DIABETIC KETOACIDOSIS PROTOCOL
2019 REVISION
www.bcchildrens.ca/endocrinology‐diabetes‐site/documents/dkaslides.pptx

DIAGNOSIS OF DKA
• hyperglycemia: glucose ≥11.1 mmol/L
• acidosis: pH <7.3 or HCO₃⁻ <15 mmol/L
• ketones in blood and/or urine
• ~10–20% of kids with new‐onset T1D present in DKA
• DDx: hyperglycemic hyperosmolar state

SEVERITY OF DKA

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>&lt;7.3</td>
<td>&lt;15</td>
</tr>
<tr>
<td>moderate</td>
<td>&lt;7.2</td>
<td>&lt;10</td>
</tr>
<tr>
<td>severe</td>
<td>&lt;7.1</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

DKA: PATHOPHYSIOLOGY
• metabolic effects of insulinopenia
  • glucose uptake into muscle, fat, liver
  • ~gluconeogenesis, ~glycogenolysis, ~lipolysis, ~ketogenesis
• hyperglycemia, obligate diuresis
• ~stress hormones aggravate situation
• metabolic acidosis: ketones, lactate
• huge losses of H₂O, Na⁺, K⁺, HCO₃⁻, Pi

RATIONALE FOR 2019 REVISION
• The PECARN FLUID Trial demonstrated that fast vs slow rehydration for DKA seems to be equivalent with respect to:
  • brain injury (0.9%)
  • short‐term memory
  • post‐event memory
  • IQ
  • serious adverse events
• some suggestion (not significant) that faster rehydration:
  • led to less ~ in GCS
  • led to faster ~ in short‐term memory scores in sickest patients

Diabetes Care 2006;29:1150–1159
DKA PROTOCOL 2019: GENERAL PRINCIPLES

• 10–20 mL/kg fluid push up front, repeat if CV status not improved
• assume 5–10% dehydration (7% for most)
• even rehydration over 24–36 h
• use of 0.45–0.9% NaCl-containing fluids
• avoid use of bicarbonate
• no insulin in the 1–2 h of treatment
• continuous insulin infusion, glucose to match
• continued use of the “two-bag” method

MODIFICATIONS FROM 2015 PROTOCOL

• more-aggressive fluid boluses are suggested at the start of therapy:
  o all patients with DKA should receive a 10-mL/kg bolus of normal saline at the beginning
  o the majority will receive a second 10-mL/kg bolus to follow
• fluid infusion rate calculations have been simplified
• fluid rehydration rates will reflect a goal to correct losses over a 36-h period (previously this was 48 h)

DKA PROTOCOLS: DISCLAIMER

• no DKA protocol has been shown to eliminate the risk of cerebral injury
• current gold standard: ISPAD Clinical Practice Consensus Guidelines 2018
• guidelines should not replace intelligent thought and should be tailored to meet the needs of each individual patient
• involve Pediatric Endocrinology early!

ISPAD 2018

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• involve Pediatric Endocrinology early!

TREKK
**DKA NURSING DOCUMENTS**

**BCCH DKA PROTOCOL 2019: TIMELINE**
- on admission: weight, vitals, assessment and stabilization
- first 30–60 minutes: fluid resuscitation
- 60 min–36 h:
  - fluid replacement
  - insulin infusion
  - addition of glucose
- throughout:
  - careful monitoring, reassessment
  - titration of fluids, electrolytes, glucose, insulin

**INITIAL ER MANAGEMENT**
- ABC's and GCS
- weigh patient
- insert large-bore IV
- check chemistries, CBG, urine/blood ketones
- evaluate dehydration
- think about underlying illness (infection, etc.)

**EVALUATING DEHYDRATION**
- best:
  - prolonged capillary refill (>1.5–2 sec)
  - abnormal skin turgor
  - abnormal respiratory pattern
- also:
  - no tears
  - weak pulses
  - cool extremities
  - HR
- poor:
  - dry mouth
  - urine output
  - BP
  - weight

**ESTIMATING DEHYDRATION (% BODY WEIGHT)**

<table>
<thead>
<tr>
<th></th>
<th>INFANTS</th>
<th>KIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>MODERATE</td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>SEVERE</td>
<td>15%</td>
<td>9 (10)%</td>
</tr>
</tbody>
</table>

**CAUTIONS IN APPROACH**
- fluid and electrolyte imbalances in patients presenting in DKA can be quite disparate:
  - kid has been drinking only water all day
  - kid has been drinking juice all day
  - kid has been vomiting all day
  - kid has been having chicken soup all day
- some kids may have insulin on board
- many patients present with an element of hyperglycemic hyperosmolar state and/or hypernatremic dehydration
BCCH PROTOCOL: 1st 60 MINUTES

- give 1st bolus of NS 10 mL/kg IV over 30 min
- most sicker patients require a 2nd NS bolus of 10 mL/kg IV over 30 min
- the sickest patients may require even more NS to stabilize HR and peripheral perfusion

BCCH PROTOCOL: 60 MINUTES–36 HOURS

- begin even rehydration over 36 h, estimating 10% dehydration:
  - 5–10 kg BW: 6.5 mL/kg/h
  - 10–20 kg BW: 6 mL/kg/h
  - 20–40 kg BW: 5 mL/kg/h
  - >40 kg BW: 4 mL/kg/h, max 250 mL/h
- start with NS + 40 mEq KCl/L, assuming patient is urinating

“TWO-BAG” METHOD

- at 60–120 min after start of 1st fluid bolus, begin insulin infusion:
  - 0.05–0.1 Units/kg/h
  - 0.5–1 mL/kg/h of 50 units Regular insulin in 500 mL NS
- when BG is <25 mmol/L and falling >5 mmol/L/h, add dextrose to IV fluids using the “two-bag” method

BCCH PROTOCOL: 60 MINUTES–36 HOURS

- aim to keep BG in the ~8–12 mmol/L range by titrating the rates of the two Bags A and B
- a general rule is to make changes of approximately 10–20% of the total rate every hour
- if the patient’s BG is lower than desired, despite maximal dextrose infusion from Bag B, you may (in order of safety):
  - cut the insulin infusion rate by ~25%, provided the acidosis is correcting
  - give the patient a small amount (1–2 mL/kg) of juice or 2–4 dextrose tablets (being mindful of the overall fluid balance)
  - change the insulin Bag C to D10/NS
  - in institutions with intensive-care capabilities, consider placing a central line and using a higher concentration of dextrose (e.g. D20) in Bag B

BCCH PROTOCOL: 60 MINUTES–36 HOURS

- at 4–6 h after initial fluids and if corrected Na⁺ is ≥145 mmol/L, stable or increasing:
  - switch Bag A to ½NS + 40 mEq/L KCl
  - switch Bag B to D10/½NS + 40 mEq/L KCl
- if unable to get K⁺ >3.5 mmol/L with IV fluids: consider PO/NG KCl
- may give 50% of K⁺ as phosphate (order by the mmol of K⁺)
- may prevent ensuing hyperchloremia, but no clear evidence of benefit
- bicarbonate: rarely if ever needed
**ONGOING MONITORING**

- BG by meter q30–60 min (may need lab BG if >30 mmol/L)
- Na⁺, K⁺, Cl⁻, HCO₃⁻, anion gap, urea, creatinine, venous pH q2–4 h
- Ca²⁺, Mg²⁺, P, q2–4 h if giving phosphate
- β-hydroxybutyrate (preferably) or urine ketones q2–4 h
- neurovital signs/GCS q30–60 min

- corrected Na⁺ = [measured Na⁺ + 0.36×(BG−5.6)]
- active osmolality = [BG + 2×(Na⁺+K⁺)]

**URINE vs BLOOD KETONES**

<table>
<thead>
<tr>
<th>URINE KETONES</th>
<th>β-HYDROXYBUTYRATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>≤0.5 mmol/L</td>
</tr>
<tr>
<td>trace (&lt;0.5 mmol/L)</td>
<td>0.6–0.9 mmol/L</td>
</tr>
<tr>
<td>small (1+, 0.5 mmol/L)</td>
<td>1.0–1.4 mmol/L</td>
</tr>
<tr>
<td>moderate (2+, 1.5 mmol/L)</td>
<td>1.5–2.4 mmol/L</td>
</tr>
<tr>
<td>large (3+, 4 mmol/L)</td>
<td>2.5–2.9 mmol/L</td>
</tr>
<tr>
<td>very large (4+, 8 mmol/L)</td>
<td>≥3.0 mmol/L</td>
</tr>
</tbody>
</table>

**FALL IN BLOOD VS. URINE KETONES IN DKA**

[Graph showing fall in blood β-hydroxybutyrate vs urine ketones]

**ACUTE KIDNEY INJURY**

- DKA should be considered a multiple organ dysfunction syndrome
- kids in DKA have a high risk (64%) of acute kidney injury (AKI)
- use Schwartz formula to calculate expected baseline creatinine:
  - EBC (µmol/L) = 36.5 × height (cm)/120
  - measured creatinine 1.5–1.99×EBC = Stage 1
  - measured creatinine 2–2.99×EBC = Stage 2
  - measured creatinine ≥3×EBC = Stage 3
- some creatinine assays have cross-reactivity with ketones!

**MECHANISMS OF CEREBRAL INJURY**

- vasogenic edema: leakage across altered BBB
  - hypoxia
  - cerebral hypoperfusion/reperfusion
  - neuroinflammation (IL-6, etc.)
  - ketones (altered BBB)
  - hypcapnia (↓ cerebral blood flow)
- other possible factors:
  - role of Na⁺–H⁺ antiporter-3 (insulin) and Na⁺–K⁺–Cl⁻ cotransporter-1
  - continued absorption of H₂O from GI tract
  - vasopressin, atrial natriuretic peptide
  - cellular edema: osmotic shifts across cell membrane

**CEREBRAL INJURY: MORTALITY**

- can be present at diagnosis before treatment
- usually occurs in first 12–24 hours of treatment
- DKA still has ~0.5–1% risk of cerebral injury
- ~25% mortality rate, ~35% serious morbidity rate
- 70–80% of diabetes-related deaths in kids <12
- greatest contributor (~50%) to mortality of DKA, not hyperglycemia or shock
- subclinical CI with subtle sequelae may be frequent in DKA
BASELINE RISK FACTORS FOR CI

• infants and young children
• new-onset (3.3% vs. 0.23% in known pts)
• long-standing symptoms
• ↑ serum Na⁺, ↓ serum Na⁺
• ↓ pCO₂ (even adjusting for pH), ↓ pH (most acidic)
• ↑ plasma urea, ↑ serum K⁺, ↑ hematocrit (most dehydrated)
• “sickest looking”?

TREATMENT-RELATED RISK FACTORS FOR CI

• too-rapid fall in “corrected Na⁺”
  o Na⁺ + [0.36 × (glucose – 5.6)]
• failure of uncorrected Na⁺ to rise
• too-rapid fall in “active osmolality”
  o glucose + [2 × (Na⁺ + K⁺)]
• bicarbonate therapy
• early (<60 min) insulin Rx or large insulin boluses
• fluids ≥4 L/m²/24 h or ≥50 mL/kg in 1st 4 h

CEREBRAL INJURY: SYMPTOMS

• severe headache
• change in sensorium: irritability, confusion, inability to arouse
• dilated pupils, papilledema, cranial nerve palsies
• posturing, incontinence
• decreased O₂ saturation
• Cushing’s triad
  o bradycardia
  o hypertension
  o irregular respirations

CEREBRAL INJURY: TREATMENT

• elevate head of bed
• reduce fluid rate by ⅓
• mannitol 20% 0.5–1 g/kg (2.5–5 mL/kg) IV over 15 min
• NaCl 3% 2.5–5 cc/kg IV over 15 min
• intubate if pending respiratory failure
• mild hyperventilation
• no known role for dexamethasone
• early Dx and Rx improve outcome

OTHER COMPLICATIONS OF DKA

• hypokalemia*, hypocalcemia, hypomagnesemia, hypophosphatemia*
• hyperchloremic acidosis
• hypoglycemia
• peripheral venous*, dural sinus, basilar artery thrombosis
• pulmonary embolism*, pulmonary edema*, pneumothorax, aspiration pneumonia*, ARDS
• rhabdomyolysis*
• acute pancreatitis*
• intracranial hemorrhage, cerebral infarction
• acute kidney injury*

*HHS > DKA

HYPERGLYCEMIC HYPEROSMOLAR STATE

• hyperglycemia: glucose >33.3 mmol/L
• hyperosmolality: osmolality >320 mOsm/kg
• small ketonuria, absent-to-small ketonemia
• absence of significant acidosis: pHven >7.30, pHart >7.25, HCO₃⁻ >15
• obtundation, combativevness, seizures (~50%)”
• seen in T2D, obese, blacks
• also seen in T1D drinking lots of pop
• can have mixture of DKA and HHS
HHS vs. DKA
• ↑ hyperosmolality, ↑ hyperglycemia
• ↑ dehydration, ↑ fluid Rx needed
• ↑ electrolyte loss
• ↓ acidosis, ↑ HCO₃⁻
• may not need much or any insulin
• ↑ risk of shock, thrombosis, rhabdomyolysis
• ↓ risk of cerebral injury

TREATING HHS
• assume 12–15% dehydration
• fluids: 20 cc/kg NS, then balance Na⁺ content:
  o intravascular needs vs. lowering osmolality
• K⁺: 20 mEq/L KCl + 20 mEq/L KPhos
• insulin: 0.025 U/kg/h if BG won’t ↓ with fluids
• lower Na⁺ by ~0.5 mmol/L/h
• lower glucose by ~3–5 mmol/L/h

HHS ALGORITHM

RECURRENT DKA
• most often seen in:
  o very small kids with GI illness
  o unsupervised kids
  o non-compliant teens
  o insulin pump site problems
• nearly all cases of recurrent DKA are preventable!
• get an A1C!

DKA PREVENTION (BC PEDIATRIC SOCIETY)

EDU WEBSITE
http://endodiab.bcchildrens.ca
REFERENCES


• Translating Emergency Knowledge for Kids (TREKK Canada): http://trekk.ca.


• BC Children’s Hospital ePOPS (Electronics Policies, Order Sets, Procedures and Standards): https://epops.bchbc.ca.