Iv Insulin Infusion Protocol for Critically-Ill Adult Patients in the ICU Setting

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Why is Glucose Control Important in the ICU?
Stress Hyperglycemia

↑ Counterregulatory hormones
- Cortisol
- Catecholamines
- Glucagon
- Growth Hormone

↑ Glucose production

↓ Glucose utilization

↑ Glucose
↑ FFAs

↑ Lipolysis

↓ FFAs

Kitabchi AE, Diabetes Care 24:131, 2001
Hyperglycemia: An Independent Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes

Total In-patient Mortality

- Normoglycemia: 1.7%
- Known Diabetes: 3.0%
- New Hyperglycemia: 16.0% *

* P < 0.01

Umierrez GE et al, J Clin Endocrinol Metab 87:978, 2002
Hyperglycemia and Pneumonia Outcomes

<table>
<thead>
<tr>
<th>BG (mg/dl)</th>
<th>&lt; 110</th>
<th>110 - &lt;198</th>
<th>198 - &lt;250</th>
<th>≥250</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Admission glucose (mg/dl)
- Mortality
- Hospital Complications

* : p < 0.05 vs BG < 198 mg/dl (11 mmol/l)

N= 2,471 patients with CAP

McAllister et al, Diabetes Care 28:810-815, 2005
Hyperglycemia in Hospitalized Patients

- Hyperglycemia (>200 mg/dL x 2) occurred in 38% of hospitalized patients
  - 26% had known history of diabetes
  - 12% had no history of diabetes

- Newly discovered hyperglycemia was associated with:
  - Longer hospital stays
  - Higher admission rates to intensive care units
  - Less chance to be discharged to home (required more transitional or nursing home care)

Hyperglycemia in Hospitalized Patients

- High-risk for bacterial infection
  - Surgery
  - Catheters
  - Intravenous Access

- Problems with wound healing

- Problems with tissue and organ perfusion

- Nice sugar study the largest trial to date intensive insulin therapy is associated with increased hypoglycemia and increased mortality

- Therefore it is recommended to maintain blood glucose level between 140 - 180 mgs

- A lower blood glucose target (not less than 100mgs) may be appropriate in selected patients
140-180 mg/dL (7.8-10 mmol/L)

Critically ill

2009 AACE/ADA Consensus Statement

## NICE-SUGAR Study Outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Intensive Group</th>
<th>Conventional Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning BG (mg/dL)</td>
<td>118 ± 25</td>
<td>145 ± 26</td>
</tr>
<tr>
<td>Hypoglycemia (≤ 40mg/dL)</td>
<td>206/3016</td>
<td>15/3014</td>
</tr>
<tr>
<td>28 Day Mortality (p=0.17)</td>
<td>22.3%</td>
<td>20.8%</td>
</tr>
<tr>
<td>90 Day Mortality (p=0.02)</td>
<td>27.5%</td>
<td>24.9%</td>
</tr>
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</table>
Diabetes Mellitus Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) trial

- People with diabetes who suffer an acute myocardial infarction (MI) are at markedly increased risk of future cardiovascular morbidity and mortality.

- The DIGAMI study compared "conventional" anti-diabetic therapy to intensive insulin therapy consisting of acute insulin infusion during the early hours of MI and thrice-daily subcutaneous insulin injection for the remainder of the hospital stay and a minimum of 3 months thereafter.

- 1-year mortality was statistically significant.
Inpatient glycaemic targets

- Insulin infusion to control hyperglycaemia
- Starting threshold no higher than 180 mg/dL
- Maintain BG between 140 and 180 mg/dL
  - Possible greater benefit at lower end of range
- Somewhat lower targets may be appropriate in selected patients
- Targets <110 mg/dL are not recommended

<table>
<thead>
<tr>
<th>Not recommended</th>
<th>May be appropriate</th>
<th>Recommended</th>
<th>Not recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;110 mg/dL</td>
<td>110–140 mg/dL</td>
<td>140–180 mg/dL</td>
<td>&gt;180 mg/dL</td>
</tr>
</tbody>
</table>
**Titration of insulin dose according to blood glucose level**

<table>
<thead>
<tr>
<th>Blood glucose levels (mg/dl)</th>
<th>Dosage of insulin infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>No insulin to be given</td>
</tr>
<tr>
<td>100-149</td>
<td>1-1.5 units/hour</td>
</tr>
<tr>
<td>150-199</td>
<td>2 units/hour</td>
</tr>
<tr>
<td>200-249</td>
<td>2.5 units/hour</td>
</tr>
<tr>
<td>250-299</td>
<td>3 units/hour</td>
</tr>
<tr>
<td>300-349</td>
<td>3.5 units/hour</td>
</tr>
<tr>
<td>350-399</td>
<td>4 units/hour</td>
</tr>
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</table>
Basal Insulin

Long-acting, non-peaking insulin is preferred as it provides continuous insulin action, even when the patient is fasting.

Required in all patients with T1DM

Many patients with T2DM will require basal insulin in the hospital

Can be estimated to be about 1/2 of the total daily dose (TDD) of insulin
Diabetes Treatment algorithm
• This algorithm is not intended to be used for those individuals with type 1 diabetes, diabetic ketoacidosis or hyperglycemic hyperosmolar states.
• Target Range for Glycemic Control: 80–140 mg/dL (Generally 110 mg/dL)
1. Standard drip 100 units/100 mL 0.9% NaCl. Approved IV insulins include Regular, aspart and glulisine

2. Start IV insulin therapy when glucose is above target range. Insulin infusions should be discontinued when
   a. Patient has no history of diabetes and is receiving <1 Unit/hour
   b. Patient receives 1st dose of SC basal + bridging dose of fast analog or R
• 3. Bolus dose and Initial Infusion rate: Divide initial glucose level by 100, then round to nearest 0.5 units for bolus AND initial infusion rate Examples:

1) Initial glucose=326 mg/dL: 326÷100=3.26, round to 3.5: IV bolus 3.5 units + start infusion @ 3.5 units/hour

2) Initial glucose=174 mg/dL: 174÷100=1.74, round to 1.5: IV bolus 1.5 units + start infusion @ 1.5 units/hour
4. Intravenous Fluids

- Most patients will need 5–10 g glucose per hour D5W or D5W½NS at 100–200 mL/hour or equivalent (TPN, enteral feeding, etc.)
5. Adjusting the Infusion:

- Algorithm 1: Start here for most patients.
- Algorithm 2: For patients not controlled with Algorithm 1, or start here if s/p CABG, solid organ or islet cell transplant, receiving glucocorticoids etc. or patient with diabetes receiving >80 units/day of insulin as an outpatient.
- Algorithm 3: For patients not controlled on Algorithm 2. NO PATIENT STARTS HERE without authorization from the endocrine service.
- Algorithm 4: For patients not controlled on Algorithm 3. NO PATIENT STARTS HERE
<table>
<thead>
<tr>
<th>Glucose</th>
<th>Algorithm 1</th>
<th>Glucose</th>
<th>Algorithm 2</th>
<th>Glucose</th>
<th>Algorithm 3</th>
<th>Glucose</th>
<th>Algorithm 4</th>
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<tbody>
<tr>
<td>&lt;70</td>
<td>Off</td>
<td>&lt;70</td>
<td>Off</td>
<td>&lt;70</td>
<td>Off</td>
<td>&lt;70</td>
<td>Off</td>
</tr>
<tr>
<td>70–109</td>
<td>0.2</td>
<td>70–109</td>
<td>0.5</td>
<td>70–109</td>
<td>1</td>
<td>70–109</td>
<td>1.5</td>
</tr>
<tr>
<td>110–119</td>
<td>0.5</td>
<td>110–119</td>
<td>1</td>
<td>110–119</td>
<td>2</td>
<td>110–119</td>
<td>3</td>
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<tr>
<td>120–149</td>
<td>1</td>
<td>120–149</td>
<td>1.5</td>
<td>120–149</td>
<td>3</td>
<td>120–149</td>
<td>5</td>
</tr>
<tr>
<td>150–179</td>
<td>1.5</td>
<td>150–179</td>
<td>2</td>
<td>150–179</td>
<td>4</td>
<td>150–179</td>
<td>7</td>
</tr>
<tr>
<td>240–269</td>
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<td>240–269</td>
<td>5</td>
<td>240–269</td>
<td>8</td>
<td>240–269</td>
<td>16</td>
</tr>
<tr>
<td>300–329</td>
<td>4</td>
<td>300–329</td>
<td>7</td>
<td>300–329</td>
<td>12</td>
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<td>24</td>
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<tr>
<td>&gt;360</td>
<td>6</td>
<td>&gt;360</td>
<td>12</td>
<td>&gt;360</td>
<td>16</td>
<td>&gt;360</td>
<td>32</td>
</tr>
</tbody>
</table>

<60 = Hypoglycemia (See #8 for treatment)
• Moving from Algorithm to Algorithm:
  ➢ Moving Up: When glucose remains outside the target range after titrating insulin
  ➢ Moving Down: When glucose is <70 mg/dL x 2 or decreases >60 mg/dl in 1 hour
7. Patient Monitoring:

- Hourly venous (lab) determinations until glucose <450 mg/dL; then capillary glucose (finger sticks) q 1 hour until glucose is within goal x 4 hours; then every 2 hours x 4 hours; If stable, decrease monitoring to every 4 hours

- Hourly monitoring indicated for critically ill patients even if the glucose is stable

- In hypotensive patients (BP <80/60), capillary glucose values may be inaccurate. Obtain venous blood for glucose determinations
• If any of the following occur, temporarily resume hourly glucose monitoring, until glucose is again stable (2–3 consecutive values within target range):
  ➢ Any change in insulin infusion rate
  ➢ Significant changes in clinical condition
  ➢ Starting or stopping pressor or steroid therapy
  ➢ Starting or stopping dialysis
  ➢ Starting, stopping or changing rates of TPN, PPN or tube feedings
8. Treatment of Hypoglycemia (Glucose <60 mg/dL)
- Discontinue insulin drip AND
- Give D50W IV Glucose 40–60 mg/dL 12.5 g (1/2 amp)
- Glucose <40 mg/dL 25.0 g (1 amp)
- Recheck glucose every 15–30 minutes and repeat D50W IV as above. Restart insulin drip,
- one algorithm lower, when glucose >80 mg/dL x 2
9. Notify the physician:
   - For patients not responding to Algorithm 1 or 2.
   - For hypoglycemia which has not resolved after administration of D50W IV and discontinuation of the insulin drip.
10. Transition from IV insulin to SC insulin: “Basal-Analog” Method
a. Calculate Total Daily Dose (TDD) for subcutaneous insulin
   \[ TDD = \frac{\text{Infusion rate/h}}{x} \times 20h \]
b. First dose SQ insulin includes [basal insulin + bridging dose aspart, glulisine, lispro or R] \times 1
   - 1. If patient will begin eating give:
     - Half TDD as basal glargine, detemir* or NPH* Plus
     - Bridging insulin** @ 10% of basal insulin dose
     - Stop IV insulin
     - Continue primary I.V.
   - 2. If patient will continue NPO, TPN or tube feeding give:
     - All TDD as basal glargine, detemir* or NPH* Plus
     - Bridging insulin** @ 5% of basal insulin dose
     - Stop IV insulin and continue primary I.V.
c. Proceed to “Inpatient Management of Insulin in the Non-Critical Care Setting” algorithm for management of daily basal insulin, prandial + supplemental insulin
• No evidence-based data on inpatient transition from I.V. insulin to detemir. If detemir is selected, expect to use at least 25% greater dose than glargine. If the dose of detemir is <0.6 units/Kg, use half bid. If NPH is used as a basal insulin the dose is 2/3 of the TDD (whether or not the patient is eating) and is distributed bid as 2/3 A.M. and 1/3 H.S. or may be divided equally and given q 6h.
• R (regular insulin) is not preferred as a bridging or prandial insulin
Thanks for your attention