
<tr>
<th>Glucose</th>
<th>11.5-14mmol/L</th>
<th>14.1-17mmol/L</th>
<th>17.1-20mmol/L</th>
<th>20.1-24mmol/L</th>
<th>&gt;24mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Give 3 units insulin IVP and start @ 2 units/hr</td>
<td>Give 6 units insulin IVP and start @ 2 units/hr</td>
<td>Give 8 units insulin IVP and start @ 2 units/hr</td>
<td>Give 10 units insulin IVP and start @ 2 units/hr</td>
<td>Call MD for orders</td>
</tr>
</tbody>
</table>

### Ongoing Insulin Infusion:

#### Below Desired Range (7-11.5mmol/L)

<table>
<thead>
<tr>
<th>Glucose Level</th>
<th>Infusion Rate of 1-3 units/hr</th>
<th>Infusion Rate of 4-6 units/hr</th>
<th>Infusion Rate of 7-9 units/hr</th>
<th>Infusion Rate of 10-12 units/hr</th>
<th>Infusion Rate of 13-16 units/hr</th>
<th>Infusion Rate of &gt; 16 units/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.5mmol/L</td>
<td>D/C Infusion and give 1 amp D50 IVP</td>
<td>D/C Infusion: Re-check glucose in 1 hour. If &gt;7, re-start but decrease rate by 1 unit/hr.</td>
<td>D/C Infusion: Re-check glucose in 1 hour. If &gt;7, re-start but decrease rate by 2 unit/hr.</td>
<td>D/C Infusion: Re-check glucose in 1 hour. If &gt;7, re-start but decrease rate by 3 unit/hr.</td>
<td>Decrease Infusion by 50%</td>
<td></td>
</tr>
<tr>
<td>3.5-4.5mmol/L</td>
<td>D/C Infusion: Re-check glucose in 1 hour. If &gt;7, re-start but decrease rate by 1 unit/hr.</td>
<td>Decrease Infusion by 2 units/hr</td>
<td>Decrease Infusion by 3 units/hr</td>
<td>Decrease Infusion by 4 units/hr</td>
<td>Decrease Infusion by 5 units/hr</td>
<td>Decrease Infusion by 6 units/hr</td>
</tr>
<tr>
<td>4.6-5.5mmol/L</td>
<td>Decrease Infusion by 1 unit/hr</td>
<td>Decrease Infusion by 2 units/hr</td>
<td>Decrease Infusion by 3 units/hr</td>
<td>Decrease Infusion by 4 units/hr</td>
<td>Decrease Infusion by 5 units/hr</td>
<td>Decrease Infusion by 6 units/hr</td>
</tr>
<tr>
<td>5.6-7mmol/L</td>
<td>Decrease Infusion by 1 unit/hr</td>
<td>Decrease Infusion by 2 units/hr</td>
<td>Decrease Infusion by 3 units/hr</td>
<td>Decrease Infusion by 4 units/hr</td>
<td>Decrease Infusion by 5 units/hr</td>
<td>Decrease Infusion by 6 units/hr</td>
</tr>
</tbody>
</table>

#### In Desired Range (7-11.5mmol/L)

<table>
<thead>
<tr>
<th>Glucose Level</th>
<th>Infusion Rate of 1.5 units/hr</th>
<th>Infusion Rate of 6-10 units/hr</th>
<th>Infusion Rate of 11-16 units/hr</th>
<th>Infusion Rate of &gt; 16 units/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.5-14mmol/L</td>
<td>Give 2 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 3 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 3 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>14.1-17mmol/L</td>
<td>Give 3 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 5 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 5 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>17.1-20mmol/L</td>
<td>Give 8 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 8 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 8 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>20.1-24mmol/L</td>
<td>Give 10 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 10 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 10 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>&gt; 24mmol/L</td>
<td>Call Physician for New Order</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Above Desired Range (7-11.5mmol/L)

<table>
<thead>
<tr>
<th>Glucose Level</th>
<th>Infusion Rate of 1.5 units/hr</th>
<th>Infusion Rate of 6-10 units/hr</th>
<th>Infusion Rate of 11-16 units/hr</th>
<th>Infusion Rate of &gt; 16 units/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.5-14mmol/L</td>
<td>Give 2 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 3 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 3 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>14.1-17mmol/L</td>
<td>Give 3 units insulin IVP and increase Infusion by 1 unit/hr</td>
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<td>17.1-20mmol/L</td>
<td>Give 8 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 8 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 8 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>20.1-24mmol/L</td>
<td>Give 10 units insulin IVP and increase Infusion by 1 unit/hr</td>
<td>Give 10 units insulin IVP and increase Infusion by 2 units/hr</td>
<td>Give 10 units insulin IVP and increase Infusion by 3 units/hr</td>
<td>Call Physician for New Order</td>
</tr>
<tr>
<td>&gt; 24mmol/L</td>
<td>Call Physician for New Order</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Management of Hypoglycemia

- Varied definitions < 60mg/dL, Sx?
- Dextrose 50% IVP
  - 25 – 50 ml ½ - 1 amp
  - 12.5 - 25 gm
- Glucagon (Subcutaneous, IM or IV)
  - 0.5 - 1 mg repeat in 20 min if needed
  - Self-injectors available
- Oral
  - O. J., glucose tabs, et. al.
  - Sublingual sugar
Pearls, Aphorisms & Lagniappe

- If a little is good, a lot is not necessarily better
- Halitosis is better than no breath at all.
- The enemy of good is better.
- When at first you don’t succeed, consult.
- The ignorance of facts does not make them disappear.
- Man who looks at leopard through bamboo pole sees only one spot.
- Often the therapy is worse than the disease.
- Primum non noncere.
- When you are up to part of your anatomy in alligators, it is hard to remember that your primary purpose was to drain the swamp.
- Illegitimi non carborundum.
- Nutrition Week 2004 - Practice Posters N44, 63, 65
A.S.P.E.N. Rhoads Research Foundation
Request for Proposals

- Intensive Glycemic Control in Critically Ill Patients Receiving TPN

- Purpose
  - The principal objective of this request is to support meritorious hypothesis-driven clinical research that examines the role of intensive glucose management in critically ill patients receiving total parenteral nutrition (TPN).

http://www.nutritioncare.org/research/rpf_03.pdf
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http://www.barrocas.com/Library/library.htm
abarroc@tulane.edu
Kaplan-Meier Curves Showing Cumulative Survival of Patients Who Received Intensive Insulin Treatment or Conventional Treatment in the Intensive Care Unit (ICU)
