
پیام خدا

DIABETIC KETOACIDOSIS

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INTRODUCTION

- DKA is the leading cause of morbidity and mortality in children with type ١ diabetes mellitus.
- It occurs at the time of diagnosis of type ١ diabetes , ٣٠ to ٤٠ % of children .
- In children with established diabetes, ٦ to ٨ % per year .
- DKA can also occur in children with type ٢ diabetes.

DEFINITION OF DKA

- Presence of **all** of the following in a patient with diabetes:

➢ **Hyperglycemia** – BS >٢٠٠ mg/dL

➢ **Ketosis** –Ketones in the blood (>٣ mmol/L beta-hydroxybutyrate) or urine ("moderate or large" urine ketones)

➢ **Metabolic acidosis** – Venous pH <٧٫٣ or serum bicarbonate <١٨ mEq/L

DEFINITION OF Hyperglycemic Hyperosmolar State

- It is a hyperglycemic emergency, which is distinguished from classic DKA by:

➢ **Marked hyperglycemia** (BS>٦٠٠ mg/dL)

➢ **Minimal acidosis** (venous pH >٧٫٢٥ or arterial pH >٧٫٣ and serum bicarbonate >١٥ mmol/L)

➢ **Absent to mild ketosis**

➢ **Marked elevation in serum osmolality** (>٣٢٠ mOsm/kg)

➢ **Altered consciousness**

DKA at initial presentation of type ١ diabetes mellitus

Risk Factors :

- Young age (<٥ years of age and especially <٢ years)
- Delayed diagnosis of diabetes (reduced access to medical care)
- Low socioeconomic status
- Children living in countries with low prevalence of type ١ diabetes

DKA in established type 1 diabetes mellitus

Risk factors :

- Poor metabolic control
- Gastroenteritis with vomiting and dehydration
- Peripubertal and pubertal adolescent girls
- History of psychiatric disorders
- Limited access to medical care
- Inadvertent or intentional omission of insulin

CLINICAL FEATURES

- Polyuria (glucose-induced osmotic diuresis)
- Nocturia
- Enuresis
- Polydipsia (increased urinary water losses)
- Fatigue
- Weight loss
- Vaginal or cutaneous moniliasis

CLINICAL FEATURES

- Abdominal pain
- Polyphagia may be present early in the course of the illness.
- Once insulin deficiency becomes more severe and ketoacidosis develops, appetite is suppressed.

CLINICAL FEATURES

- Hyperventilation and deep (Kussmaul) respirations
- Fruity breath odor secondary to exhaled acetone

CLINICAL FEATURES

- Clinical signs of intravascular volume depletion (tachycardia, poor peripheral perfusion, and decreased skin turgor)
- ٥ to ١٠ % fluid deficit

CLINICAL FEATURES

- Neurologic findings (drowsiness, lethargy, and obtundation to coma)
- Cerebral injury occurs in ۰٫۳ to ۰٫۹ % of cases of DKA in children and is the leading cause of mortality.

Laboratory abnormalities

❑**Blood glucose**

- >٢٠٠ mg/dL is generally required for the diagnosis of DKA .

Laboratory abnormalities

- DKA with normal or near-normal glucose levels :

✓Pregnancy

✓Use of sodium-glucose cotransporter ٢ inhibitor medications

✓Administered insulin prior to arrival in the emergency department

Laboratory abnormalities

❑**Acidosis**

- Insulin deficiency and increased plasma concentrations of glucagon, cortisol, and epinephrine increase glucose production, lipolysis, and ketogenesis, which collectively contribute to the development of both hyperglycemia and ketoacidosis.

Laboratory abnormalities

❑**Ketosis**

➢Acetoacetate is the initial ketone formed and is reduced to beta-hydroxybutyrate (BOHB) or decarboxylated to acetone.

➢**Blood or serum BOHB** : ≥٣ mmol/L

➢**Urine ketones**

Laboratory abnormalities

➢ **Urine ketones**

- **Nitroprusside test strip** reacts with **acetoacetate** and **acetone** but not BOHB.
- This test may give a false impression of persistent ketoacidosis during recovery from DKA.
- During recovery from DKA, BOHB is converted to acetoacetate and acetone, which are excreted in urine for many hours after the serum BOHB concentration has returned to normal.

Laboratory abnormalities

❑Serum sodium

- Patients with DKA have a total body sodium deficit ranging from ٥ to ١٣ mmol/kg.
- Despite this deficit, their initial serum sodium concentrations can vary widely, ranging from hyponatremia to hypernatremia.

Laboratory abnormalities

- Hyperglycemia tends to **lower** the serum sodium because it increases the plasma osmolality, resulting in movement of water from the intracellular to the extracellular space, thus lowering the serum sodium by dilution.
- Patient's sodium status can be estimated by calculating a "corrected" plasma sodium concentration.
- The measured serum sodium is reduced by ***١/٦ mmol/L for every ١٠٠ mg/dL*** increase in the blood glucose concentration above ١٠٠ mg/dL.

Laboratory abnormalities

- Glucosuria-induced osmotic diuresis tends to **raise** the serum sodium because of water loss in excess of sodium.
- If water intake is inadequate (which may be a particular problem in hot weather and in infants and young children who cannot independently access water), hypernatremia may occasionally occur.

Laboratory abnormalities

- If hyperlipidemia is present, the measured serum sodium may be reduced due to a laboratory artifact (pseudohyponatremia).

Laboratory abnormalities

❑Serum phosphate

- Children with DKA are in negative phosphate balance because of decreased phosphate intake and phosphaturia caused by glucosuria-induced osmotic diuresis.
- At presentation, the serum phosphate concentration is usually normal or even slightly elevated because both insulin deficiency and metabolic acidosis cause a shift of phosphate out of the cells .
- This transcellular shift is reversed and phosphate levels typically decline during DKA treatment.

Laboratory abnormalities

❑**Blood urea nitrogen and creatinine**

- Patients with DKA often have elevated BUN concentrations, which correlate with the degree of hypovolemia .
- Many children with DKA have acute increases in serum creatinine compared with baseline, reflecting acute kidney injury .
- AKI occurs in ۴۳ to ۶۴ percent of children with DKA and is more common in children with more severe acidosis and circulatory volume depletion.
- Cross reaction to ketones

Laboratory abnormalities

- Ca , K , Mg

INITIAL RAPID ASSESSMENT

➢ **Clinical assessment**

- Measure vital signs
- Measure weight
- Estimate the degree of dehydration
- Assess the neurologic state

INITIAL RAPID ASSESSMENT

- **Laboratory tests**
- ✓Blood glucose
- ✓Electrolytes
- ✓BUN and creatinine
- ✓VBG
- ✓Calcium, phosphorus, and magnesium

INITIAL RAPID ASSESSMENT

✓CBC

- Is not essential .
- If a CBC is performed, typical findings include elevated WBC with increased neutrophils.
- These findings are characteristic of DKA and do not help to identify children with infection.

INITIAL RAPID ASSESSMENT

✓HbA1C

- Unnecessary for management of DKA.

✓Diabetes-associated antibodies

- Glutamic acid decarboxylase antibodies, insulin auto-antibodies, islet cell antibodies are not useful for management of DKA.

INITIAL RAPID ASSESSMENT

➢ **Assessment of severity**

Assessment of severity of diabetic ketoacidosis in children [1,2]

Defining features	Severe	Moderate	Mild
Venous pH	<7.1	7.1 to <7.2	7.2 to <7.3
Serum bicarbonate (mEq/L)	<5	5 to 9	10 to <18

Severity of DKA

parameter	mild	moderate	severe
Volume deficit(%)	٣-٥	٦-١٠	١٠-١٥
Blood sugar	٢٠٠-٤٠٠	٤٠٠-٦٠٠	⬆ ٦٠٠
BUN	⬇ ٢٥	٢٥-٣٠	⬆ ٣٠

INITIAL RAPID ASSESSMENT

➢ **Disposition**

- All patients with DKA should be managed in a unit with personnel and facilities capable of frequent monitoring of clinical symptoms, fluid status, and laboratory results.

INITIAL RAPID ASSESSMENT

- PICU is appropriate for patients with severe DKA or signs of or risk factors for cerebral injury, which include:

✓Altered consciousness

✓Age younger than five years

✓Severe acidosis (venous pH <٧٫١)

✓Low $pCO_{٢}$ (≤٢٠ mmHg)

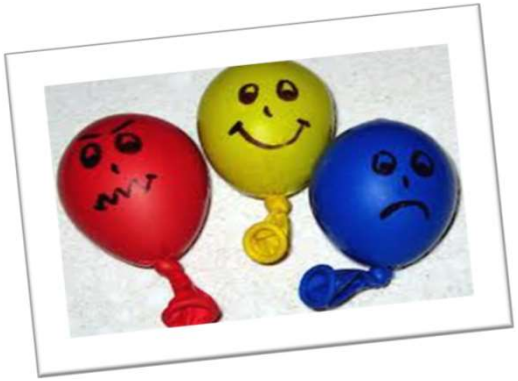
✓High BUN

✓Significant hyper- or hypokalemia, or other severe electrolyte disturbances.

Management of DKA

The goals of management

- Improvement of circulatory volume and tissue perfusion
- Reduction of serum glucose and plasma osmolarity
- Correction of electrolyte imbalance
- Resolution of ketosis
- Identification and prompt treatment of comorbid precipitating causes.

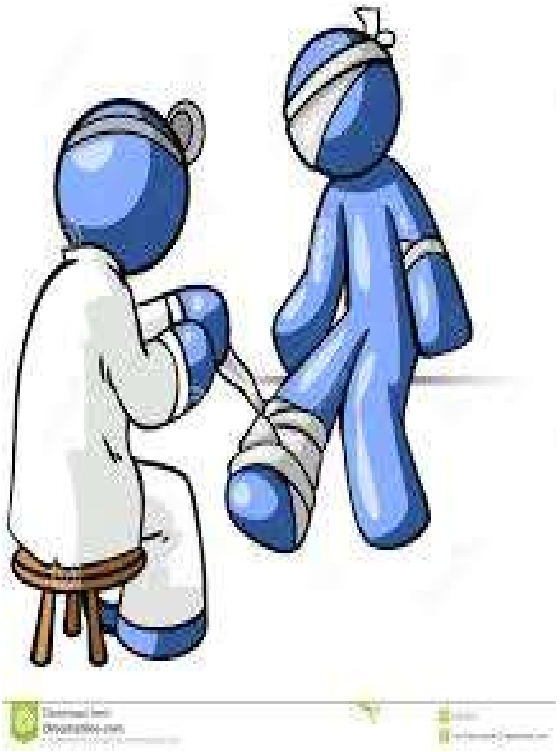


management

١. Fluids – type/rate

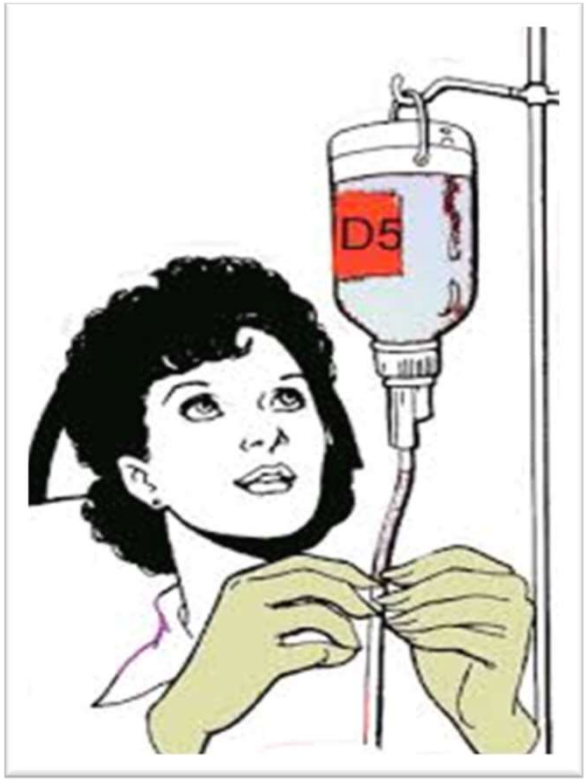
٢. Insulin – type/delivery/dose

٣. Electrolytes replacement



Fluid therapy

- Initial therapy
- Maintenance
- Deficit



Initial therapy

- ١ST hour ١٠ - ٢٠ ml / kg N/S OR RL

- If and only if the effective circulating volume is still compromised, an additional infusion of ١٠ mL/kg can be given over the next hour.

Maintenance+ Deficit

- ٢nd – ٣٦th hour deficit +maintenance

  ١st -١٢ hr ½ D + ½ M

  ١٢nd -٣٦hr ½ D + M

case

کودک ۶ ساله با وزن ۲۵ کیلوگرم و deficit = ۷ %

مایع نگهدارنده

۱۰ × ۱۰۰ cc = ۱۰۰۰ cc

۱۰ × ۵۰ cc = ۵۰۰ cc

۵ × ۲۰ cc = ۱۰۰ cc

۱۶۰۰ cc maintenance

case

- Deficit = ٧ %
- ٢٥٠٠٠ × ٧ = ١٧٥٠٠٠ ÷ ١٠٠ = ١٧٥٠ cc deficit

١st -١٢ hr ½ D + ½ M (٨٧٥ + ٨٠٠ cc)

١٢nd -٣٦hr ½ D + M (٨٧٥ + ١٦٠٠ cc)

Fluid therapy

- BW > ٣٢ kg
- ١٫٥ – ٢ maintenance

Fluid therapy

Up to : ۴ L / m۲ / day

٢/٥ L/m٢/day
Deficit ٤٨-٧٢hours

- ١- BS > ٨٠٠mg/dl
- ٢- Na corrected >١٤٥meq/l
- ٣- Rapid falling in Na corrected

Type of fluid

- BS > ٣٠٠ mg/dl : N/S
- ٢٠٠ <BS < ٣٠٠ mg/dl : D/W ٥% in ٧٥ meq/L Na
- ١٠٠ <BS< ٢٠٠ mg/dl : D/W ٧٫٥% in ٧٥ meq /L Na
- BS <١٠٠mg/dl : D/W ١٠% in ٧٥ meq /L Na

.

Fluid Therapy in adult

- ۱۰۰۰ mL normal saline first hour

- Then normal or ۰/۴۵% saline at ۲۵۰ to ۵۰۰ mL/h, depending on serum sodium concentration.(۴-۱۴ cc/kg/hr)

Electrolytes replacement

Electrolyte replacement

- K: ٢ th hr
- K>٥٫٥ No kcl
- K=٣٫٥-٥٫٥ ٤٠ meq/L IV
- K=٢٫٥-٣٫٥ ٠٫٥-١meq/kg kcl ١٥% IV (١ hr)

  ٤٠-٦٠ meq/L IV

  Monitor K hourly

K < ۲/۵

۱meq/kg KCL ۱۵% IV within ۱ hour

Withhold insulin infusion

Monitor K hourly

to avoid:

arrhythmia

cardiac arrest

respiratory muscle weakness

INSULIN

- Since ٢nd hr :

  ٠/١ IU / kg / hr

- K < ٢/٥ → Insulin hold

Insulin therapy

- If the patient shows marked sensitivity to insulin, as in some **younger** or **malnourished** children, it may be necessary to decrease the insulin infusion rate to avoid hypoglycemia (٠/٠٥ units/kg/hour)

Insulin therapy

- If facilities to administer intravenous insulin are not readily available, SC or IM insulin can be used as initial therapy.

- Combination of volume depletion and secondary sympathetic activation decrease local perfusion, initially leading to inconsistent absorption.

BICARBONATE

- No need to it.

Indication of Bicarbonate therapy

- *life-threatening hyperkalemia*

- *Severe acidosis : Ph < ۶/۹ and*
  - *Hypotension*
  - *Shock*
  - *Arrhythmia*

Resistant to Treatment

- Infection
- Dehydration
- Inadequate insulin
- Out of date insulin
- Hypocalemia …..

Monitoring

- Treatment of DKA requires close monitoring of the patient's clinical condition, including changes in :

✓Vital signs

✓Neurologic status

✓Fluid status

✓Metabolic state

Monitoring of children during treatment for diabetic ketoacidosis

Parameter	Frequency	Comments
Vital signs	Hourly	Decrease in heart rate (not related to sleep or rehydration) or severe hypertension suggest possible cerebral injury.
Fluid intake and output	Hourly	Ensure ongoing positive fluid balance.
Neurologic status	At least hourly	Use GCS or similar assessment (refer to UpToDate content on cerebral injury in children with DKA).
Blood glucose	Hourly	Use a point-of-care meter, but cross-check with laboratory tests to ensure correlation.
Blood BOHB	Every 2 to 4 hours, if available	Perform if test is available. Resolution of DKA is indicated by BOHB ≤1 mmol/L (10.4 mg/dL).
Electrolytes, BUN, creatinine, venous blood gas	Every 2 to 4 hours	Timing of initiating potassium replacement depends on initial serum potassium level (refer to UpToDate topic text). **Calculate the anion gap:** ▪ Anion gap = sodium − (chloride + bicarbonate) ▪ Normal anion gap = 12±2 (in mEq/L or mmol/L); indicates resolution of DKA* **Calculate the corrected sodium concentration:** ▪ Corrected sodium = measured sodium + 1.6 (glucose − 100 mg/dL)/100 **NOTE** – For glucose measured in mmol, use: (glucose − 5.56)/5.56
Calcium, magnesium, phosphorus	Every 4 to 6 hours	More frequent measurements may be required for patients with significant derangements in these laboratory values.
ECG monitoring	Continuous, if available	Required for patients with severe DKA or significant electrolyte abnormalities (particularly potassium), but recommended for all patients.

Discontinuing the insulin infusion

- Venous pH >٧٫٣ or serum bicarbonate >١٨ mEq/L
- Blood glucose <٢٠٠ mg/dL
- Patient is tolerating oral intake

Time of feeding

If

- the patient wishes
- Conscious
- No vomiting

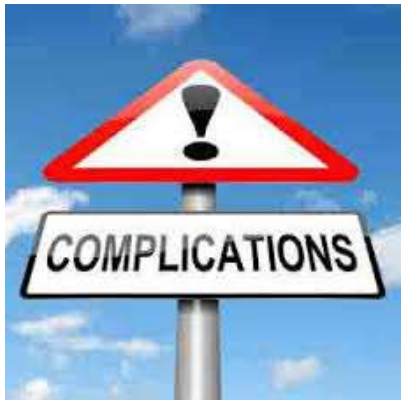
TREATMENT OF MILD DIABETIC KETOACIDOSIS

- Older children and adolescents with established diabetes and mild DKA can frequently be managed in the emergency department.
- These patients often improve substantially after intravenous (IV) fluid therapy and subcutaneous insulin administration.
- Rapid-acting insulin can be given at an initial dose of ٠٫١ units/kg every one to two hours.
- Regular insulin (given every four hours) has also been used in these circumstances .

COMPLICATIONS AND MORTALITY

- Reported mortality rates for DKA are consistent in developed countries, from ۰٫۱۵ to ۰٫۵۱ %

- Cerebral edema accounts for the majority of deaths (۶۰ to ۹۰ percent).



warning signs and symptoms of cerebral edema

- Headache
- Inappropriate decrease in heart rate
- Recurrence of vomiting
- Changes in neurologic status
- Rising blood pressure
- Decreased oxygen saturation

Risk Factors for Brain edema

At PRESENTATION

- Age (<٥ yr)
- First episode vs. known diabetic
- Severity of acidosis at presentation

(pH < ٧٫١, pCO٢ < ١٠)

- Severity of dehydration at presentation

(high urea)

DURING TREATMENT

- Starting Insulin with or right after the fluid bolus
- > ٤ lit/m^{٢}/day fluids
- > ٤٠ ml/kg fluids in the ١st ٤ hrs
- Fall in or no rise in [Na^{+}] as glucose drops with therapy
- $NaHCO_{٣}$ administration

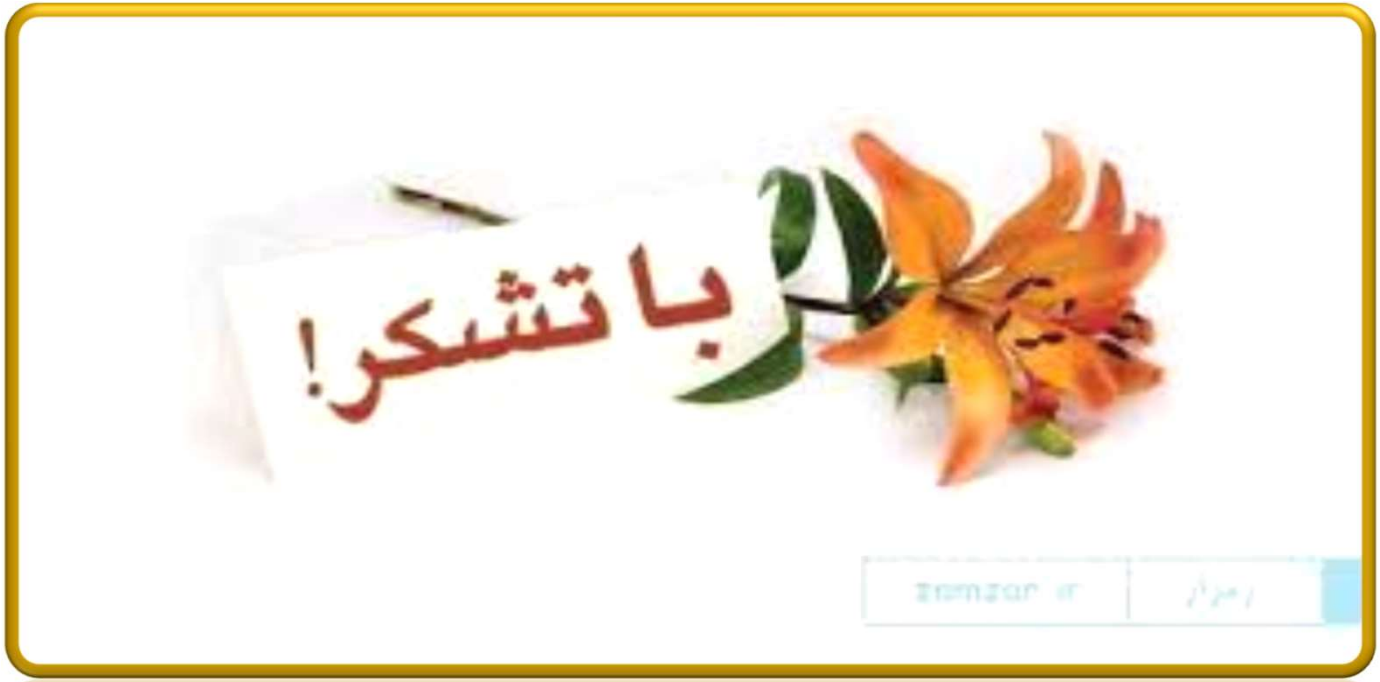
Treatment:

- Restriction of fluid (۱/۳)

- Manitol ۰٫۲۵ – ۱ gr/kg/۲۰ min

- Hypertonic saline(۳%) ۵-۱۰ ml/kg/۳۰ min

- Intubation and hyperventilation


با تشکر!