PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**Diabetic Ketoacidosis.**" These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Diabetic Ketoacidosis

Developed by Dr. Carly Rumley and Dr. Jessica Foulds for PedsCases.com.
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Introduction

Hello, my name is Carly Rumley and I am a resident doctor at the University of Alberta. This podcast was developed with Dr. Jessica Foulds, a paediatrician and clinician educator at the University of Alberta and Stollery Children's Hospital in Edmonton, Alberta, Canada. In this PedsCases Podcast, we will discuss Diabetic Ketoacidosis and the different ways it can present. For a detailed review of Type 1 Diabetes, please review the two-part PedsCases podcast by Dr. Alkarim Velji and Dr. Rose Girgis.

By the end of this podcasts, listeners will be able to:

- Recognize and diagnose Diabetic Ketoacidosis, otherwise known as DKA
- Review an approach for the management of patients with DKA, including looking for a trigger
- Highlight important differences in the management of pediatric versus adult DKA

Let's start by reviewing some basics of glucose metabolism. Pancreatic beta cells are stimulated by increased blood glucose to release insulin into the bloodstream. Insulin causes the body cells to take up glucose while the liver stores excess glucose as glycogen. When there is a decrease in blood glucose levels, pancreatic alpha cells are stimulated to release glucagon into the bloodstream. This causes the liver to break down glycogen and glucose is released into the bloodstream.

In diabetes mellitus, hyperglycemia happens because of an insulin deficiency or a reduced effectiveness of insulin. Diabetes in children can be diagnosed with one of the three following lab values:

1. Fasting plasma glucose ≥7.0 mmol/L or
2. Random plasma glucose ≥11.1 mmol/L or
3. Plasma glucose ≥ 11.1 mmol/L after a 2 hour 75 gram oral glucose tolerance test (OGTT)

Note that glycosylated hemoglobin or HbA1c cannot be used to diagnose T1DM in children, adolescents, or pregnant women. A repeat test of any of the above is required to make the

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diagnosis if the patient does not have hyperglycemic symptoms such as polyuria, polydipsia, polyphagia, weight loss, or blurry vision.

Now, let's review T1DM in comparison to T2DM and other types of diabetes in childhood. T1DM is an autoimmune disease characterized by absolute insulin deficiency due to immune mediated beta cell destruction. Up to 80% of beta cells can be destroyed before diabetes symptoms are present. The onset is usually before age 30 but 45% of patients are diagnosed before the age of 10. T1DM is the most common endocrine condition in childhood and one of the most common childhood chronic conditions. Risk factors for T1DM include a personal or family history of other autoimmune diseases such as Graves, myasthenia gravis, autoimmune thyroid disease, celiac disease, or pernicious anemia. T1DM is treated with insulin, usually basal-bolus or via a continuous subcutaneous insulin infusion using an insulin pump. A rough rule of thumb is a total daily insulin requirement of 0.3-0.5 units/kg/day which can be increased to 0.5-0.7 units/kg/day. An acute and life-threatening complication of T1DM is diabetic ketoacidosis, the focus of our podcast today. DKA is the leading cause of morbidity and mortality for pediatric patients with T1DM.

Clinical Case

To learn about the recognition, diagnosis, and management of DKA, let's think of our approach to an 8-year-old girl, Katie Corner, presenting with vomiting and abdominal pain to the Paediatric emergency room. She is alert and oriented, tachycardic with a heart rate of 115, tachypneic with a respiratory rate of 23, blood pressure of 108/65, temperature 39 C, and her oxygen saturation is 97%.

The questions to ask on history would be those that you would ask any child presenting with abdominal pain: onset of symptoms, location of abdominal pain, sick contacts, diarrhea, nausea, vomiting, weight loss, fatigue, and toxic ingestions. You would also ask questions related to the urinary tract such as frequency of urination, dysuria, and assess her level of dehydration. Always include a thorough review of systems. Then ask for medications, medical conditions, allergies, social and surgical history, and family history of medical conditions (specifically autoimmune conditions as outlined above).

Katie's parents report that her only past medical history is type 1 diabetes mellitus which was diagnosed when she was 6 years old and she now takes insulin for it. She has had good glycemic control and no previous hospitalizations with DKA.

On physical exam, Katie has GCS 15/15, normal pupil response, dry oral mucous membranes, 3 second capillary refill time, left unilateral lower lung crackles but no Kussmaul respirations, normal S1 and S2 heart sounds, soft but tender abdomen. She has no skin changes over her injection sites. You note a fruity odour on her breathe and her beside glucose measurement is 20 mmol/L.

For children with known diabetes, DKA **most often** results from poor management on sick-days or failure to take insulin. Patients with poor metabolic control, previous DKA episodes, difficulty with family circumstances, or those of peripubertal age or adolescent females are at higher risk of presenting in DKA. We must now consider the potential causes for her

hyperglycemia. The 8I approach can be used for patients with or without known diabetes. Regardless of history you should always consider why the patient is presenting now: what is their trigger? The 8 I's are as follows:

1. Infection
2. Iatrogenic (ex. glucocorticoids, tacrolimus, atypical antipsychotics)
3. Intoxication
4. Insulin missed
5. Initial presentation
6. Ischemia / Infarction
7. Intra-abdominal process (ex. pancreatitis, cholecystitis)
8. Intra-operative/ peri-operative stress

So how does hyperglycemia result in DKA? In the setting of insulin deficiency, there is an increase in counter regulatory hormones such as glucagon, cortisol, catecholamines, and growth hormone. DKA can occur in the setting of a lack of insulin or increased stress such as surgery or infection. Unopposed hepatic glucose production leads to hyperglycemia which leads to osmotic diuresis, leading to dehydration, electrolyte disturbances and pseudohyponatremia due to the water shift to the extra-cellular space. Fat mobilization leads to an increase in free fatty acids, leading to ketoacidosis and a metabolic acidosis. The body is deplete in potassium, but serum potassium can be normal or elevated due to a shift of potassium from intracellular fluid to extracellular fluid. The plasma osmolality is increased.

We will briefly discuss hyperosmolar hyperglycemic state (HHS), which is a complication from T2DM that has some similarities and differences to DKA. HHS can be precipitated by similar triggers as DKA, such as sepsis, stroke, or myocardial infarction. The small amount of insulin present can inhibit lipolysis and prevent ketosis. Signs and symptoms of HHS are hyperglycemia, hyperosmolality, and dehydration. A metabolic acidosis is usually absent unless the precipitant itself leads to acidosis. The treatment for HHS is similar to DKA.

Clinical Presentation

The frequency of DKA as the initial presentation for pediatric T1DM is 30%, but reports have varied from 15-67%. Children under six years of age or those from an adverse socioeconomic background are more likely to present in DKA as the initial presentation of T1DM. Be mindful that just because it is an initial presentation of T1DM with DKA does not mean you should stop thinking about other triggers. You don't want to miss the pneumonia that pushed the patient over the edge to present this way.

DKA should be considered when a patient presents with polyuria, polydipsia, polyphagia, weight loss, fatigue, nausea and vomiting, and abdominal pain. Less common, but more severe presentations include a fruity or acetone odor on the breath, Kussmaul respirations which are a deep, labored pattern of breathing, obtundation, or dehydration.

Diagnosis

What is the definition of DKA? DKA is defined as the following:

- Venous pH <7.3,
- Bicarbonate of less than 15 mmol/L,
- Ketonemia or ketonuria, and
- Hyperglycemia with blood glucose >11 mmol/L.

Therefore, initial bloodwork in a patient with suspected DKA includes electrolytes, glucose, venous blood gas, and a urinalysis for ketones. In addition to diagnostic bloodwork one should also monitor serum electrolytes, urea, creatinine, calcium, phosphorus, magnesium and serum osmolality. Consider ordering a chest x-ray, an ECG, and blood or urine cultures based on clinical suspicion. Always obtain an accurate patient weight.

Expected results for a patient in DKA would be a normal or high potassium, increased creatinine and urea, ketonemia, decreased PO4, and increased osmolality. Urine is positive for glucose and ketones. If DKA is a first presentation of T1DM, consider testing for autoimmune thyroid diseases, with TSH and thyroperoxidase antibodies.

Children with T1DM presenting with DKA who are on insulin pump therapy, should have their insulin pumps disconnected and remain off the insulin pump until the most responsible healthcare provider deems it appropriate to restart.

Let's get back to our case. Katie's laboratory results are back, and her venous blood gas shows pH 7.2, bicarbonate 12, glucose 20 mmol/L, Na of 131, K of 4.5, Ca 2.25, Mg is 0.8, Phosphorus 1.0, and a urinalysis shows 2+ ketones, negative for nitrites or leukocytes. Creatinine is 90, urea is 7. These laboratory results confirm DKA, and her CXR shows a left lower lobe pneumonia. What is the appropriate management for a patient with DKA?

Treatment

The cornerstone of DKA management is careful rehydration and insulin therapy. The patient should be NPO initially and on continuous cardio respiratory monitoring. The initial management of DKA depends on how the patient clinically presents.

There are different approaches to manage patients with DKA, therefore listeners should refer to their own institutional protocol. We will outline two general approaches that are used for illustrative purposes. Alberta Health Services (AHS) guidelines at the Stollery Children's Hospital dictate that if the patient presents in decompensated shock, then the patient should receive a 10 mL/kg IV normal saline (0.9% NaCl) bolus with re-assessment of vitals and neurological exam. A repeat bolus may be indicated based on the patient's hemodynamic status. Alternatively, it the patient presents with moderate to severe dehydration but no evidence of shock, they should receive a 7-10 mL/kg IV normal saline (0.9% NaCl) bolus over one hour, with close monitoring and re-assessment. After initial fluid resuscitation, calculate the hourly fluid rate by adding the maintenance rate to the patient's fluid deficit, which is the total fluid deficit minus the volume already given, divided by 48 hours. Alternatively, the Ontario Diabetes protocol suggests running 3.5-5 mL/kg/hr for patients

without vascular compromise, or 5-7 mL/kg/hr for patients with vascular compromise after the first hour. After the first hour, you should also start an insulin infusion. Please see the PedsCases website for a link to the Ontario Diabetes protocol flowchart.

When thinking about what fluids to run, I would consider using the mnemonic “KID”.

K is for potassium: KCl 40 mmol/L should be added to saline solutions when the serum K is <5 mmol/L and the patient is voiding. This is because patients with DKA are total body K depleted regardless of what the measured serum K is. Another electrolyte to monitor is the corrected Na. The serum Na is expected to rise with treatment of the DKA with decreasing glucose concentration. The patient would be expected to get hyponatremic secondary to hyperglycemia; for every increase in blood glucose of 10 mmol/L there is on average an expected decrease in Na by 3 mmol/L. Refer to the attached PDF on the PedsCases website for clarification on these formulas and more.

I is for insulin: The insulin infusion should be its own separate bag (often referred to as Bag C in centers that use a three bag system) and should be started at 0.1 units/kg/hour, 1-2 hours after the IV fluids have been started. **Do not administer an insulin bolus**. The target is a blood glucose 8-15 mmol/L. A rough rule of thumb is to target a drop in blood glucose of 5 mmol/L per hour, and not faster. The insulin therapy is imperative to resolving the acidosis.

D is for dextrose: In a center that uses a three bag system Bags A and B will have NS with KCl and variable amount of dextrose (for example NS + 40 mEq KCl/L in Bag A and D12.5 NS + 40 mEq KCl/L in Bag B). The dextrose concentration that the patient receives is determined by the proportions given from Bag A and B and can be adjusted by changing the rates of the bags instead of switching bags of fluid. Dextrose should be started when the patient’s blood glucose has improved and to avoid precipitous drops in glucose or osmotic shifts. Change the fluid to start 5% dextrose with normal saline when the blood sugar drops to below 15 mmol/L.

Hourly vitals, accurate fluid intake and output, regular bedside glucose checks and neuro vitals should be taken. With respect to lab tests ordered, serum electrolytes, and VBG need frequent monitoring with urea, creatinine, calcium, phosphate, beta hydroxybutyrate less frequently, but should be assessed during the course of treatment.

The main complication from DKA to watch out for is cerebral edema. Signs and symptoms include headache, restlessness, irritability, or increased drowsiness. More serious signs of cerebral edema are neurological signs such as non-reactive pupils, cranial nerve palsies, slurred speech, incontinence, slowing heart rate, rising blood pressure, or decreased oxygen saturation. Rapid action is essential if a patient has suspected cerebral edema: if you have not already been in contact with a tertiary care center with experience managing pediatric DKA it is essential to contact your local pediatric intensive care resources and pediatric endocrinology referral center. Think about if the patient will require ICU admission, which is usually indicated if they are intubated, fluctuating GCS, signs of cerebral edema, young age, or with severe acidosis. If you suspect cerebral edema, the most important thing to do is in the mean-time, maintain ABCs, administer high flow O2 by non-rebreather mask,

elevate the head of the bed to 30 degrees, order mannitol or 3% hypertonic saline. Consider intubation or a cranial CT scan.

Cerebral edema generally occurs within the first 24 hours, and occurs in 0.3-1% of children with DKA and has a mortality rate of 21-24%. Those at highest risk for cerebral edema are young children, newly diagnosed patients with T1DM, and those receiving insulin boluses, rapid hypotonic fluid administration, or sodium bicarbonate. During treatment, patients are at a higher risk of developing cerebral edema if there is a failure of serum sodium to rise as predicted after insulin and fluid therapy, severity of acidosis, and a higher BUN.

Prognosis and Complications

The prognosis of DKA is a 2-5% mortality in developed countries. Morbidity can result from sepsis, respiratory complications, thromboembolic complications, cerebral edema, cardiac arrhythmia, and pancreatic enzyme elevations. An altered level of consciousness and vomiting associated with DKA increases the risk for aspiration and a nasogastric tube should be considered. Cardiac arrhythmias can be seen with hyper- or hypokalemia. Elevations in serum amylase and lipase can be seen in 40% of pediatric patients with DKA, but often does not represent acute pancreatitis, which should be diagnosed clinically.

It is important to discuss the control and management of diabetes with the patient and family before discharge. For the newly diagnosed patient with T1DM intensive interdisciplinary pediatric diabetes education is essential. Supporting patients and families to avoid subsequent DKA episodes requires close follow-up. Increasing the frequency of blood glucose testing, increasing parental involvement in taking insulin, frequent visits with the diabetes care team, and psychological counseling can be helpful.

Case Resolution

As we turn our attention back to Katie, orders for her include NPO, and hourly vitals, fluid input and output, and capillary blood glucose. Electrolytes were monitored by VBG every 4 hours, and BUN, creatinine, Ca, PO4, and beta hydroxybutyrate were monitored every 4 hours initially.

Her body weight was 27 kg. With regards to fluid requirements, Katie was not in decompensated shock, and was assessed to have moderate dehydration so was treated with NS 10 mL/kg IV over one hour, or 270 mL. As per the Stollery Children's Hospital guidelines (see formula sheet), Katie will then receive 95 mL/hr as her total hourly rate, which is distributed between two bags, one of saline and one of dextrose. KCl at 40 mmol/ L was added to the saline bag as Katie's potassium was normal and she was voiding. Katie's initial blood glucose was 20 mmol/L; therefore, when her glucose dropped to below 15 mmol/ L, the IV bag with Dextrose was added to target 5% dextrose (D5NS) with 40 mmol/ L KCl. Insulin infusion at a rate of 0.1 units/kg/hr was added two hours after the fluid therapy was initiated to target a blood glucose of 8-15 mmol/ L. Katie's pupils remained equal and reactive, she maintained her level of responsiveness and normal neurological status, and her tachycardia improved with fluid therapy.

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Summary

Let's review some key take home points for this podcast on Diabetic Ketoacidosis.

1. Criteria for the diagnosis of Diabetic Ketoacidosis. Remember, DKA is defined as the following:
    - Venous pH <7.3,
    - Bicarbonate of less than 15 mmol/L,
    - Ketonemia or ketonuria, and
    - Hyperglycemia with blood glucose >11 mmol/L.

2. Review the possible triggers for an episode of DKA. The 8 I's are helpful to aid in remembering: infection, iatrogenic, intoxication, insulin missed, initial presentation, ischaemia / infarction, intra-abdominal process, or intra-operative or peri-operative stress.

3. Review the essential components of treating pediatric DKA. Remember in diagnosing T1DM in pediatric patients, HbA1c is not used. The symptoms of DKA can be non-specific, such as polyuria, polydipsia, polyphagia, weight loss, fatigue, nausea and vomiting, and abdominal pain. More severe presentations can include a fruity or acetone odour on the breath, Kussmaul respirations, obtundation, or dehydration.

4. When managing DKA, remember fluids are the cornerstone of treatment. Use the mnemonic "KID." K is for potassium, which should be added to saline solutions when serum K is <5 mmol/L and the patient is voiding. I is for insulin. Do not administer an insulin bolus. The target is a drop in blood glucose of 5 mmol/L/hour, and not faster. The target is a blood glucose of 8-15 mmol/ L. D is for dextrose. Change the fluid to Start 5% dextrose with normal saline when the blood sugar drops to below 15 mmol/L.

Overall, we have discussed that DKA can have different presentations, and is important to keep in your differential as it can present in a non-specific way. Early recognition, appropriate labs and monitoring, and fluid resuscitation is essential in the management of a patient with diabetic ketoacidosis. Remember, refer to your local institutional protocol for specific details on managing a patient with DKA. Thanks for listening, and stay tuned for more PedsCases podcasts!

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References:

1. AHS Diabetic Ketoacidosis Guideline, Stollery Children's Hospital, Document #STOL-2.2

2. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes 2013;37(suppl 1):S1-S212.

3. Emergency Room Management Guidelines for the Child with Type 1 Diabetes. Ontario Ministry of Health and Long Term Care.
http://www.health.gov.on.ca/english/providers/pub/diabetes/child_pocketcard.pdf

4. Toronto Notes 2016

5. Uptodate
    1. Levitsky, L. L. Epidemiology, presentation, and diagnosis of type 1 diabetes mellitus in children and adolescents. In: UpToDate.
    2. Haymond, M. W. Cerebral edema in children with diabetic ketoacidosis. In: UpToDate.

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