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ALASKA NATIVE DIABETES TEAM

Diabetes Dispatch

Hyperglycemic Crises:

Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State

Newsletter compiled by Sarah Bowen, PharmD Candidate

Hyperglycemic crisis can occur in patients with both Type 1 and Type 2 diabetes. The most recognized crisis is diabetic ketoacidosis (DKA), which is more often found in younger Type 1 patients. Type 2 patients can present with DKA; however, hyperosmolar hyperglycemic crisis (HHS) is more common, especially in older patients. The purpose of this article is to differentiate between DKA and HHS and to summarize the current treatment guidelines for DKA and HHS.

Pathology

DKA consists of a "triad" of symptoms, including hyperglycemia, metabolic acidosis, and increased ketone concentrations. These symptoms are the result of the complete (or near complete) absence of insulin and an increase in counterregulatory hormones (glucagon, catecholamines, growth hormone, and cortisol). As a result, patients have blood glucose levels above 250mg/dL, sometimes exceeding 600 mg/dL. This increase in blood sugar draws water out of the cell leading to osmotic diuresis and, as a result, dehydration. Further complicating the situation is the loss of electrolytes that occur with diuresis. Because the patient does not have insulin to utilize glucose as an energy source, the body turns to lipolysis for energy, creating excess ketone bodies, which can cause an elevated anion gap metabolic acidosis.

The pathophysiology of HHS is very similar to DKA, but differs in that patients have higher blood glucose values and do not typically present with ketoacidosis. Because HHS occurs in Type 2 patients, there is normally some insulin being produced by the pancreas. This small amount of insulin is enough to stop the lipolysis which creates the ketones in DKA, but is not sufficient to utilize glucose as energy. As a result, blood glucose levels are much higher in HHS than in DKA, at times exceeding 900 mg/dL. This leads to an even greater loss of water and electrolytes, thereby causing a more severe dehydration than what is seen in DKA.

Causes

Any type of stressful event that can increase counterregulatory hormones can cause DKA or HHS in a patient with diabetes. Infection is the most common underlying cause, typically urinary tract infections or pneumonia. Also, patients who refrain from taking their insulin can precipitate an event. Certain medications can increase the risk of DKA and HHS and require close monitoring when used in patients with diabetes.

Drugs which ↑ risk of HHS and DKA	
Corticosteroids	Diuretics
Sympathomimetics	Calcium Channel Blockers (CCBs)
α / β Adrenergic Blockers	Phenytoin

Treatment

Fluid Replacement

In both DKA and HHS, fluid replacement is key. Using IV fluids first allows for quicker symptom resolution without the need for high dose insulin. To begin replacement, 0.9% NaCl should be infused at a rate of 15-20 mL/kg/h or 1-1.5 liters during the first hour. After initial treatment with fluid, the patient's corrected sodium (Na^+) value should be calculated to account for Na^+ lost during osmotic diuresis. Corrected Na^+ can be found using the following equation:

If the Na^+ value is normal or high, the fluid

$$Na_{corrected} = Na_{serum} + [0.016 \times (glucose - 100)]$$

should be changed to 0.45% NaCl and given at a rate of 250-500 mL/h. If the corrected Na^+ is low, continue to use 0.9% NaCl at a decreased rate of 250-500 mL/h.

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Objectives:

- Identify treatment methods, prevention techniques, and complications of DKA and HHS
- Discuss carbohydrate counting with sugar alcohols
- Discuss tips for air travel for patients with diabetes.

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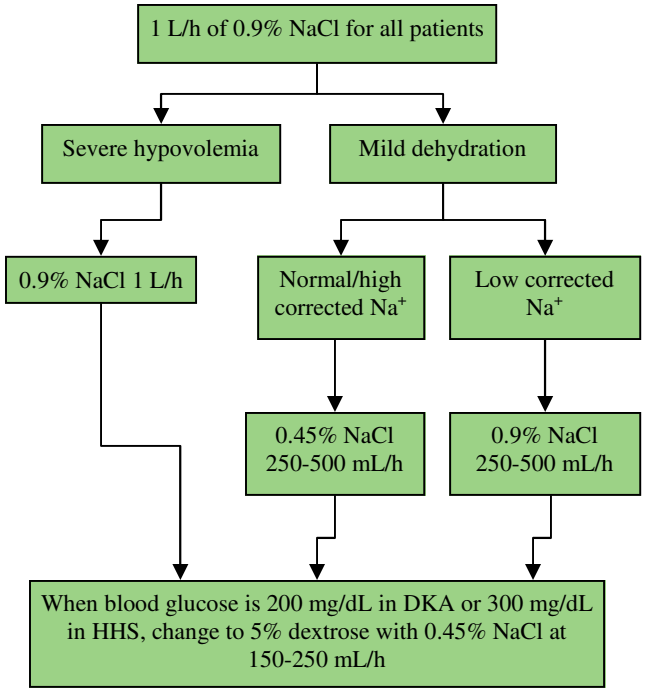
Hyperglycemic Crises

When serum glucose levels reach 200 mg/dL in a DKA patient or 300 mg/dL in a patient with HHS, dextrose should be added to the fluid to avoid hypoglycemia. Dextrose 5% with 0.45% NaCl can be used at a rate of 150-250 mL/h.

Figure 1: Fluid replacement algorithm



Insulin

Insulin therapy should be started following the administration of the first liter of fluid. The most recent American Diabetes Association Consensus Statement on Hyperglycemic Crisis states it is no longer required to give a bolus dose of insulin prior to a continuous insulin infusion. If it is decided to use a bolus, a 0.1 unit/kg bolus of IV regular insulin should be used, followed by a 0.1 unit/kg/h continuous insulin infusion. When a bolus dose is not used, an IV continuous infusion of 0.14 unit/kg IV regular insulin should be started. Serum glucose should be monitored, and if they do not decrease by at least 10% within the first hour, then a 0.14 unit/kg bolus dose should be administered followed by continuation of the previous insulin infusion.

When serum glucose reaches 200 mg/dL in DKA or 300 mg/dL in HHS, the IV infusion should be reduced to 0.02-0.05 unit/kg/h until resolution of DKA or HHS. The goal serum glucose ranges are 150-200 mg/dL in DKA and 200-300 mg/dL in HHS.

Once DKA or HHS has resolved , a patient may be transitioned to subcutaneous insulin, while overlapping IV infusion for 1-2 hours to avoid relapse into the hyperglycemic crisis. In treatment naïve patients, a 0.5 unit/kg/day subcutaneous insulin can be given in a basal-bolus dosing style. Those previously treated with insulin should continue their home dose.

Potassium

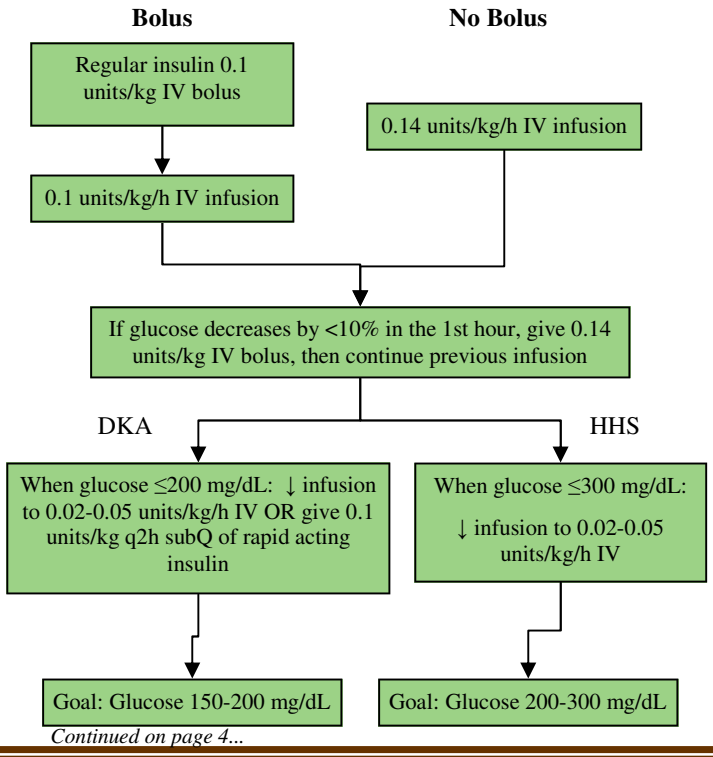
Hypokalemia is the most serious electrolyte derangement associated with both DKA and HHS, which can led to life-threatening cardiac arrhythmias if left untreated. Upon presentation, patients may have a pseudohyperkalemia due to the intracellular supply of potassium (K^+)following water out of the cell and into the serum. This potassium is eventually lost during osmotic diuresis. As a result, deficits of potassium can be greater than 4 mEq/L in both DKA and HHS.

For K^+ replacement, there are two key values to remember: 3.3 mEq/L and 5.2 mEq/L. If K^+ is less than 3.3 mEq/L, insulin should be held and 20-30 mEq/h of K^+ should be administered until $K^+ > 3.3$ mEq/L. Between 3.3-5.2 mEq/L, 20-30 mEq of K^+ should be given in each liter of fluid to maintain 4-5 mEq/L. K^+ can be replaced as ⅔ potassium chloride and ⅓ potassium phosphate to replete phosphate and decrease risk of hyperchorlemia. If $K^+ > 5.2$ mEq/L, K^+ replacement is not needed, but K^+ should be monitored every 2 hours, as it is likely to decrease with insulin treatment. For resistant hypokalemia, magnesium should be monitored and replaced if needed due to magnesium being essential for K^+ to move intracellularly.

Figure 2: Potassium replacement

<3.3 mEq/L	3.3-5.2 mEq/L	>5.2 mEq/L
Hold insulin and give 20-30 mEq/h K^+	Give 20-30 mEq K^+ in each liter of IV fluid	Do not give K^+ Check K^+ every 2 hours
Goal: $K^+ \geq 3.3$ mEq/L	Goal: K^+ 4-5 mEq/L	Goal: K^+ 4-5 mEq/L

Figure 3: Insulin treatment algorithm



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Air Travel with Diabetes

Traveling can be stressful for anyone, but it is especially stressful for those individuals with diabetes. In order to make the process of packing supplies easier, a few important points for patients to remember are listed below:

- Always bring more medication and supplies than what you expect to use.
- Patients should pack all supplies in their carry-on. Items permitted through security include insulin vials and pumps, syringes when accompanying injectable medications, glucose meters and supplies, cleaning agents, glucagon kits, and a sharps container.
- Carry on raisins, glucose tablets, or candy in case of hypoglycemia.
- The patient is not required to have a prescription for supplies; however, it is recommended to have one in case of breakage, loss, and for documentation that the medication is yours.
- Liquid medications including insulin, Symlin, glucagon, and Byetta are permitted, even if they are in containers greater than 3.4oz. They should be declared to TSA agents at security and should be in zip-lock bags if <3.4 oz and not bagged if >3.4oz.
- If patients are concerned about medications being sent through the x-ray or about going through the x-ray with a pump, the patient can request a visual inspection and pat-down. If they are sent through the x-ray, make sure the insulin and supplies are stored properly afterwards to avoid breakage.
- In order to speed up the screening process, there is a notification card that can be printed out for patients to carry during travel that will let TSA know they have diabetes. This can be accessed at the TSA website under "disability documentation."

References:
1.Fact sheet-Air travel and diabetes. American Diabetes Association Web site. http://www.diabetes.org/assets/pdfs/know-your-rights/public-accommodations/air-travel-and-diabetes.pdf. Assessed July 12, 2012.
2.Air travel and diabetes. American Diabetes Association Web site. http://www.diabetes.org/living-with-diabetes/know-your-rights/discrimination/public-accommodations/air-travel-and-diabetes/. Assessed July 12, 2012.
Image from: http://gamecollage.com/news/apple-design-awards-and-airport-security-dont-mix/

Accounting for Sugar Alcohols

In order for patients to feel less guilty about giving into their sweet tooth, they might turn to "sugar free" or "no sugar added" candies. The marketing for these products can lead people to overindulge because many patients believe that they are not eating sugar so they are able to eat as much as they want.

Actually, a lot of these treats are sweetened with sugar alcohols, which still contain calories. These sweeteners tend to have about 55-67% of the calories one gets from sugar. So, when patients do chose to eat these foods, it is important they know how to account for those carbohydrates. A basic rule of thumb is that for items which contain >5 g of carbohydrates listed as sugar alcohols, multiply the grams of sugar alcohol by 1/2. Subtract the resulting number from the total carbohydrates to get a more realistic idea of how many carbohydrates are actually being absorbed.

Common Sugar Alcohols		
Glycerol	Mannitol	Xylitol
Isomalt	Sorbitol	Lactitol

Although they are lower calorie alternatives to sugar, overconsumption of sugar alcohols should be avoided, as they can led to nausea, bloating, and hyperglycemia.

Nutrition Facts
Sugar Free hard candy
Serving Size: 3 pieces (45 g)

Amount Per Serving

Calories 162
Calories from fat 53

	% Daily Value*
Total Fat 6 g	10%
Saturated Fat 4 g	30%
Cholesterol 7 mg	2%
Sodium 25 mg	1%
Total Carbohydrate 15 g	4%
Sugars 0 g	
Sugar Alcohol 10 g	
Protein 1 g	

*Percent Daily Values are based upon a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65 g	80 g
Sat Fat	Less than	20 g	25 g
Cholesterol	Less than	300 mg	300 mg
Sodium	Less than	2,400 mg	2,400 mg
Total Carbohydrate		300 g	375 g
Dietary Fiber		25 g	30 g

Calories per gram:
Fat 9 Carbohydrate 4 Protein 4

The total carb count tells you how many grams of fiber, sugar, and sugar alcohols are in 1 serving

~50% of sugar alcohols are absorbed. This is important for patients to know when calculating carb counts.

How to calculate a carb count with sugar alcohols:
10 g of sugar alcohol x (1/2)= 5 g of carbs
15 g of total carbs– 5 g of carbs= 10 g of carbs
So, the carbohydrate count absorbed per serving is ~**10 g**

References:
1. Counting sugar alcohols. UCSF Web site. http://dtc.ucsf.edu/living-with-diabetes/diet-and-nutrition/ understanding-carbohydrates/counting-carbohydrates/learning-to-read-labels/. Accessed July 12, 2012.
2. Sugar alcohols: Reduced calorie sweeteners. American Diabetes Association Web site. http: www.diabetes.org/food-and-fitness/food/what-can-i-eat/sugar-alcohols.html. Accessed July 12, 2012.

Hyperglycemic Crises (continued from page 2)

Bicarbonate

In cases of extreme acidosis, bicarbonate (HCO_3) replacement can be used. This is not often recommended, because acidosis normally resolves with adequate fluid replacement and insulin administration. Bicarbonate is only recommended when pH is <6.9. At this point, 100 mmol of sodium bicarbonate (2 ampules) should be added in 400 mL of sterile water with 20 mEq of KCl and given at a rate of 200 mL/h for 2 hours until venous pH is >7. This infusion should be repeated every 2 hours until pH is >7.

Phosphate

Replacement of phosphate is only needed in severe depletion to prevent respiratory depression and cardiac dysfunction. In DKA, if phosphate levels fall below 1 mg/dL, replacement with 20-30 mEq/L potassium phosphate can be used, not to be exceed a rate of 1.5 mL/h of potassium phosphate. There are no current studies of phosphate replacement in HHS.

Complications

With the treatment of DKA and HHS, there are some complications that can arise if a patient's pH or blood glucose level is corrected too quickly. One such issue is hypoglycemia, which occurs if too much insulin is given. To avoid this, dextrose should be added to IV fluid when blood glucose levels are at goal. At this time, insulin infusion rates should be slowed in the method previously mentioned. Cerebral edema and adult respiratory distress syndrome both occur due to the presence of excess water in the brain and the lungs, respectively. In order to prevent these sometimes fatal complications, it is important to slow the rate of fluid infusion after the initial hour of fluid replacement. Hyperchloremic metabolic acidosis is common in most patients with DKA or HHS, due to the excess amount of chloride in replacement fluids. Once the patient resumes normal diuresis and approaches baseline metabolic function, this issue typically resolves.

Resolution

DKA is defined as "resolved" when blood glucose is <200 mg/dL and when two of the following conditions have been met: serum $HCO_3 \geq 15$ mEq/L, venous pH > 7.3, or anion gap ≤ 12 mEq/L. For resolution of HHS, a patient must have a normal serum osmolality (275 to 295 mOsm/kg) and regain normal mental status.

Prevention

The easiest way to prevent these complications is to encourage frequent monitoring of blood glucose at home, especially when the patient is sick. HHS tends to develop over several days, allowing patients to detect upward trends in their blood glucose. The onset of DKA tends to occur more quickly, but with checking blood glucose multiple times a day, it can be caught in its early stages. Additionally, patients on insulin therapy need to be educated on the importance of taking their insulin, even when they are not eating due to nausea or vomiting. Regimens should be adjusted to account for decreased carbohydrate intake, but not stopped completely in order to avoid extremely high blood glucose levels. Patients and their diabetes team should develop a "sick day" plan that helps patients determine when they should call their provider or report to the emergency department to treat potential DKA or HHS. Sick day plans for patitents with type 1 diabetes may include checking the urine for ketones when blood glucose remain elevated. Finally, patients on insulin pumps should always have a back-up delivery method of insulin for times of pump malfunction. Typically, this includes an extra vial of insulin and subcutaneous needles the patient can use to self-administer insulin. As with most complications of diabetes, it is easier to prevent the occurrence of DKA and HHS

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1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 32:1335-1343, 2009
2. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ, Kreisberg RA, Malone JI, Wall B: Management of hyperglycemic crises in patients with diabetes mellitus (Technical Review). *Diabetes Care* 24: 131- 153, 2001
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Goal-The goal of the Diabetes Dispatch is to increase the reader's knowledge of diabetes treatments and technologies and to provide the most current information on new drugs, therapies, and devices.

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Continuing Education Quiz

Diabetes Dispatch: Fall 2012

1) DKA has which of the following characteristics?
   a. Ketosis
   b. Acidosis
   c. Hyperglycemia
   d. All of the above

2) Medications that can increase the risk DKA and HHS include all of the following except:
   a. Corticosteriods
   b. β– Blockers
   c. Sympathomimetic agents
   d. ACE inhibitors

3) True or False: Infections, such as urinary tract infections (UTIs), are a common cause of DKA and HHS

4) One of the most serious electrolyte derangements in DKA and HHS which can cause cardiac arrhythmias is:
   a. Hyponatremia
   b. Hypokalemia
   c. Hypophosphatemia
   d. Hypocalcemia

5) When should bicarbonate be used when treating DKA and HHS?
   a. All patients should receive bicarbonate
   b. Only patients with DKA or HHS due to infection
   c. DKA and HHS patients with a pH<6.9
   d. Patients with blood glucose >750mg/dL

6) True or False: DKA usually develops over several days, while HHS develops suddenly.

7) JJ is a 48 year old male with Type 2 diabetes, who has presented to the ER with suspected HHS. His blood glucose is 850mg/dL, pH 7.4, potassium 3.6mEq/L, and has physical findings indicative of severe dehydration. What do you do first?
   a. Start 1 liter of 0.9% NaCl over 1 hour
   b. Administer 0.14 unit bolus of IV regular insulin
   c. Give 20-30 mEq/hour of potassium as ⅔ potassium chloride and ⅓ potassium phosphate
   d. Give 1 liter of 5% dextrose with 0.45% NaCl over 1 hour

8) Which of the following blood glucose levels would be within the appropriate range to change to 5% dextrose with 0.45% NaCl in a patient with DKA?
   a. 450 mg/dL
   b. 188 mg/dL
   c. 600 mg/dL
   d. 378 mg/dL

9) Can patients with diabetes pack syringes for insulin in their carry-on baggage?
   a. Yes. Syringes are allowed, as long as they have a copy of the original prescription.
   b. Yes. Syringes are allowed when with injectable medications
   c. No. Patients do not need them during flight.
   d. No. Needles are too dangerous to have in flight.

10) A patient with diabetes wants to have a "sugar-free" candy bar, but doesn't know how many carbohydrates she should count. The candy bar has 40g of total carbohydrates, 0 g of sugar, 24g of sugar alcohol, and 0g of fiber. What should you tell her?
   a. 40 grams of carbs
   b. 64 grams of carbs
   c. 28 grams of carbs
   d. None of the above. The candy bar is sugar-free.

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To obtain CPE credit for this lesson you must answer the questions on the quiz (70% correct required) return the quiz and evaluation tool. Should you score less than 70%, you will be asked to repeat the quiz. This activity is accredited for 1.0 hour CPE (0.1CEU). Upon satisfactory completion, AKPhA will report participant CPE to CPE Monitor within 60 days of completion. Upon request, the cost to print and mail a statement of credit is $20.00.

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