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Managing hyperglycaemic emergencies: an illustrative case and review of recent British guidelines

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ABSTRACT – Diabetic ketoacidosis and hyperosmolar hyperglycaemic syndrome are important hyperglycaemic emergencies seen in patients with diabetes. Occasionally, differentiation between the two conditions can be difficult. We present the case of a patient whose hyperglycaemic emergency was managed in a way that could have adversely influenced the outcome. We also discuss important aspects of the new Joint British Diabetes Societies Guidelines on the management of hyperglycaemic emergencies.

KEY WORDS: diabetic ketoacidosis, hyperosmolar hyperglycaemic syndrome, Joint British Diabetes Societies Guidelines

Introduction

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the two most serious metabolic complications of diabetes mellitus (DM). The two conditions share similar pathophysiological mechanisms, involving a reduction in insulin action and production, combined with increased levels of counter-regulatory hormones (glucocorticoids, glucagon and catecholamines). In DKA, the lack of insulin combined with increased catecholamine levels leads to lipolysis, fatty acid production and ketogenesis; whereas in HHS, residual beta-cell function is sufficient to prevent lipolysis but not hyperglycaemia.[1] The main difference between the clinical presentations of DKA and HHS is that the former usually presents acutely, whereas the latter has a more subacute presentation.[2] Other differences in presentation have been suggested by the American Diabetes Association (Table 1).

HHS is manifested by marked elevation of blood glucose, severe dehydration, hyperosmolality (often with hypernatraemia) and only mild ketosis. Rapid administration of insulin and correction of hyperglycaemia are the mainstays of treatment for DKA, but rapid correction of glucose and sodium in HHS can be undesirable because of the rapid shifts in osmolality that result.[3,4]

We present a case of a patient who was admitted with marked hyperglycaemia, whose initial management led to rapid a drop in their blood glucose levels and significant neurological deterioration. We discuss the importance of distinguishing between HHS and DKA in the emergency department, and review the latest Joint British Diabetes Societies guidelines on recognition and management of hyperglycaemic emergencies.

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Table 1. American Diabetes Association diagnostic criteria for diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic syndrome (HHS).

	Diabetic ketoacidosis			
	Mild	**Moderate**	**Severe**	**HHS**
Plasma glucose (mmol/l)	> 14	> 14	> 14	> 33
pH	7.25–7.30	7.0–7.24	<7.0	>7.30
Serum HCO3 (mEq/l)	15–18	10 to <15	<10	>15
Serum ketones	Positive	Positive	Positive	Small
Urine ketones	Positive	Positive	Positive	Small
Serum osmolality (mOsm/kg)	Variable	Variable	Variable	>320
Anion gap	>10	>10	>12	Variable
Mental state	Alert	Alert/ drowsy	Stupor/ coma	Stupor/coma

Case presentation

A 38-year-old African man presented as an acute patient to the emergency department with a five-day history of confusion, disorientation and a recent collapse. He lived alone, but on the day of admission, he had been found by a friend to be difficult to rouse, confused and incontinent of urine. His friend stated that the patient had no past medical history of note, but had been unwell with severe fatigue for around four weeks. He had been unable to work but had not sought medical assistance. He drank around 16 units of alcohol per week, and did not smoke cigarettes.

On admission, it was noted that the patient was overweight (although his actual weight was not initially known) and clinically severely dehydrated. His pulse was 120 regular, his blood pressure 75/36 mmHg and his temperature 35.4ºC. Blood glucose on venous gas analysis was 68 mmol/l (normal range 4–7 mmol/l). The patient was found to have metabolic acidosis on arterial blood gas (pH 7.27, lactate 3.2 mmol/l , bicarbonate 17 (18–28) mmol/l, pO_2 12.3 (10–13) kPa, pCO_2 3.4 (4.4–6) kPa). Urine tests showed glycosuria (4+) and ketonuria (+). Plasma ketone testing was not available. Sodium was 154 (135–145) mmol/l, potassium 5.4 (3.5–5.0) mmol/l, urea 36 (2.5–6.7) mmol/l and creatinine 290 (60–96) umol/l.

A presumptive diagnosis of diabetic ketoacidosis and acute renal failure was made, and the patient was treated in the emergency department with rapid infusion of intravenous 0.9% saline, 12 units of actrapid insulin, and thereafter a continuous

6 units/h intravenous infusion of insulin. He was transferred to the Intensive Therapy Unit (ITU) where he was seen six hours into his admission by the diabetes team. They recognised that the diagnosis was more likely to be HHS, and stopped his intravenous insulin infusion. The patient's calculated serum osmolality on admission was 412 (285–295) mOsm/kg H_2O. By the time that the insulin infusion was stopped after six hours, the patient's venous glucose had fallen to 26 mmol/l. Sodium rose in the first 24 hours from 154 mmol/l to 172 mmol/l, during which time the patient was treated with 0.9% saline and Hartman's fluids.

By the evening of admission, the patient required ventilation because of poor respiratory effort and possible aspiration pneumonia. For the next four days, his glucose levels remained stable at around 20 mmol/l with low-dose insulin infusion (0–2 units/h). His renal failure and hypernatraemia improved with intravenous fluid therapy, without the need for haemofiltration. Nevertheless, the patient remained poorly rousable when off sedation, and magnetic resonance imaging of the brain showed evidence of cerebral oedema and pontine lesions consistent with central pontine myelinolysis. He had a prolonged stay on ITU, and when finally extubated, showed evidence of significant brain injury. EEG confirmed reduced cortical activity. The patient required low-dose insulin to maintain euglycaemia with percutaneous gastrostomy feeding, and he was transferred to the regional brain injury unit for further rehabilitation.

Discussion

Hyperglycaemic emergencies are an important cause of mortality and morbidity in patients who have diabetes. Difficulty in classifying these patients has been highlighted recently.[5] The diagnosis of an acute hyperglycaemic emergency is relatively straight forward, but distinguishing between diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) can sometimes be challenging. The likely reason for our patient's acidosis was his acute renal failure and poor tissue perfusion, rather than ketoacidosis. His low concentrations of urine ketones were probably due to starvation ketosis, which is commonly seen in HHS, and are the reason why the previous name of hyperosmolar non-ketotic coma (HONK) was changed to HHS. We believe that the patient's neurological deterioration could have been worsened by the rapid correction of his glucose levels during the first six hours of admission. We further believe that the very high glucose levels measured on admission, coupled with the patient's hypernatraemia, ethnicity (HHS is more common amongst African-Caribbeans) and weight should have prompted concern that this was more likely to be HHS rather than DKA. There are a number of previous case reports of neurological sequelae resulting from rapid glucose correction in HHS.[6–9]

Joint British Diabetes Societies (JBDS) guidelines on management of DKA

These guidelines were published in 2010, and present a new paradigm for the diagnosis and management of DKA in the UK.[10] Diagnostic criteria for DKA remained unchanged (plasma glucose >11 mmol/l, ketonaemia >3 mmol/l, acidosis [bicarbonate<15 mmol/l] and/or pH <7.3). The important areas of change in practice are as follows:

1 The guidelines stress the importance of bedside plasma ketone testing, which can help in guiding diagnosis and treatment. This, however, requires the training of staff in use of meters for the measurement of plasma ketone as well as regular quality-assurance checks on these meters. Therefore, many hospitals have yet to implement ketone testing.
2 The guidelines suggest the use of venous, rather than arterial, blood-gas monitoring for the diagnosis and monitoring of acidosis, along with the monitoring of electrolyte changes during the course of treatment.
3 The guidelines advocate the use of fixed-rate intravenous insulin infusions (FRIVII) rather than sliding-scale insulin infusions (0.1 units/kg/h).
4 The guidelines do not suggest the need for a bolus insulin dose prior to intravenous insulin infusion.
5 The guidelines suggest continuation of long-acting subcutaneous insulin from admission to facilitate conversion of intravenous insulin to subcutaneous insulin rapidly on recovery.

Targets for treatment include a reduction of the blood ketone concentration by around 0.5 mmol/l/h, an increase in venous bicarbonate by 3 mmol/l/h, reduction in capillary blood glucose by 3 mmol/l/h and maintenance of serum potassium at concentrations between 4.0 and 5.0 mmol/l.

The guidelines give clear suggestions on the investigation, monitoring and subsequent management of patients with DKA. They also exhort the early involvement of the diabetes team in the management of such patients.

Joint British Diabetes Societies (JBDS) guidelines on management of HHS

There is little randomised trial evidence for the correct management of HHS, and many previous guidelines have extrapolated the fluid and insulin therapies used in DKA.[11] Rapid infusion of insulin is an appropriate treatment for DKA as this is usually an acute phenomenon that is not associated with significant changes in osmolality.[10] By contrast, HHS frequently presents over a much longer time period. Rapid reductions in glucose levels are undesirable in HHS as they can lead to large shifts in water and sodium status resulting from rapid changes in serum osmolality.[3] Indeed, rehydration alone will lead to an initial fall in plasma glucose of between 5–11 mmol/l. Subsequently, low-dose insulin infusion might be required, ensuring that the fall in glucose levels is not too precipitous. Another important aspect of the management of HHS that is not relevant to DKA is the use of full anti-coagulation because of the high risk of thrombotic events resulting from severe dehydration.[12]

The recently published JBDS guidelines on the management of HHS have highlighted the important differences in management

of DKA and HHS.[13] They state that the diagnosis of HHS is based on characteristic features of hypovolaemia, marked hyperglycaemia (>30 mmol/l) without significant ketonaemia or acidosis, and hyperosmolality (>320 mOsm/kg), but that some patients can present with a mixed picture of DKA and HHS, or with lactic acidosis if sepsis, metformin therapy or renal failure are apparent.

The guidelines encourage gradual normalisation of osmolality, and suggest the following management pathway:

1 Measure or calculate osmolality frequently to monitor progress using osmolality = $2Na^+$ + glucose + urea, and use venous blood-gas analysis for frequent monitoring after baseline samples.
2 Use 0.9% saline, with or without potassium but without insulin.
3 Careful fluid-balance monitoring is encouraged, with an aim of achieving a positive fluid balance of 3–6 litres within the first 12 hours and 100% of estimated fluid losses by 24 hours. Rate of replacement is influenced by the patient's co-morbidities (for example, their cardiac and/or renal function). Typical fluid losses are estimated to be 110–220 ml/kg (ie 10–22 l for a person weighing 100 kg).
4 Careful monitoring and charting of blood glucose, osmolality and sodium levels at intervals of 1–2 hourly is advocated. The guidelines state that an initial increase in sodium is frequently seen in HHS, and that this is not an indication for hypotonic fluids. Use of 0.45% saline is advocated only if osmolality is not falling despite adequate fluid resuscitation.
5 Low-dose intravenous insulin (0.05 units/kg/h) is advocated only if significant ketonaemia (3-OH Butyrate >1 mmol/l) or ketonuria (>2+) is seen at presentation or if plasma glucose is falling at a rate of less than 5 mmol/h despite adequate fluid replacement. The guidelines suggest that treatment should aim to maintain blood glucose levels at 10–15 mmol/l for first 24 hours.
6 Frequent fluid assessment is advocated to ensure no signs of fluid overload.
7 Prophylactic full anticoagulation is advocated to reduce the risk of venous thromboembolism and stroke.
8 Identification and treatment of underlying precipitants (eg sepsis) is advocated.
9 HHS patients are at high risk of foot ulceration, and careful daily foot checks are necessary.

Conclusions

The diagnosis of a hyperglycaemic emergencies is usually straightforward, but differentiation between DKA and HHS can sometimes be difficult, particularly as type 2 diabetes is now more common in younger age groups. In African Caribbean patients, a condition known as ketosis-prone type 2 diabetes (a genuine presentation with DKA, but with no subsequent requirement for insulin) can also make the situation more complex.[14]

This patient illustrates the importance of distinguishing between DKA and HHS in those presenting with acute hyperglycaemic emergencies, as the insulin therapies required by the two conditions are very different. Familiarity with the new guidelines and the early involvement of the diabetes team are important in managing such cases.

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