Glucose Management in Critically Ill Patients

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OBJECTIVES

- Understand the impact of glycemic control on clinical outcomes for critically ill surgical and medical patients
- Review current guidelines and glycemic targets for critically ill patients
- Implement strategies for safe and effective glycemic control during the ICU stay and on transition out of the ICU
- Management of Hyperglycemic Crisis: DKA and HHS

DISCLOSURES

- I do not have any relevant financial disclosures.
THE IMPACT OF HYPERGLYCEMIA IN CRITICALLY ILL PATIENTS

CAUSES OF INPATIENT HYPERGLYCEMIA

- Illness related “stress” – counter regulatory hormones and cytokines cause insulin resistance
- Undiagnosed diabetes mellitus
- Medications: steroids, immunosuppressants, sympathomimetics, anesthetic agents, octreotide
- Parenteral and enteral nutrition
- Physical Inactivity
- Inappropriate insulin use e.g. Sliding scale insulin

LINK BETWEEN HYPERGLYCEMIA AND POOR OUTCOMES: POTENTIAL MECHANISMS

Metabolic stress response
- Stress hormones and peptides
- Glucose
- Insulin
- Ketones
- Lactate
- Reactive O2 species
- Transcription factors
- Secondary mediators

- Immune dysfunction
- Infection dissemination
- Organ dysfunction
- Protracted hospital stay
- Mortality

Hyperglycemia and Mortality in Critically Ill Patients

- Mortality risk from hyperglycemia is greater in patients without a diagnosis of diabetes.
- Patients with diabetes: n = 78,142
- Patients without diabetes: n = 180,898

Hyperglycemia and Mortality in Acute Myocardial Infarction

16,871 patients with acute myocardial infarction

Association between Mean BG and In-Hospital Mortality After Multivariable Adjustment (Reference: Mean BG 100 to <110)

HYPERGLYCEMIA INCREASES MORTALITY IN CABG PATIENTS

Mortality Increases With Increases in Average Glucose Levels

Post-CABG

Mortality %

(N = 2,110)

1.8%
P = 0.001

1.8% 5.0%

Glucose <200 Glucose >200

CABG = coronary artery bypass graft


HYPERGLYCEMIA INCREASES MORTALITY IN CABG PATIENTS

Mortality %

Average Postoperative Glucose (mg/dL)

<150 150-175 175-200 200-225 225-250 >250

1.2% 10.0% 14.0% 12.0% 10.0% 6.0%


OUTCOMES OF TREATING HYPERGLYCEMIA IN CRITICAL ILLNESS
PORTLAND DIABETES PROJECT:
REDUCTION IN DEEP STERNAL WOUND INFECTION RATES

SQI = subcutaneous insulin; CII = continuous insulin infusion.

Anthony Fournary MD
1999 CONM

INTENSIVE INSULIN THERAPY (IIT) IN CRITICALLY ILL (SURGICAL) PATIENTS

N = 1,548


INTENSIVE INSULIN THERAPY IN CRITICALLY ILL (SURGICAL) PATIENTS

**IIT IN CRITICALLY ILL MIXED (MEDICAL AND SURGICAL) ICU PATIENTS**

<table>
<thead>
<tr>
<th>BG target 80-140 mg/dl</th>
<th>N = 1,600</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mortality</td>
</tr>
<tr>
<td></td>
<td>29.3%</td>
</tr>
</tbody>
</table>

*Infectious complications were not statistically significant


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**BENEFITS OF TIGHT GLYCEMIC CONTROL: OBSERVATIONAL STUDIES AND EARLY INTERVENTION TRIALS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Population</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furnary, 1999</td>
<td>ICU</td>
<td>DM undergoing open heart surgery</td>
<td>65% ↓ infection</td>
</tr>
<tr>
<td>Furnary, 2003</td>
<td>ICU</td>
<td>DM undergoing CABG</td>
<td>57% ↓ mortality</td>
</tr>
<tr>
<td>Krinsley, 2004</td>
<td>Med/Surg ICU</td>
<td>Mixed, no Cardiac</td>
<td>29% ↓ mortality</td>
</tr>
<tr>
<td>Malmberg, 1995</td>
<td>CCU</td>
<td>Mixed</td>
<td>28% ↓ mortality After 1 year</td>
</tr>
<tr>
<td>Van den Berghe, 2001*</td>
<td>Surgical ICU</td>
<td>Mixed, with CABG</td>
<td>42% ↓ mortality</td>
</tr>
<tr>
<td>Lasa, 2004</td>
<td>OR and ICU</td>
<td>CABG and DM</td>
<td>60% ↓ A Fib post op survival 2 yr</td>
</tr>
</tbody>
</table>

*RCT, randomized clinical trial


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**DIGAMI 2 – A NEGATIVE STUDY**

- 1253 T2 DM patients with AMI
- Randomized to 3 groups:
  - #1 – iv insulin + glucose ≥24 hours followed by MDI SC insulin
  - #2 – iv insulin + glucose ≥24 hr followed by usual care
  - #3 – Usual Care by physician
- No differences in mortality

*Deficiencies:
1. Only 50% recruitment
2. Underpowered analysis
3. Target glucose levels NOT met

INTENSIVE GLUCOSE MANAGEMENT IN RCTS SHOWING NO BENEFIT

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Setting</th>
<th>Primary Outcome</th>
<th>ARR</th>
<th>RRR</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van den Berghe 2006</td>
<td>1200</td>
<td>MICU</td>
<td>Hospital mortality</td>
<td>2.7%</td>
<td>7.0%</td>
<td>0.94* (0.84-1.06)</td>
<td>N.S.</td>
</tr>
<tr>
<td>HI-5 2006</td>
<td>240</td>
<td>CCU-AMI</td>
<td>6-mo mortality</td>
<td>-1.8%*</td>
<td>-30%*</td>
<td>NR</td>
<td>N.S.</td>
</tr>
<tr>
<td>Giscanti 2007</td>
<td>1101</td>
<td>ICU</td>
<td>ICU mortality</td>
<td>-1.5%</td>
<td>-10%</td>
<td>1.10 (1.04-1.16)</td>
<td>N.S.</td>
</tr>
<tr>
<td>VISEP 2008</td>
<td>537</td>
<td>ICU</td>
<td>28-d mortality</td>
<td>1.3%</td>
<td>5.0%</td>
<td>0.80* (0.68-1.00)</td>
<td>N.S.</td>
</tr>
<tr>
<td>De La Rosa 2008</td>
<td>504</td>
<td>ICU-MICU</td>
<td>28-d mortality</td>
<td>-4.2%*</td>
<td>-13%*</td>
<td>NR</td>
<td>N.S.</td>
</tr>
<tr>
<td>NICE-SUGAR 2009</td>
<td>6104</td>
<td>ICU</td>
<td>3-mo mortality</td>
<td>-2.6%</td>
<td>-10.6</td>
<td>1.14 (1.02-1.28)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

NICE-SUGAR TRIAL: IDEAL TARGET IN ICU PATIENTS

- Intensive: Glucose 80-110 mg/dL
- Conventional: Glucose 140-180 mg/dL

- Average am glucose
  - 118 (IT) vs. 145 mg/dL
- Increased mortality in IT
  - 27.5% (IT) vs. 24.9%
- OR for death = 1.4 (except in trauma and corticosteroid therapy)
- Hypoglycemia (BG < 40)
  - 6.8% (IT) vs. 0.5%
- No significant benefits in secondary outcomes
GLUCO-CABG: IDEAL TARGET IN CABG PATIENTS

- RCT, N=302 with 2 targets: 100-140 mg/dL vs 140-180 mg/dL
- Insulin infusion in ICU if glucose >140 mg/dL followed by SC insulin regimen during the entire hospital stay and for 90 days postop
- Composite postoperative complications: mortality, wound infection, pneumonia, bacteremia, respiratory failure, acute kidney injury and major cardiovascular events
  - in patients without diabetes, there were ~20% fewer postoperative complications
  - in patients with diabetes, no difference

Healthcare Utilization and Costs

**DIGAMI 1**
- Gain in life-years: 0.94 years
- Cost per life-year gained: Euro 18,900
- Per Swedish standards, this is highly cost effective

**CABG Patients**
- Each 50 mg/dL BG increase was associated with:
  - Longer Post op days: 0.76 days
  - Higher hospital Charges: $2,824
  - Higher hospital costs: $1,769

Costs in Intensive Care Unit

**Leuven Study**
- Decreased ICU length of stay: 2.0 days
- Decreased ICU costs: 2,638 Euros/patient
- No difference in ward length of stay

**Stamford Study**
- Net decrease in costs: $1,580 per patient
- Decrease in ICU LOS: 0.3 median days (p=0.005)
- Decrease in Non-ICU days: 1 calendar day (p=0.54)
**Abstract**

COST SAVINGS IN PATIENTS TREATED WITH IIT- TIRUMPH STUDY

Pre and post implementation of Intensive Insulin Protocols in ICU

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Change in Outcome (Decreased Patients Included) No: 31,139 (2003 to 2007)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total LOS Costs</td>
<td>-$7,580 (-$13,643, -$1,180)*</td>
</tr>
<tr>
<td>Direct Variable Costs</td>
<td>-$4,960 (-$8,998, -$850)*</td>
</tr>
<tr>
<td>Total ICU costs</td>
<td>-$5,916 (-$17,999, -$2,176)*</td>
</tr>
<tr>
<td>Direct variable ICU costs</td>
<td>-$5,316 (-$6,218, -$577)*</td>
</tr>
<tr>
<td>Total LOS</td>
<td>-0.25 (-1.55, .99)</td>
</tr>
<tr>
<td>ICU days</td>
<td>-1.80 (-2.78, -0.89)*</td>
</tr>
<tr>
<td>Mortality</td>
<td>-.026 (-.06, .0006)</td>
</tr>
<tr>
<td>Average glucose per patient day (mg/dL)**</td>
<td>-9.18 (-12.49, -5.97)*</td>
</tr>
</tbody>
</table>

*Denotes significance at p ≤ 0.05. 95% empirical, bias-corrected bootstrapped confidence intervals shown in parentheses.

Sadhu et al. Diabetes Care 2008; 31(8): 1556-1661
Sadhu et al. Abstract - ADA 70th Scientific Session 2010

**HYPOGLYCEMIA IN CRITICALLY ILL PATIENTS**

- 22.4% of patients had hypoglycemia defined as glucose ≤ 81 mg/dL, at least once
- Mortality Rates:
  - Hypoglycemia → 36.6%
  - No hypoglycemia → 19.7%
- Mortality increased with severity of hypoglycemia
- Therapy at time of hypoglycemia:
  - 32.7% were receiving insulin
  - 67.3% were not (spontaneous)
- Insulin therapy was not a significant predictor of hospital mortality in a multivariate analysis

Two centers; N= 4946


**HYPOGLYCEMIA DUE TO INSULIN THERAPY**

40 hospitals: 7820 acute myocardial infarction patients admitted with hyperglycemia
Subsequent hypoglycemia during hospitalization (< 60 mg/dL)

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>No hypoglycemia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>m(mg/dL)</td>
<td>m(mg/dL)</td>
</tr>
<tr>
<td>Glucose level</td>
<td>86</td>
<td>59</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>14.1</td>
<td>13.4</td>
</tr>
</tbody>
</table>

- Increased in-hospital mortality if hypoglycemia occurred
- Hypoglycemia was associated with increased mortality in non insulin treated patients BUT NOT in patients treated with insulin

AACE/ADA/STS TARGET GLUCOSE LEVELS IN ICU PATIENTS

- **ICU setting:**
  - Starting threshold of no higher than 180 mg/dL
  - Once IV insulin is started, the glucose level should be maintained between **140 and 180 mg/dL**
  - Lower glucose targets (**110-140 mg/dL**) may be appropriate in selected patients (Cardiothoracic surgery)
  - Targets <110 mg/dL or >180 mg/dL are **NOT recommended**

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STRATEGIES TO ACHIEVE GLYCEMIC CONTROL IN CRITICALLY ILL PATIENTS

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ADMISSION #1 – CHEST PAIN

- 68 year old male admitted with chest pain and found to have AMI and CHF
- Type 2 DM for 14 years, HTN, Hyperlipidemia, Gout
- Outpatient DM Meds: Metformin 1000mg bid, Glyburide 5mg bid
- Exam: Lungs with rales, 2+ LE edema
- Labs: Admission glucose 316 mg/dL HgbA1c 9.3%, creatinine 2.5, LFT's 2.5 x upper limit of normal
- Echo shows LVEF 25%
- Admitted to CCU after cardiac catheterization with glucose now 250 mg/dL

**How should we treat this patient?**

1. Continue metformin and increase the dose of glyburide to 10 mg bid
2. Start **SLIDING SCALE** subcutaneous insulin Q4-6 hours
3. Start insulin infusion with a glucose target of 110-140 mg/dL
4. Start insulin infusion with a glucose target of 140-180 mg/dL
INDICATIONS FOR INTRAVENOUS INSULIN THERAPY: SUMMARY

- Diabetic Ketoacidosis
- Hyperglycemic Hyperosmolar Syndrome
- Critical care illness (surgical, medical)
- Post cardiac surgery
- Myocardial infarction or cardiogenic shock
- NPO status in Type 1 diabetes
- Labor and Delivery
- Organ Transplantation


ADMISSION #1 – CONTINUED

- Over the next 24 hours, the glucose control improved into the desired target and he is medically optimized
- He now has proceeds to surgery and has a 3 vessel CABG
- Postop, he is admitted to the surgical ICU on epinephrine and vasopressin drips for hypotension
- His initial glucose in the ICU is 251 mg/dl

How do we manage his glucose?
1. SLIDING SCALE insulin Q 4-6 hours
2. Start long and short acting insulin for basal-bolus insulin therapy
3. Start Insulin Infusion with a glucose target of 110-140 mg/dl
4. Start Insulin Infusion with a glucose target of 140-180 mg/dl

ADMISSION #1 – CONTINUED

- Over the next 24 hours, the glucose control reaches target range and has been stable
- Pressors are weaned off and he is extubated
- A diet is ordered and plans are started to transfer to the floor

What do we do next?
1. Restart metformin and increase glyburide dose to 10mg bid
2. Turn off insulin infusion and immediately start SLIDING SCALE insulin Q 0.4-6 hours
3. Transition to a long + short acting insulin for basal-bolus insulin therapy
TRANSITION FROM IV TO SC
INSULIN - FACTORS TO CONSIDER

1. Stability of the insulin infusion rate
   - Initial rates when glucose is uncontrolled can be high and then as it stabilizes, the rates may decrease.
   - Ideally use at least 6 hours of stable glucose and infusion rates.

2. Nutrition status while on infusion
   - If patient was eating without prandial insulin coverage, the glucose abruptly rises after food, followed by significant increase in insulin infusion rates.
   - If the patient was on TPN or tube feedings, will there be a upcoming change in nutrition?

3. Level of glucose control
   - Some % of the total IV insulin requirements is used to calculate the SC insulin dose.
   - If glucose was not at target, may need to increase the conversion factor.

4. Other factors influencing insulin infusion rate
   - Medications: Corticosteroids, vasopressors
   - Organ function: acute renal failure
   - Resolving infection

TRANSITION FROM IV TO SC
INSULIN - EXAMPLE

- Use approx. 50-80% of stable 24 hour IV insulin requirements (if not wean for 24 hours, can extrapolate over a recent stable period).
  - 70 units x 0.7 = 49 units (total 24 hour SC insulin dose).

- For glargine/detemir + lispro/aspart regimen:
  - 50% Basal: 49 x 0.5 = 25 units.
  - 50% Nutritional divided Q fixes: 8 units.
  - Use a corrective algorithm in addition to scheduled prandial.

- For NPH + lispro/aspart regimen:
  - 2/3 NPH - divided into two doses: 49 x 2/3 = 16 units before breakfast and bedtime.
  - 1/3 Nutritional, divided TID with meals = 5 units before each meal.
  - Always discontinue the insulin drip two hours after the first long acting subcutaneous insulin dose.

ADMISSION #2: FEVER

- 66 year old female admitted with fever of 103°F, SOB and hypotension.
- Intubated, on pressors and admitted to Medical ICU.
- Found to have a multilobar pneumonia with SIRS.
- No history of Type 2 Diabetes but has HTN, Hyperlipidemia, CAD, COPD.
- Labs: Glucose = 225 mg/dL, repeat accucheck 253 mg/dL. HgbA1c = 6.3%. Creatinine = 1.8. AST/ALT = normal.

How should we treat this patient?

1. No therapy needed as this is acute hyperglycemia and not diabetes.
2. Start SLEDING SCALE Subcutaneous insulin 4-6 hours.
3. Start Insulin Infusion with a glucose target of 110-140 mg/dL.
4. Start Insulin Infusion with a glucose target of 140-180 mg/dL.
ADMISSION #2: CONTINUED

- Patient was managed on insulin infusion and reached the target
- Over the next 48 hours, patient is supported with mechanical ventilation, Norepinephrine, stress dose hydrocortisone, iv antibiotics
- Still not improved and TPN is started due to ileus
- Insulin infusion has been titrated up to 6-10 units/hr and she is requiring >180 units of IV insulin per 24 hours
- Labs: Cr = 2.6, LFTS now 3x normal

What is the next step?
1. Change to sliding scale insulin
2. Transition to basal bolus subcutaneous insulin regimen
3. Add NPH or Lantus in addition to iv insulin infusion
4. Add Regular insulin into the TPN formula

ADMISSION #2 - ADDING INSULIN IN TPN

- Insulin is more effective when added to the TPN
- Delay in preparation of TPN, often 12-24 hours later requires planning
- Watch for clinical and medication changes and plan insulin in TPN in advance to avoid hypoglycemia.
- Evidence for dosing is limited but expert opinion:
  - DM: 1 unit per 12-15 grams of dextrose in addition to basal bolus insulin regimen
  - No DM: 1 units per 15-20 grams of dextrose with rapid acting correction insulin

ADMISSION #3

- 33 year old female with Type 1 Diabetes managed on an insulin pump
- Developed nausea and vomiting and was brought to ED due to increasing lethargy
- On presentation: Shallow and rapid respirations, minimally responsive Glucose 750 mg/dl, Sodium 129 mg/dl, Bicarb 9, Cr 1.4

What is the diagnosis?
1. Gastroenteritis
2. Insulin pump failure
3. Acute kidney injury
4. All of the above
DKA AND HHS: DIAGNOSTIC CRITERIA

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH</td>
<td>Mild (plasma glucose &gt;250 mg/dl)</td>
<td>Moderate (plasma glucose &gt;250 mg/dl)</td>
</tr>
<tr>
<td></td>
<td>7.25–7.30</td>
<td>7.00 to &lt;7.24</td>
</tr>
<tr>
<td>Serum bicarbonate (mg/dl)</td>
<td>15–18</td>
<td>10 to &lt;15</td>
</tr>
<tr>
<td>Urine ketone</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Serum ketone</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Effective serum osmolality</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Anion gap</td>
<td>&gt;10</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert</td>
<td>Alert/drowsy</td>
</tr>
</tbody>
</table>

DIAGNOSTIC CRITERIA

- glucose >250 mg/dl

DKA/HHS TREATMENT PROTOCOL

- IV Fluids
  1. 0.9% Saline at 500-1,000 ml/h for 2 h, then
  2. 0.45% saline at 250-500 mL/h until blood glucose <250 mg/dL, then
  3. Dextrose 5% in 0.45% saline at 150-250 ml/h until resolution of DKA
**DKA/HHS TREATMENT PROTOCOL**

- **Potassium Replacement**
  1. If initial $K^+$ > 5.5 mmol/L, do not give K but recheck every 2 hours
  2. Add $K^+$ as needed based on subsequent values
    1. $K^+ = 4$-5.5 mmol/L, add 20 mmol/L of KCL to IV fluid
    2. $K^+ = 3$-4 mmol/L, add 40 mmol/L of KCL to IV fluid
    3. $K^+ = <3$ mmol/L, give 10-20 mmol of KCL per hour until serum $K^+ >3$ mmol/L, then add 40 mmol/L of KCL to IV fluid

**DKA/HHS TREATMENT PROTOCOL**

- **IV Insulin Therapy**
  1. Give IV bolus of regular insulin of 0.1 U/kg
  2. Start continuous insulin infusion at 0.1 U/kg/h
  3. When blood glucose <250 mg/dL:
    - Change IV fluids to 0.45% saline
    - Reduce insulin infusion rate to 0.05 units/kg/h to keep glucose = 200 mg/dL until resolution of DKA

**DKA/HHS TREATMENT PROTOCOL**

- **Transition to SQ insulin therapy**
  - Continue insulin infusion until resolution
    - DKA: glucose <200 mg/dL, bicarbonate ≥ 18 mEq/L, pH ≥ 7.30, and anion gap ≥ 14 mEq/L
    - HHS: serum osmolality <320 mOsm/kg and glucose ≤ 250 mg/dL with recovery of mental status
  - SQ insulin therapy
    - Previous DM: restart home insulin regimen if adequate glycemic control before admission
    - New diagnosis: Total daily dose of 0.5-0.8 U/kg/day of body weight
    - REMEMBER to administer the first basal SQ dose 2-4 hours PRIOR to discontinuation of IV insulin therapy
DKA/HHS TREATMENT PROTOCOL

- **Bicarbonate**
  1. If arterial pH < 6.9, administer 44.6 mEq of sodium bicarbonate in 200ml of 0.45% saline over 1 h until pH increases to 6.9-7.0
  2. Do not give bicarbonate if pH > 7.0

- **Laboratory Assessment**
  Admission: CBC with differential, complete metabolic panel, venous or arterial pH, and serum β-hydroxybutarate, HgbA1c. Consider cardiac, CV, infection or substance abuse workup if indicated
  During Treatment: basic metabolic profile, venous pH, phosphorus, and β-hydroxybutarate
  Glucose monitoring: capillary blood glucose every 1.2 h at the bedside

SQ INSULIN PROTOCOLS

- **SQ rapid acting insulin every 1 h (SQ-1h):**
  1. Initial dose SQ: 0.2 U/kg of body weight, followed by 0.1 U/kg/h
  2. When BG < 250 mg/dL, change IVF to D5%-0.45% saline and reduce SQ rapid acting insulin to 0.05 unit/kg/h to keep glucose ≈ 200 mg/dL until resolution of DKA

- **SQ rapid acting insulin every 2 h (SQ-2h):**
  1. Initial dose SQ: 0.3 U/kg of body weight, followed by 0.2 U/kg 1 h later, then
  2. SQ rapid acting insulin at 0.2 U/kg every 2 h
  3. When BG < 250 mg/dL, change IVF to D5%-0.45% saline and reduce SQ rapid acting insulin to 0.1 U/kg every 2 h to keep glucose ≈ 200 mg/dL until resolution of DKA

SQ LISPRO VS IV REGULAR INFUSION FOR DKA

<table>
<thead>
<tr>
<th>Study or insulin type</th>
<th>Stolte et al., 2003 (104 U)</th>
<th>Tresidder et al., 2002 (104 U)</th>
<th>Tresidder et al., 2002 (104 U)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin type</strong></td>
<td>Regular</td>
<td>Regular</td>
<td>Regular</td>
</tr>
<tr>
<td><strong>Age and Gender</strong></td>
<td>Male (52), Female (48)</td>
<td>Male (52), Female (48)</td>
<td>Male (52), Female (48)</td>
</tr>
<tr>
<td><strong>Type of diabetes</strong></td>
<td>Type 2</td>
<td>Type 2</td>
<td>Type 2</td>
</tr>
<tr>
<td><strong>Time to achieve</strong></td>
<td>18 h</td>
<td>12 h</td>
<td>12 h</td>
</tr>
<tr>
<td><strong>Glucose (mg/dL)</strong></td>
<td>150 (20)</td>
<td>150 (20)</td>
<td>150 (20)</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>120 (20)</td>
<td>120 (20)</td>
<td>120 (20)</td>
</tr>
<tr>
<td><strong>Weight loss (kg)</strong></td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td><strong>Hyperglycemic events</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Intravenous fluids</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Data from Vincent and Noreau, Diabetes & Metabolism 39: 293-305, 2013*
GLP-1 RECEPTOR ANTAGONIST THERAPY IN CRITICALLY ILL PATIENTS

**Advantages:**
- Glucose-dependent insulin stimulation prevents hypoglycemia
- Glucagon inhibition may be useful in the maladaptation of the stress response
- Suppression of hepatic glucose
- Increased tissue insulin sensitivity
- Potential cardiovascular benefits with improved cardiac function, reduced infarct size
- Less nursing time to monitor glucose and administer insulin

**Disadvantages:**
- Small, limited studies investigating use in critically ill patients
- Usually compared to placebo, not insulin
- High incidence of GI side effects
- Rescue insulin therapy often needed
- Long term effects unknown
- More studies needed

Schwarz S, D’Antona, RA. Diabetes Care 2013 Vol 36 (7):2112
Umpierrez GE, Korytkowski M. Diabetes Care 2013 Vol 36 (7):2112

THANK YOU FOR YOUR ATTENTION!