Diabetic Emergencies

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“I need someone well versed in the art of torture—do you know PowerPoint?”

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I have No Financial Disclosures
Goals

- DKA treatment guidelines (Peds vs Adult)
- *Interesting* pathophysiology
- Cerebral Edema
- Controversies

**Diabetic Ketoacidosis (DKA)**

- Hyperglycemia (glc>250)
- Ketonemia
- Anion Gap Metabolic Acidosis (pH<7.3  HCO3<18) (gap >10)

*Kitabchi et al, Hyperglycemic Crises in Adult Patients with Diabetes, Diabetes Care, 2009*
Hyperosmolar Hyperglycemic State (HHS)

- High serum osmolality (>320mOsm/kg)
- High glucose (>600)
- No or small acidosis / ketonemia

Kitabchi et al, Hyperglycemic Crises in Adult Patients with Diabetes, *Diabetes Care*, 2009

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Insulin  Stress Hormones

Feast <---> Famine

Normal Glucose
**Get Sick / No Insulin**

- Insulin << Stress Hormones

- Muscle Tissues → LIVER

- Hyperglycemia!

- Osmotic Diuresis

- Dehydration Acidemia Electrolytes Renal Impairment

- Cortisol

- Catechol

- GLUCAGON

- Fat

- FFA

- KetoACIDS KETONES

**Goals of Treatment**

- ABCs
- Underlying Cause
- Volume deficit and dehydration
- Correct electrolytes, especially K+
- Reverse acidosis and treat glucose
- Treat Cerebral edema
- Do no harm
16 y F h/o IDDM

- BP = 153/84  P = 146  R = 30  T = 97
  Sat = 97%  Wt = 175 lbs
- Glucometer = “high”
- Complains of “pain all over”
- Looks sick, ?AMS, smells of ketones

IV, 02, Monitor

- ABC’s and D
- Move to appropriate room in your ED
- Find underlying cause and treat it.
- “When the sugar is high…You got to treat the reason why!”
Why?

Urine
Xrays
Cultures/Lactate
Tox?
Pregnant? PID?
PE, MI, Abdominal pathology, Skin, Thyroid, meds, Zebras?

More on labs…

- Ca, Mg, Phos
- EKG
- Beta hydroxybutyrate vs serum ketones vs urine ketones?
- ABG or VBG
What do you want to do?

1. Insulin SQ, 1-2 liter NS bolus
2. Insulin IV bolus, 1-2 liter NS bolus
3. Insulin IV bolus followed by insulin drip, 1-2 liter NS bolus
4. 1-2 liter NS bolus, wait for study results for further care

There is universal agreement that the most important initial therapeutic intervention in DKA is appropriate fluid replacement followed by insulin administration.

Joint British Diabetes Societies Inpatient Care Group
The Management of Diabetic Ketoacidosis in Adults
March 2010
“Fluids come first ‘cuz they’re dyin of thirst!”

- Adult deficit~ 6L in DKA, ~9L HHS
- Prerenal→Volume = Crystalloid
- All patients start on single bolus over 1 hr.
- Kids 10-20ml/kg, Adults 1-2L
- More if in shock, less if heart dz
Get Sick / No Insulin

Cortisol
Catechol
GLUCAGON

Insulin << Stress Hormones

Muscle Tissues LIVER Fat

Hyperglycemia!

KetoACIDS KETONES

Osmotic Diuresis

Dehydration Acidemia Electrolytes Renal Impairment

Total Body K+ is Low...

- Osmotic diuresis
- Vomiting

↓↓Volume↑↓aldosterone↑↓kidneys↑↓
spare Na/H2O, waste K+

- Typical deficit = 3-5mmol/kg
But **serum** K+ is usually normal or high

- Due to low pH?
- Due to insulin deficiency mostly


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Know your serum K+ level before giving insulin

- Stat K+
- EKG

“Keep insulin at bay… until you know the K+”
**Hypokalemia**

- Must replete before insulin if $K^+ < 3.3$
- Add 20mEq to 1 liter NS if hemodynamically unstable
- If stable, add 40-60mEq to 1 liter 1/2 NS and run over 2 hrs.
- Oral load?

**Hyperkalemia**

- Best treatment is fluids and insulin
- Consider bicarb and calcium for life-threatening hyperkalemia (ekg changes)
- You will probably still have to give potassium later on!
Goals of Treatment

- ABCs
- Underlying Cause
- Volume deficit and dehydration
- Correct electrolytes, especially K+
- Reverse acidosis and treat glucose
Insulin when K+ is OK

- Adults: 0.1 unit/kg bolus → 0.1 unit/kg/hr drip

- Or…. 0.14 units/kg/hr drip only

- Kids don’t get bolus…just the drip at 0.1

The bolus swole us.
When glc < 200-300…
Continue insulin drip at 0.05-0.1 units/kg/hr
Add 5% dextrose to the 1/2NS (+/- K+)

The cure for acidosis is *insulin*… *Not* a normal sugar!

Your Studies Come Back
- WBC = 31, Hgb = 13.3, Plt = 422
- Na = 123, K = 5.9, Cl = 87, bicarb = 5, BUN = 20, Cr 1.3, glc = 812.
- Large acetone
- Gap = 31
- UA, preg, u tox, LFTs, cxr = neg
- EKG = sinus tach, o/w neg
How’s our Patient?

- Therapy so far = 2 liters NS
- BP = 120’ s/70’ s HR = 130’ s RR = 30
- Altered?

ABG

- pH = 6.855
- pCO2 = 9.7
- PO2 = 126
- Bicarbonate = 1.7
What do you want to do?

1. One more liter NS, start insulin, give bicarb
2. Two more liters NS, start insulin
3. NS at 200ml/hr, start insulin
4. Give mannitol, send to CT scanner

Cerebral Edema

- 0.3% to 1% of pediatric DKA
- 21% to 24% mortality
- 21% to 26% permanent neuro morbidity
- 57% to 87% of all DKA deaths
Who’s at risk?

- Younger
- New onset DKA (67%)
- Higher BUN
- Low pCO2
- Low pH
- Failure of Na to rise appropriately

Glaser et al, NEJM, 2001
Edge et al, Diabetologia, 2006
Hoorn et al, J Pediatr, 2007
Lawrence et al, J Pediatr, 2005

When does it happen?

- Typically becomes clinical 4-12 hours after initiation of treatment
- Some are already symptomatic when they arrive…

Krane et al, NEJM, 1985
Hoffman et al, American Journal of Neuroradiology, 1988
Symptoms and Signs of Cerebral Edema

- Headache
- Recurrence of vomiting
- Inappropriate slowing of heart rate
- Rising blood pressure
- Decreased oxygen saturation
- Change in neurological status:
  - Restlessness, irritability, increased drowsiness, incontinence
  - Specific neurologic signs, e.g., cranial nerve palsies, abnormal pupillary responses, posturing

http://care.diabetesjournals.org/cgi/content/full/29/5/1150

Should I get a CT?

- If you are really concerned, CT can help establish baseline or reveal other sequelae
- CE is clinical diagnosis
- CT has false positives and negatives

Muir et al, *Diabetes Care*, 2004
Krane et al, *NEJM*, 1985
Treatment of Cerebral Edema

- Mannitol 0.25-1g/kg bolus
- 3% NaCl 5-10mL/kg over 30 minutes

Wolfsdorf et al, *Diabetes Care*, 2006
Jeha et al, *UpToDate*, 2008

Did I cause the cerebral edema?
**Osmotic Edema Theory**

- Treatment drops intravascular osms --> water shifts into brain --> swelling
- Aggressive IVF and insulin BAD

The bolus swole us.

*Edge et al, Diabetologia, 2006*
*Hoorn et al, J Pediatr, 2007*
*Levin et al, Pediatr Crit Care Med, 2008*

**Vasogenic Edema Theory**

- Hypoperfusion --> injury --> reperfusion injury
- Supported by MRI studies
- No link between rate of fluid or insulin administration.
- Strong link with severity of illness

*Glaser et al, J Pediatr, 2004*
*Glaser et al, J Pediatr, 2008*
*Lawrence et al, J Pediatr, 2005*
*Figueroa et al, Endocrine Research, 2005*
*Glaser et al, NEJM, 2001*
*Hom et al, Annals Emerg Med, 2008*
Pediatric Fluids Summary

- Treat shock and sepsis with NS boluses
- If stable after first 10-20ml/kg bolus…
- Start 1.5x - 2x maintenance (add K+)
- Add dextrose when glc<300

Wolfsdorf et al, Diabetes Care, 2006
Dunger et al, Pediatrics, 2004
Jeha et al, UpToDate

Should I give her bicarb?

- Increased risk of cerebral edema
- May cause other bad things
- No evidence that it helps
- ARF or diarrhea?

Bicarb in the brain causes swelling and pain
Yeah, but what about that pH?

- Treat perfusion problems with fluids
- Treat infection with fluids and abx
- Treat ketoacidemia with insulin
- Watch for hyperchloremic acidosis

Should I give Bicarb to Adults?

- May cause bad things
- No evidence that it helps
- Diarrhea or ARF?
- Consider in low pH and severe cardiac dz?

Kitabchi et al, Hyperglycemic Crises in Adult Patients with Diabetes, Diabetes Care, 2009
How is our Patient?
3 hours later…

- 3.5 liters of NS, insulin gtt at 10 units/hr
- BP = 130/70  HR = 120’ s  RR = 30’ s
- Na = 129,  K = 6,  Cl = 98,  CO2 < 5,
- glc = 621, gap = ≥ 26
- Corrected Na = 141 (from 140)
- Mental status?

**TABLE 1.** Mean Arterial Blood pH, Plasma Bicarbonate Concentrations, and Fractional Shortening of the Left Ventricle during Systole in 10 Patients before and after Correction of Ketoadidosis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>At Base Line</th>
<th>After Correction of Ketoadidosis</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial blood pH</td>
<td>7.07±0.2</td>
<td>7.42±0.05</td>
<td>0.005</td>
</tr>
<tr>
<td>Plasma bicarbonate (mmol/liter)</td>
<td>6.9±4.9</td>
<td>22.8±2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>104±20</td>
<td>98±23</td>
<td>0.33</td>
</tr>
<tr>
<td>Left ventricular fractional shortening (%)†</td>
<td>37.8±3.9</td>
<td>36.6±2.6</td>
<td>0.26</td>
</tr>
</tbody>
</table>

*P values were calculated with the Wilcoxon test.
†The mean normal value is 36±6 percent.
What if I have to intubate?

- Treat shock before intubating if possible
- Take your absolute Best shot
- Immediate blood gas
- Bicarb?

Ventilation Goals

- Avoid hyperventilation
- May decrease intracranial blood flow and worsen cerebral edema
- Aim for pt’ s own pC02

Phos?

- Treat if severe <1mg/dl
- Can use Kphos
- Phos replacement can drop calcium, so monitor.

Wolfsdorf et al, Diabetes Care, 2006

Central Line?

- Children in DKA ↑ risk DVT
- DKA suggested prothrombotic state
- Avoid it if you can.

Worly et al, Pediatrics, 2004
Gutierrez, Crit Care Med, 2003
When are you done?

• Close the gap (bicarb may still be low)
• Eating and drinking
• Transition to SQ insulin

Summary

• ABCD’s
• Find and treat underlying cause
• Fluid resuscitate
• Treat the K+
• No insulin until you know the K+
Special Peds Considerations

- Expand volume with NS 10-20ml/kg bolus over 1-2 hours. Repeat x1 prn.
- Gentle rehydration at 1.5-2 x maintenance to avoid cerebral edema…(maybe)
- No insulin bolus…only use drip (usually 0.1unit/kg/hr)
- Avoid bicarb, central lines, ABG’s (use venous or capillary samples)
- Treat cerebral edema with mannitol or hypertonic saline (3%)

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<table>
<thead>
<tr>
<th></th>
<th>Peds</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Bolus</td>
<td>NO</td>
<td>+/-</td>
</tr>
<tr>
<td>Insulin Drip</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Bicarb</td>
<td>NO</td>
<td>+/-</td>
</tr>
<tr>
<td>Fluids</td>
<td>CAUTIOUS (unless shock)</td>
<td>Less cautious</td>
</tr>
<tr>
<td>Central line</td>
<td>AVOID</td>
<td>OK</td>
</tr>
<tr>
<td>Infection</td>
<td>Less Common</td>
<td>More Common</td>
</tr>
</tbody>
</table>
### Important Formulae

- Anion Gap = (Na) - (Cl) - (HCO3)
- Effective osmolality = 2xNa + glc/18
- Corrected Na = Na + [(glc - 100) x 0.016]
- Alternative equation =>
  - Corrected Na = Na + [ΔSG ÷ 42]

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<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucose (mg/dl)</strong></td>
<td>&gt;250 mg/dl</td>
<td>&gt;600 mg/dl</td>
</tr>
<tr>
<td><strong>Arterial pH</strong></td>
<td>7.25–7.30</td>
<td>&gt;7.30</td>
</tr>
<tr>
<td><strong>HCO3 (mEq/l)</strong></td>
<td>15–18</td>
<td>&gt;15</td>
</tr>
<tr>
<td><strong>Ketones</strong></td>
<td>Positive</td>
<td>Small</td>
</tr>
<tr>
<td><strong>Serum Osm</strong></td>
<td>Variable</td>
<td>&gt;320</td>
</tr>
<tr>
<td><strong>Anion gap</strong></td>
<td>&gt;10</td>
<td>&lt;12</td>
</tr>
<tr>
<td><strong>Mental status</strong></td>
<td>Alert/drowsy</td>
<td>Stupor/coma</td>
</tr>
</tbody>
</table>

Kitabchi et al, Hyperglycemic Crises in Adult Patients with Diabetes, *Diabetes Care*, 2009
Correct the sodium…it’s not as low as it looks!

- Corrected serum Na = Measured serum Na + \[\Delta SG \div 42\]

- where \(\Delta SG\) is the increment above normal in the serum glucose concentration (in mg/dL).

- So for our case Na = 123 + (812-100)/42 = 140

Peds Hourly Maintenance IVF
The 4,2,1 Rule

- 4mL/kg per hour for 1st 10kg
- 2ml/kg per hour for 2nd 10kg (11-20kg)
- 1ml/kg per hour for every kg over 20kg

- Example 55kg child =
- 4x10 + 2x10 + 1x35 =95ml/hr
VBG vs ABG

- pH - 0.05 lower than arterial pH
- pO2 - 40-50 instead of 100
- pCO2 - about 5 higher than arterial pCO2 (45 rather than 40)

DKA Aphorisms

- If the sugar is high... you got to treat the reason why.
- Fluids come first, cuz they’re dyin’ of thirst.
- Keep insulin at bay...until you know the K+.
- “The bolus swole us.”
- Bicarb in kids brain causes swelling and pain.