EM CASES SUMMARY

Episode 147 HHS Recognition & Management

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DKA and HHS are two distinct entities that exist on the spectrum of diabetic emergencies. HHS is characterized by the *triad* of severe hyperglycemia (>33.3 mmol/L or >600 mg/dL), elevated serum osmolality (>320 Osm/kg), and altered level of awareness (LOA). HHS occurs without significant ketoacidosis, the anion gap is variable and patients often present with profound volume depletion. Importantly, HHS can occur concurrently with DKA making the ED diagnosis even more challenging.

Differentiating DKA from HHS

DKA	HHS
Hyperglycemia	Severe hyperglycemia (elevated osmolality)
Metabolic acidosis	pH > 7.3
Ketonemia (elevated beta-hydroxybutyrate)	Minimal or negative ketonemia
Volume depletion	Profound volume depletion
Young > Elderly, T1DM > T2DM Acute presentation	Elderly > Young; T2DM, 20% without hx of T2DM illness
Acute presentation	Longer, protracted course of illness

How do patients with HHS become severely hyperglycemic, dry and altered?

In HHS, there is relative insulin deficiency or resistance, leading to impaired glucose utilization, resulting in severe hyperglycemia and subsequent dehydration from osmotic diuresis. However, there is sufficient insulin to suppress ketogenesis (thus minimal or no ketones), but not enough to control hyperglycemia. This insidious process permits ongoing osmotic diuresis and progressive volume depletion. Increased counter-regulatory hormones in HHS can also exacerbate this cycle of hyperglycemia and further volume depletion through decreased insulin sensitivity, increased glycogenolysis and gluconeogenesis.

This is the reason why patients with HHS often present with a protracted course of illness.
In contrast, DKA is a state of **absolute insulin deficiency**. In order for the body to meet its basic metabolic demands, fatty acid metabolism/ketosis occurs. Patients in DKA often present much sooner in their course of illness as their body cannot tolerate the ketotic/acidotic state.

Finding the cause of HHS is of paramount importance

The mortality rate of HHS is considerably higher than DKA partly because it more often targets older people with concurrent illnesses.
HHS is often precipitated by similar conditions seen in DKA including: infection (pneumonia, UTI, intra-abdominal etc.), insulin deficiency (medication access/non-adherence, inter-current illness (ACS, PE, stroke etc.) and inadequate hydration. Use the mnemonic 5 "I"s plus drugs if that helps you remember the triggers.
Pearl: *Mortality in HHS is frequently due to an underlying cause rather than the complications of the condition itself; a thorough investigation for the cause should always be undertaken.*

Filling the tank: HHS fluid resuscitation

Osmotic diuresis from profound hyperglycemia results in significant volume depletion. Fluid resuscitation will help restore intravascular volume and help normalize plasma hyperosmolality. Our experts recommend using POCUS to help guide fluid resuscitation and avoid fluid overload.

- Use NS or RL for initial fluid replacement
- American Diabetes Association (ADA): 1000-1500mL NS over 1 hr, then adjust to hemodynamic and electrolyte status, and maintain between 250 and 500 mL/hr
- ADA: Patients with a normal or high corrected sodium can be switched to 0.45% sodium chloride after the first hour of fluid replacement
- ADA: Add dextrose (D5W) when the blood glucose falls below 16.7 mmol/L (300 mg/dL)

Correcting the massive potassium deficit in HHS before starting insulin

Patients with HHS have large total body potassium deficits that must replaced after adequate renal function (urine output) is assessed. The initial potassium lab report is commonly normal or high due to intracellular shifts secondary to volume contraction.

- ADA: 20-30 mmol (20-30 mEq) potassium per liter of infusion fluid when serum potassium <5.2 mmol/L
- UK: 40 mmol (40 mEq) potassium per litre of infusion fluid when serum potassium <5.5 mmol/L
- Evidence is lacking to support either recommendation over the other
- Potassium must be replaced prior to initiation of insulin therapy as insulin further promotes an intracellular shift of potassium; it is recommended that insulin should not be started if the serum potassium is <3 mmol/L (<3 mEq/L) to avoid worsening of hypokalemia

Restoring metabolic homeostasis with insulin in HSS

In contrast to DKA where insulin therapy is used to close the gap, in HHS, the purpose of insulin is to restore metabolic homeostasis to allow for glucose utilization in a relative insulin deficient state.
The optimal time to start intravenous insulin in the management of HHS has not been determined.

- ADA: "Start intravenous insulin after initiation of fluid resuscitation and correction of any hypokalemia"

The optimal starting dose of intravenous insulin in the management of HHS has not been determined

- ADA: "Start intravenous insulin at either a fixed weight-based dose of 0.14 units/kg/h or at a fixed weight-based dose of 0.1 units/kg/h after a 0.1 units/kg bolus"

The rate of intravenous insulin should be adjusted to achieve an adequate drop in blood glucose

- ADA: "If plasma glucose does not decrease by 3-4 mmol/L/h (50-75 mg/dL/h) from the initial value in the first hour, the insulin infusion should be increased every hour until a steady glucose decline is achieved. When blood glucose is < 16 mmol/L (<300 mg/ dL), adjust dextrose or intravenous insulin rate to maintain concentrations in the 14-16 mmol/L (250-300 mg/dL) range until HHS has resolved."

Key take home points for HHS recognition and ED management

1. Clues that point to the diagnosis of HHS are protracted illness with progressive altered LOA and a high serum osmolarity – there may not be an anion gap metabolic acidosis
2. HHS and DKA can occur concurrently making the diagnosis challenging
3. Identify the underlying cause which is the most common cause of death in HHS patients – use the mnemonic 5 “I”s plus drugs if that helps you remember the triggers
4. HHS patients usually require aggressive fluid resuscitation but be careful not to fluid overload; use POCUS to help assess volume status
5. Correct the potassium deficit in HHS before starting insulin

References

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