Diabetic Ketoacidosis

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Status:
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A The preponderance of data supporting this statement is derived from level 1 studies, which meet all of the evidence criteria for that study type

B The preponderance of data supporting this statement is derived from level 2 studies, which meet at least one of the evidence criteria for that study type

C The preponderance of data supporting this statement is derived from level 3 studies, which meet none of the evidence criteria for that study type or are derived from expert opinion, commentary or consensus

Study types and evidence criteria are defined at http://pier.acponline.org/criteria.html

7. Drug Therapy: Recognize that therapy of DKA will correct the hyperglycemia, dehydration, metabolic acidosis, and the precipitating event. A B

7.1 Begin rehydration for DKA immediately. B C

Specific recommendation:
- Begin treatment with normal saline (0.9% sodium chloride).
- Reassess fluid replacement hourly.
- Switch to 0.45% sodium chloride after the initial bolus if the serum sodium is high or normal.
- Begin fluid infusion at an initial rate of 15 to 20 mL/kg·h depending on the fluid deficit; switch to dextrose containing fluids once the blood sugar level is approximately 250 mg/dL.
- Use extra caution in children, who have higher incidence of cerebral edema associated with DKA therapy, and in children at risk of pulmonary edema.
- See table Drug Treatment for Diabetic Ketoacidosis.

Rationale:
- Rehydration alone will lower the blood sugar level, replace the fluid deficit, and improve insulin sensitivity.

Evidence:
- Recommendations for management are presented (1; 16).

Comments:
- None.

7.2 Begin insulin therapy when serum electrolytes are available. B

Specific recommendation:
- Begin treatment with iv regular insulin if serum potassium is ≥3.3 mEq/L.
- If K is <3.3 mEq/L, hold insulin, replace K at 40 mEq/h and monitor frequently.
- Use an initial bolus of approximately 0.15 U/kg·h iv, followed by an infusion of 0.1 U/kg.
- If the blood glucose is <250 mg/dL, begin treatment with 5% or 10% dextrose in water and monitor therapy using the anion gap and presence of serum ketones.
- See table Drug Treatment for Diabetic Ketoacidosis.

Rationale:
- Insulin is required to treat the hyperglycemia and ketosis.
- Insulin results in a shift of potassium from the extracellular space to the

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intracellular space; therefore, treatment with insulin in the hypokalemic patient could result in profound hypokalemia and serious arrhythmias.
- Insulin therapy is required to suppress ketosis.
- Inadequate therapy results in prolongation of the ketosis and elevation in anion gap.

Evidence:
- Early reduction in insulin therapy because of normalization of blood glucose will prolong the duration of DKA (20).
- Low-dose insulin therapy is as effective as older high-dose regimens (21).

Comments:
- Cardiac monitoring may give an indication of potassium concentration and allow early administration of insulin if there is evidence of hypokalemia.

7.3 Monitor potassium levels closely and replace potassium deficit in all patients with DKA. B C

Specific recommendation:
- Measure serum potassium at baseline, at 1 hour, then every 2 hours during initial therapy.
- Consider ECG and cardiac monitoring to monitor potassium status.
- Initiate potassium therapy once the serum potassium level is <5.5 mEq/L unless the patient is anuric or in significant renal failure.
- If potassium level is <3.3 mEq/L, replace at 40 mEq/h; if potassium is >3.3 and <5.5 mEq/L, replace at approximately 20 mEq/h; use 2/3 as KCl and 1/3 as KPO_4.
- See table Drug Treatment for Diabetic Ketoacidosis.

Rationale:
- Most patients with DKA have a total body deficit of potassium despite elevated or normal potassium levels at baseline.
- Potassium shifts into the extracellular fluid because of the acidotic state and insulin deficiency.

Evidence:
- Retrospective studies and reviews of DKA show a decrease in total body potassium that increases with insulin therapy (1; 12).

Comments:
- None.

7.4 Determine the need for bicarbonate therapy. B C

Specific recommendation:
- Consider bicarbonate therapy only if pH is ≤7.0.
- If pH is <6.9, give 100 mmol $NaHCO_3$ in 400 mL of water at 200 mL/h.
- If pH is 6.9 to 7.0, give 50 mmol of $NaHCO_3$ in 200 mL of sterile water.
- Deliver each infusion at a rate of 200 mL/h and repeat every 2 hours until the pH is >7.0.

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• See table Drug Treatment for Diabetic Ketoacidosis.

Rationale:

• Bicarbonate therapy remains controversial and the benefits of bicarbonate, even if pH is <7.0, are not clear.

Evidence:

• Numerous studies have shown the lack of benefit of bicarbonate therapy in patients with DKA (22; 23; 24).
• The American Diabetes Association recommendations from January 2001 suggest the use of bicarbonate if pH 7.0 or less (12).
• Note that bicarbonate therapy in children may be even more controversial (25).

Comments:

• None.

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1 Studies that meet all of the evidence criteria for that study type

2 Studies that meet at least one of the criteria for that study type

3 Studies that meet none of the evidence criteria for that study type or are derived from expert opinion, commentary, or consensus

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The number in parentheses at the end of the reference citations identify PubMed abstracts, which can be found on the National Library of Medicine's web site http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

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Glossary

ABG	arterial blood gas
BP	blood pressure
CBC	complete blood count
CSF	cerebrospinal fluid
CVA	cerebrovascular accident
CXR	chest x-ray
DKA	diabetic ketoacidosis
ECG	electrocardiography
iv	intravenous
MI	myocardial infarction
sc	subcutaneous
UTI	urinary tract infection

Drug Treatment for Diabetic Ketoacidosis

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
Insulin (regular insulin; insulin aspart; insulin lispro; insulin glulisine; isophane insulin [NPH]; lente insulin; ultralente insulin; insulin glargine; insulin detemir; insulin lispro, insulin lispro protamine; insulin aspart, insulin aspart protamine; regular insulin, isophane insulin [NPH]; semilente insulin; protamine zinc insulin [PZI])	Corrects insulin deficiency and overcomes insulin resistance. Allows shift of glucose into cells and suppresses hepatic glucose production	Initial bolus of 0.15 U/kg, then 0.1 U/kg·h iv. Hold insulin until K is >3.3 mEq/L	Correct hyperglycemia and stop ketogenesis	Hypoglycemia, hypokalemia. Low-dose insulin less likely to cause hypoglycemia or hypokalemia	Once blood glucose level is ~250 mg/dL, switch fluids to include dextrose 5%-10%. Target blood glucose to 150-250 mg/dL. Once DKA is resolved, bicarbonate >15 mEq/L, and pH >7.3, can decrease to 0.5 U/h and begin sc insulin. Overlap therapy for at least 1 hour. If blood glucose does not respond to insulin, may need to increase dose
Potassium	Replace potassium deficit	Replace at rate of 40 mEq/h if K is <3.3 mEq/L. Use 20 mEq/h if >3.3 and <5.0-5.5 mEq/L	Reverse hypokalemia and associated complications	Risk of over treatment leading to hyperkalemia. Use cautiously in anuric patients and only if K+ is <3.3 mEq/L	Monitor potassium at least every 2 hours until normal. KCl is most common form of potassium replacement. Can use 2/3 KCl and 1/3 KPO_4 to prevent excessive Cl levels
Sodium bicarbonate	Corrects metabolic acidosis	If pH is <6.9 give 100 mmol $NaHCO_3$ in 400 mL water at 200 mL/h. If pH is 6.9 to 7.0, give 50 mmol of $NaHCO_3$ in 200 mL sterile water at 200 mL/h, repeat every 2 hours until pH is >7	By correcting severe metabolic acidosis, decreases risk of cardiac arrhythmias, decreases cardiac output, cerebral vasodilitation	Hypokalemia, metabolic alkalosis, ketoacid overproduction. Other theoretical risks include: paradoxical CSF alkalosis, altered tissue oxygenation, increased CO_2 production	Consider use if arterial pH ≤7.0 Infuse slowly, to prevent shift of potassium to intracellular space

Table Continued...

Drug Treatment for Diabetic Ketoacidosis

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
Fluid therapy	Volume expansion	Initial bolus of 0.9% NaCl, ~1 L in first hour (15-20 mL/kg·h), continue 0.9% NaCl if fluid deficit is large or corrected serum Na and osmolality are high. Once major deficit is corrected, and corrected serum Na is normal or high, use 0.45% NaCl, continue at 4-14 mL/kg·h	Corrects dehydration, improves insulin sensitivity, improves hyperkalemia, improves metabolic acidosis	Fluid overload, cerebral edema (may be associated with rapid change in serum osmolality)	Careful monitoring of fluid status is needed; estimate volume depletion using physical exam. Orthostatic tachycardia ~10% fluid deficit, orthostatic drop ~15%-20% deficit, supine hypotension ~20% decrease in extracellular fluid volume
Glucose therapy	Provide adequate blood glucose level while maintaining insulin therapy	Once glucose is between 250-300 mg/dL, begin 5% dextrose with 0.45% NaCl at 150-200 mL/h. Maintain insulin infusion at 0.05-0.1 U/kg·h, use 10% dextrose if needed	Allows continuation of adequate insulin therapy that is required to treat the metabolic acidosis and stop ketogenesis	May require ongoing adjustment of insulin dosage to maintain glucose ~150-200 mg/dL	Early reduction or cessation of insulin therapy because of normalization or low blood glucose may result in worsening of DKA and delay of cure
Phosphate therapy	Replacement	20-30 mEq of KPO_4 over several hours. Add to replacement fluid if serum PO_4 is <1 mg/dL	Correct severe hypophosphatemia	Risk of hypocalcemia	Although phosphate level may be low, replacement is not necessary except in unusual circumstances of extremely low phosphate level. Phosphate administration may lead to severe hypocalcemia and deposition of calcium phosphate. If phosphate is used, monitor calcium levels. Use 20-30 mEq of KPO_4 over several hours if needed

CSF = cerebrospinal fluid; DKA = diabetic ketoacidosis; iv = intravenous; sc = subcutaneous.