ABC don't ever forget glucose

Introduction

This article summarizes the diagnosis and acute management of glucose-based emergencies for the foundation year doctor, principally focusing on hypoglycaemia and the hyperglycaemic emergencies of diabetic ketoacidosis and hyperglycaemic hyperosmolar state. The causes of hyperglycaemia and hypoglycaemia are given in *Table 1*.

Hyperglycaemia

Hyperglycaemia may be an indicator of, or cause of, acute illness depending upon the causative aetiology. Diabetic ketoacidosis and hyperglycaemic hyperosmolar state occur in type 1 and 2 diabetes mellitus respectively and demonstrate the severe end of the spectrum. The difference between diabetic ketoacidosis and hyperglycaemic hyperosmolar state highlights the fundamental physiological difference between an absolute lack of insulin and insulin resistance or relative lack.

Biochemical investigation of hyperglycaemia, along with the clinical signs (*Table 2*), aims to identify features suggestive of diabetic ketoacidosis or hyperglycaemic hyperosmolar state so that appropriate management can be implemented. Capillary blood glucose levels are a useful starting point, but are prone to error outside of the reference interval and should be followed up with an urgent laboratory sample.

If diabetic ketoacidosis is suspected, a venous blood gas will suffice unless the patient has a decreased conscious level or a compromised airway when an arterial blood gas is required (Kelly, 2006). Hyperglycaemic hyperosmolar state is diagnosed by hyperglycaemia in the presence of a serum osmolality greater than 320 mOsm/kg (American Diabetes Association, 2006) and lack of acidosis.

Table 1. Causes of hypoglycaemia and hyperglycaemia

Hyperglycaemia	Diabetes mellitus type 1 and 2
	Physiological (stress, illness, high carbohydrate meal)
	Drug-induced
	Cushing's syndrome
	Acromegaly
	Pancreatitis
	Rare tumours (glucagonoma, phaeochromocytoma)
Hypoglycaemia	Insulin or hypoglycaemic agents
	Alcohol, high-dose salicylates
	Malabsorption
	Fasting, starvation or intense exercise
	Shock (septic)
	Chronic kidney disease, severe liver disease, adrenal insufficiency
	Rare tumours – insulinoma

Table 2. Common presenting symptoms of hyperglycaemia

Polydipsia, polyuria and nocturia
Weight loss
Fatigue
Recurrent infections
Arrhythmias
Stupor
Coma

Acute management

The management of diabetic ketoacidosis and hyperglycaemic hyperosmolar state requires advanced care and monitoring (*Table 3*). Therapy revolves around adequate rehydration, correction of hyperglycaemia and replenishing electrolytes (especially potassium). Fluid resuscitation with 0.9% saline aims to restore renal perfusion. Urine output and glucose levels should guide further intravascular resuscitation. Fluid therapy should aim to reduce the serum osmolality by ≤3 mOsmol/kg/hr to avoid pulmonary and cerebral oedema (more common in children). Intravenous resuscitation should switch to 5% dextrose with 0.45% saline once serum glucose levels are 11.1 mmol/litre in diabetic ketoacidosis or 13.9–16.7 mmol/litre in hyperglycaemic hyperosmolar state and further insulin therapy should be aimed at maintaining a glucose level between 8.3 and 11.1 mmol/litre.

In the absence of hypokalaemia (<3.3 mmol/litre) insulin should be administered, starting at 0.1 U/kg as a bolus and then continued at 0.1 U/kg/hr via intravenous infusion, aiming for a minimum initial hourly reduction in serum glucose of 2.8–3.9 mmol/litre/hr (American Diabetes Association, 2006). Dose adjustments should be guided by hourly capillary blood glucose monitoring, but if the glucose concentration does not fall by 2.8–3.9 mmol/litre/hr the insulin infusion should be doubled. Severe acidosis (pH≤7) may require bicarbonate therapy but this should only be attempted by those competent in managing the potential complications as the action of insulin

Table 3. Basic investigations for hyperglycaemic emergencies

Investigation	Rationale
Blood gas	To determine acidosis ± oxygenation
Urea and electrolytes including bicarbonate	Monitoring electrolyte depletion and renal function
Serum osmolality	>320 mOsm/Kg consistent with hyperglycaemic hyperosmolar state
Urinalysis	Ketones
Full blood count, glucose, C-reactive protein, chest X-ray	Infection screen
Electrocardiogram or cardiac monitor	Myocardial infarction may cause diabetic ketoacidosis

Dr HD Brooks *is Foundation Year 2 in Pathology,* **Dr SP Harger** *is Foundation Year 1 in Pathology and* **Dr PJ Twomey** *is Consultant Chemical Pathologist in the Department of Clinical Biochemistry, Ipswich Hospital, Suffolk IP4 5PD*

Correspondence to: Dr PJ Twomey

should raise the pH via conversion of ketoacid anions to bicarbonate.

Monitoring

Electrolyte depletion is common to both diabetic ketoacidosis and hyperglycaemic hyperosmolar state secondary to renal and gastric loss of potassium and sodium. Care with interpretation of electrolytes is required: acidosis causes a transfer of potassium from within cells to serum, usually resulting in hyperkalaemia; the expected sodium concentration after achieving normoglycaemia is usually higher (for each 5.6 mmol/litre glucose above 5.6 mmol/litre, add 1.6 mmol/litre; American Diabetes Association, 2006). Thus, close monitoring is required, especially with the instigation of insulin and fluid therapy.

Non-diabetic hyperglycaemia in acute illness

Although diabetic ketoacidosis and hyperglycaemic hyperosmolar state are the most common scenarios, hyperglycaemia in the context of acute illness also affords a poor prognosis. Evidence suggests that maintenance of normoglycaemia with insulin therapy in these patients may reduce morbidity and mortality (Langouche et al, 2007).

Hypoglycaemia

Hypoglycaemia is one of the common, yet under-diagnosed metabolic emergencies with potentially diverse aetiology, yet the vast majority of cases (99.5%) have been reported as secondary to diabetic therapy or hypoglycaemic agent abuse (Potter et al, 1982) and are easily treated with prompt diagnosis and management.

Hypoglycaemia may be categorized as biochemical or clinical. Biochemical hypoglycaemia is a plasma glucose concentration <2.8 mmol/litre that may be asymptomatic. Clinical hypoglycaemia may be acute or chronic in nature and is defined by Whipple's triad (Whipple, 1938):

- Symptoms and signs of hypoglycaemia
- A low plasma glucose of <2.2–2.5 mmol/litre (no consensus for the cut-off)
- Resolution of symptoms with glucose therapy.

Symptoms may be vague and non-specific but have a propensity to present with central and autonomic neurological disturbance (*Table 4*). Autonomic symptoms tend to present first, usually at serum glucose concentrations <3 mmol/litre, while the central neuroglycopenic presentations can occur when serum glucose concentration is <2.8 mmol/litre (Mitrakou et al, 1991).

Acute management

It is important to ascertain whether the patient is diabetic and what hypoglycaemics (oral or insulin) have been given. Beware the non-diabetic patient with access to hypoglycaemics.

Principally treat the patient rather than the results: a conscious patient will usually tolerate orange juice, jam, biscuits or hypostop. In the event of altered consciousness priority is to protect the airway, gain intravenous access (take blood for full blood count, urea and electrolytes, liver function tests, glucose and freezing (for further testing later if required)) and give a bolus of 50 ml of 50% dextrose into a large vein. Level of consciousness should return to normal within 10 minutes, if this fails (be wary of patients on β-blocker therapy) then glucagon 1 mg should be administered immediately and a 4–8-hourly infusion of 1 litre 10% dextrose started. In the acute phase monitor capillary glucose every 30 minutes with a decreasing frequency as the patient's condition improves.

Table 4. Presentations of hypoglycaemia

Autonomic	Sweating
	Anxiety
	Hunger
	Tremor
	Palpitations
Neuroglycopenic	Confusion
	Seizures
	Focal neurology
	Coma

Hypoglycaemic agents should be stopped until reinitiation is safe.

Further management

Further assessment of hypoglycaemia is required if the patient is not on treatment for diabetes, or hypoglycaemia has not been confirmed as the cause of symptoms. A referral for a 72-hour fast may be applicable outside the acute setting. Testing for glucose, insulin, C-peptide, proinsulin and μ-hydroxybutyrate may be useful in differentiating potential underlying conditions when hypoglycaemia is present but is outside of the scope of this article.

Conclusions

Both hyperglycaemic and hypoglycaemic emergencies require urgent identification, initiation of therapy and monitoring but are reversible if identified and treated early enough. BJHM

Conflict of interest: none.

American Diabetes Association (2006) Consensus statement on hyperglycaemia crises in adult patients with diabetes. *Diabetes Care* **29:** 2739–48

Kelly AM (2006) The case for venous rather than arterial blood gases in diabetic ketoacidosis. *Emerg Med Australas* **18**(1): 64–7

Langouche L, Vanhorebeek I, Van den Berghe G (2007) Therapy insight: the effect of tight glycemic control in acute illness. *Nat Clin Pract Endocrinol Metab* **3**(3): 270–8

Mitrakou A, Ryan C, Veneman T et al (1991) Hierarchy of glycaemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction. *Am J Physiol* **260:** E67

Potter J, Clarke P, Gale AE, Dave SH, Tattersall RB (1982) Insulin-induced hypoglycaemia in an accident and emergency department: the tip of an iceberg? *BMJ* **285**: 1180–2

Whipple AO (1938) The surgical therapy of hyperinsulinism. *J Int Chir* **3:** 237

Further reading

American Diabetes Association (1987) Consensus statement on self-monitoring of blood glucose. *Diabetes Care* **10:** 95

Chiasson J, Aris-Jilwan N, Bélanger R et al (2003) Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* **168**(10): 1241

Longmore M, Wilkinson I, Turmezei T, Cheung C (2007) *Oxford Handbook of Clinical Medicine.* 7th edn. Oxford University Press, Oxford

KEY POINTS

- Hypoglycaemia is common in diabetic patients and should be considered in the differential diagnosis of all acutely unwell patients.
- Diabetic ketoacidosis and hyperglycaemic hyperosmolar state require intensive monitoring of electrolytes.
- Both hypoglycaemia and hyperglycaemia are reversible if identified early enough.