



ABCD guidelines for the management of hyperglycaemic emergencies in adults

MW Savage*, A Kilvert, on behalf of the Association of British Clinical Diabetologists (ABCD)

Introduction

Diabetic emergencies are common but there is limited evidence-based assessment of management in the literature. There has been a lack of progress in research in this important clinical area and consequently there is no consensus on the optimal management of these life-threatening conditions. There is evidence that outcomes are better when the patient is managed by a specialist rather than a general physician,¹ but most units in the UK are unable to offer an on-call diabetes service and inevitably diabetic emergencies are managed by non-specialists. Many hospitals have developed local guidelines for management of diabetic emergencies but there is a need for consistency to improve the standard of care across the UK. We have developed the following guidelines on behalf of the Association of British Clinical Diabetologists (ABCD) to provide a basis for the management of diabetes-related hyperglycaemic emergencies. These guidelines are evidence based but also attempt to address the day-to-day issues that cause controversy and lead to heated debate. They were developed between 2003 and 2005 in an iterative process based on the available evidence and on the experience of practising diabetologists in the UK. We are indebted to the many colleagues who have let us see their local charts, protocols and guidelines. We (ABCD) will review them in December 2008 with the review to commence in December 2007.

The guidelines themselves are available from the ABCD website, along with a proposed Treatment

ABSTRACT

Diabetic emergencies are traditionally treated by the acute medical admitting team or the Accident and Emergency Department staff. Most will see these on a regular basis, as they are common and both type 1 and type 2 disease are increasing in prevalence. Diabetic emergencies are usually easily treated and the patients discharged. However, it is vital not to become complacent as these disorders can lead to death. It is particularly important to follow local guidance and to involve the Diabetes Team after each episode. We outline the basic management steps in the common diabetic hyperglycaemic emergencies and hope to give an insight to the non-expert. A proforma for the management of diabetic hyperglycaemic emergencies can be down-loaded from the Association of British Clinical Diabetologists (ABCD) website at: http://www.diabetologists.org.uk/ABCD_DKA_Chart.pdf. ABCD proposes this chart as an example only and is not responsible for its use; that lies with the treating doctor. Copyright © 2006 John Wiley & Sons, Ltd.

Practical Diabetes Int 2006; 23(5): 227–231

KEY WORDS

diabetes; diabetic ketoacidosis (DKA); hyperosmolar non-ketotic coma (HONK); hyperglycaemic emergencies

Chart which may be downloaded and used as it stands, or modified for local use (<http://www.diabetologists.org.uk/>).

ABCD actively encourages audit of these guidelines and invites submission of results of audits to it via the website. This will permit the iterative process to continue and allow input into the revision of these guidelines.

Diabetic ketoacidosis

These are general guidelines for management only. Treatment may need modification to suit the individual patient and frequent reassessment of the patient's condition is mandatory. Rapid treatment is essential. History and examination should not delay initial investigations and management. Diabetic ketoacidosis (DKA) usually occurs in patients with known type 1 diabetes, but may be the presenting diagnosis

– be alert to the possibility of DKA in any patient with vomiting and dehydration. Suspect DKA in patients with diabetes who are unwell, particularly if symptoms include vomiting, abdominal pain or shortness of breath.

Precipitating causes include conditions which increase circulating levels of stress hormones, such as myocardial infarction, infection, or surgical emergencies. These conditions often present with the specific symptoms and signs of the precipitating cause. Moreover, errors of insulin administration or deliberate omission of insulin are common causes of DKA.²

The diagnosis of DKA is often straightforward. Polyuria and polydipsia reflect hyperglycaemia but the important symptoms of vomiting, abdominal pain and/or shortness of breath indicate the likelihood of ketoacidosis. Symptoms of

Mark W Savage, MD, FRCP,
Consultant Physician in Diabetes, North
Manchester General Hospital,
Manchester, UK

Anne Kilvert, MD, FRCP,
Consultant Physician in Diabetes,

Northampton General Hospital,
Northampton, UK

*Correspondence to: Dr Mark Savage,
Consultant Physician in Diabetes/
Endocrinology, North Manchester General

Hospital, Pennine Acute Hospitals,
Manchester M8 5RB, UK; e-mail:
mark.savage@pat.nhs.uk

Received: 11 April 2006

Accepted: 20 April 2006



any precipitating condition may also be present.

The signs are not specific and include: dehydration; tachycardia; hypotension; hyperventilation (Kussmaul respiration); drowsiness or coma; and the smell of ketones on breath. Not everyone is able to smell ketones; to test one's ability, compare the ability to detect commercial nail-varnish remover with colleagues.

The criteria used to diagnose DKA are of course given in the title of the condition. Requirements are:

- Raised (>11.1mmol/L) blood glucose (or known diabetes).

- Ketonuria (++) or more on Dipstix® or alternatively detection of significant ketonaemia by plasma Ketostix™ or the laboratory. (Some modern blood glucose meters are able to measure blood ketones and their use may become more widespread.³ It is important not to confuse measurement of ketones with blood glucose; ensure that the correct strips are used.)

- Significant acidosis; either a serum venous bicarbonate level of <15mmol/L or, if measured, an arterial pH <7.3.

The indicators of severe DKA include the following: venous bicarbonate <10mmol/L; arterial pH <7.0 (if measured); hyperventilation; hypotension with a systolic BP <90mmHg; and a depressed conscious level. It is good practice to document the Glasgow Coma Scale. Blood glucose is not a good guide to severity due to the large number of factors that influence it, e.g. it may be reduced because of insulin administered by the patient, relatives, or primary care physician before admission.

Emergency management

Treatment should be started immediately as delay may be fatal. Obtain good intravenous (IV) access – if peripheral access is difficult, insert a central line. Commence IV saline and insulin immediately (Table 1). Consider using the Intensive or High-Dependency Units (ITU/HDU) if the patient is confused, unconscious, or hypotensive (systolic BP <90mmHg), or if venous bicarbonate is <10mmol/L (or pH

Table 1. Treatment with intravenous fluids and insulin

Intravenous fluids
<ul style="list-style-type: none"> • Give 1L 0.9% sodium chloride solution over the first hour • If BP <90 systolic consider a plasma expander • Rate of fluids thereafter depends on age/fitness of patient, typically: <ul style="list-style-type: none"> – 1L in next hour – 2L in next 2–4 hours – then 1L 4–6 hourly • Reduce rate in elderly/cardiac disease/mild DKA ($\text{HCO}_3^- >10$) • More rapid infusion increases risk of respiratory distress syndrome • Switch to 5% glucose 1L 8 hourly once BG ≤ 15mmol/L; continue 0.9% sodium chloride concomitantly if patient still volume depleted
Insulin
<ul style="list-style-type: none"> • Dilute 50units of soluble insulin to 50ml 0.9% saline in a syringe (ensure the drawing up is witnessed and signed for) • Infuse intravenously, using syringe driver, starting at 6units/hour • Give 10units soluble insulin intramuscularly if delay in starting IV anticipated • Check venous glucose at 2 hours; if glucose has not fallen check pump working and IV connections, then increase to 10u/hour • Measure capillary BG hourly • Once glucose falling, adjust insulin infusion rate according to insulin infusion schedule

<7.0). If no ITU/HDU is available then as much intensive monitoring as is practical in the circumstances is highly recommended.

Essential investigations include laboratory blood glucose; urea and electrolytes; venous bicarbonate (this can be measured on blood gas analyser); ECG; CXR; urine and blood cultures. Arterial gases should be measured if there is a reduced conscious level; respiratory distress; or if the patient is hypotensive. If the patient appears well, venous bicarbonate may suffice. Further investigations may be clinically indicated e.g. throat swab, lumbar puncture, CT brain scanning.

Other measures which must be implemented include: strict fluid balance – urinary catheter if incontinent or if no urinary output after two hours; consider inserting a central venous pressure line if the patient is elderly or has evidence of poor left ventricular function; insert a nasogastric tube if the conscious level is impaired, remembering to also protect airway; and consider thromboprophylaxis if there is severe dehydration or the patient is elderly. Broad spectrum antibiotics should be given if there is evidence

of infection (see boxed text 'Catches for the unwary' below).

Fluid and insulin replacement Fluid rate

Fluid replacement should be rapid initially, then slowed depending on the patient's response. If the patient is hypotensive, colloids may be considered but there is no evidence that this is superior to rapid crystalloid administration. Over-enthusiastic fluid replacement may lead to marked osmotic shifts with the risk of respiratory distress syndrome. It has also been linked with the rare complication of cerebral oedema, although evidence is lacking.⁴ Care should be taken with fluid replacement in at-risk groups such as: the elderly; those in renal failure; and those with a history of congestive heart failure and ischaemic heart disease.

Type of fluid

See Table 1. Most units recommend 0.9% sodium chloride solution initially. Change to 5% glucose once the blood glucose has fallen below 15mmol/L; some units prefer 10% glucose, in which case the rate of infusion of glucose and insulin

**Table 2.** Example of variable dose insulin infusion schedule

Blood glucose (mmol/L)	Insulin dose (units/hour)
>16	6
12.1–16	4
10.1–12	3
7.1–10	2
4–7	1
<4	0.5

NB

- See notes under 'Insulin' and 'Pregnancy' (below) regarding insulin resistance in septic, pregnant and obese individuals.
- If blood glucose <4 mmol/L assess patient. If confused or unrousable either apply your local hospital guidelines for the management of hypoglycaemia or contact doctor.

Table 3. Example of guide to potassium replacement

Serum potassium (mmol/L)	Potassium chloride to be added to each litre of fluid
>5.5	Nil and check K ⁺ in 2 hours
4–5.4	20mmol
<4	40mmol

Table 4. Use of bicarbonate in DKA (High Dependency Unit/Intensive Therapy Unit)

Potential harmful effects
<ul style="list-style-type: none"> • Possible hypokalaemia and arrhythmia • Exacerbation of intracellular and intracerebral acidosis due to CO₂ crossing cell membranes and blood brain barrier, when HCO₃⁻ cannot • Possible increased risk of cerebral oedema
Potential benefits
<ul style="list-style-type: none"> • Reduced cardiac irritability • Reduced respiratory discomfort • Reduction in IV chloride load and avoidance of hyperchloraemic acidosis

needs to be adjusted as necessary. If the patient is still volume depleted, 0.9% sodium chloride may be continued concomitantly. If the blood glucose rises above 15mmol/L after the change to 5% glucose, we recommend continuation of the glucose infusion and an increase in the insulin rate as necessary (according to insulin infusion schedule). Do not revert to sodium chloride infusion alone.

After changing to glucose ensure the venous bicarbonate is continuing to improve as there is a small risk of 'euglycaemic ketoacidosis'. Consider changing from 5% to 10% glucose if acidosis is slow to

resolve and the blood glucose is <10mmol/L (allows higher rate of insulin infusion).

Insulin

Low-dose IV insulin replacement is now the accepted management as the main action of insulin in this (and other conditions) is to prevent gluconeogenesis by the liver and this occurs at low blood levels of insulin.^{5–7} Tables 1 and 2 give guidance on insulin infusions as well as an *example* of an insulin infusion schedule. Be prepared to change the infusion rates if blood glucose is not falling and equipment has been checked and is functioning

normally. Some specialists prefer a constant insulin infusion of 6units/hour until the bicarbonate is above 15mmol/L; however, there is no evidence to support or refute this approach.

Insulin-resistant patients – particularly, septic and/or obese patients – may need significantly higher rates of insulin infusion and the treating doctors and nurses need to be aware of this.

Potassium

Most patients will be potassium depleted and serum potassium will fall as acidosis is corrected. Careful monitoring is required and potassium should be added to IV fluid as indicated in Table 3.

'GKI' (glucose, potassium and insulin) infusions

Some units prefer to use glucose 5% or 10%, with insulin and potassium added to the glucose solution. As far as we are aware there is no evidence to support this method, nor is there any evidence to suggest it is less safe.

Bicarbonate

Bicarbonate is usually unnecessary and may be harmful. Do not use unless pH <7.0 and the patient is not responding to rehydration and insulin. Discuss with the consultant first.⁸ We recommend that it is only used in an appropriate setting, such as ITUs or HDUs. For the pros and cons see Table 4.

Pregnancy

This is an insulin-resistant state and ketones are very dangerous for the foetus. Pregnant women with ketoacidosis should be managed in an ITU/HDU setting and a diabetologist and obstetrician should be consulted urgently. The insulin infusion schedule should be at least doubled in the third trimester.

Monitoring

Laboratory blood glucose should be measured at diagnosis and after two hours; capillary blood glucose (by meter) hourly. We recommend that urea and electrolytes and venous bicarbonate be checked after two hours from admission and then four-hourly until the patient is stable



and bicarbonate is $>15\text{mmol/L}$. An ECG monitor should be applied until the patient is stable. Ideally, blood glucose should fall by $4\text{--}6\text{mmol/L/hour}$. If this does not happen, check the insulin pump and cannulae. If the equipment is functioning normally, increase the insulin infusion rate by revising the insulin infusion schedule. Discuss with the consultant or other senior staff member.

Continuing management

- Consult the Diabetes Team as soon as possible for a decision on continuing management.
- Transfer to subcutaneous (SC) insulin once the patient is able to eat and drink normally.
- Do not stop IV insulin until SC insulin has been given.
- Urinary ketones may take some time to clear and should not delay return to SC insulin.
- Patients with known diabetes should go back to their previous insulin regimen – ask the Diabetes Team to review the regimen.
- Patients with a new diagnosis of diabetes should have short-acting insulin before meals and longer-acting insulin at bedtime based on the insulin infusion rate required to maintain a stable blood glucose, i.e. based on the rate after the acidosis resolved – for example: insulin infusion schedule at $2\text{units/hour} = 48\text{units}/24\text{hours} = \text{human soluble insulin } 12\text{units pre-meals and human isophane insulin } 12\text{units pre-bed}$. Monitor blood glucose before meals and before bed and adjust insulin doses as necessary. This is an interim measure; consult the Diabetes Team as soon as possible for advice on a long-term insulin regimen.
- If possible identify the precipitating cause of the DKA.
- Always inform the Diabetes Team so that education can be given to reduce the risk of future episodes of DKA.

Complications of DKA

Most complications are predictable from a knowledge of the biochemistry of the condition and its treatment. However, some should be emphasised.

• **Hypoglycaemia and hypokalaemia.** Monitor carefully to anticipate and prevent.

• **Aspiration.** Ensure nasogastric tube and airway protection in the unconscious patient.

• **Underlying conditions.** Ensure these are identified and treated appropriately.

• **Cerebral oedema.** This condition is uncommon but may occur, particularly in young adults.

Cerebral oedema, symptoms/signs:

- Headache.
 - Bradycardia and rising BP.
 - Change in neurological status (decreased conscious level, restlessness, irritability).
 - Focal neurological signs.
 - Convulsions.
 - Papilloedema.
- Cerebral oedema, management:*
- Exclude hypoglycaemia.
 - Discuss with consultant and transfer to ITU.
 - Give mannitol 20% 5ml/kg over 20 minutes.
 - Obtain CT scan of head to exclude other causes.

• **Hypophosphataemia.** This may occur in DKA and has been associated with a wide range of metabolic disturbances. Phosphate depletion

persists for several days after resolution of DKA.⁹ However, prospective studies have failed to show clinical benefit from phosphate replacement.¹⁰

Hyperosmolar non-ketotic coma

This condition is characterised by hyperglycaemia and high plasma osmolality without significant ketonuria or acidosis.

Clinical characteristics

Type 2 diabetes, usually in patients over 60 years. Up to 40% of cases occur in previously undiagnosed patients. The onset is often insidious with vague symptoms including confusion and drowsiness with features of dehydration. It is necessary to look for a precipitating medical condition, e.g. sepsis, myocardial infarction etc. In this condition the haemodynamic state is the best indicator of severity of illness.¹¹

Diagnosis

Hyperglycaemia (blood glucose usually $>50\text{mmol/L}$) with a calculated osmolality ($2[\text{Na} + \text{K}] + \text{glucose}$) of $>350\text{mosmoles}$ (it is not necessary to include urea as this does not con-

Catches for the unwary in DKA

- Blood glucose may not be very high and is not a guide to the severity of DKA if there has been partial treatment with insulin before admission
- Urine output may be high in the initial stages – ensure that this is measured and taken into consideration when calculating rate and volume of fluid replacement
- Urinary ketones may be negative in the early stages of DKA because Ketostix do not detect 3-hydroxybutyric acid, the main ketone body in the urine initially. If in doubt plasma ketones can be measured
- Not everyone can smell acetone. Do not rely on smell to detect ketones unless you are sure you can smell them
- If there is doubt about the reason for the acidosis, serum salicylate and lactate should be measured
- Pseudo-hyponatraemia may result from highly lipaemic serum – if the serum sodium is low this should be checked with the laboratory
- Serum potassium levels may be very high initially as acidosis drives potassium into the extracellular compartment. Potassium will fall (sometimes rapidly) during treatment as the acidosis resolves
- Raised WCC is common in DKA and does not necessarily indicate infection
- Fever may be absent initially because of acidotic vasodilatation
- Serum amylase is often elevated and does not necessarily indicate pancreatitis
- Abdominal pain is common and may be mistaken for an acute abdomen *but* if in doubt get a surgical opinion



tribute to the osmotic load); in addition serum bicarbonate is $>15\text{mmol/L}$ and the urinary ketones ++ or less on the standard Dipstix.

Management

Management is as for DKA but note the following.

- The insulin infusion rate should be halved as paradoxically these patients can be quite insulin sensitive. This should be reviewed in two hours.
- Elderly patients are more likely to need a CVP line to optimise fluid replacement.
- If serum sodium is $>155\text{mmol/L}$ consider giving 0.45% sodium chloride initially, although many units give 'normal' saline (0.9%) as this is relatively hypotonic in this situation.
- Risk of thromboembolic disease is high – anticoagulate fully if no contraindications.
- Most patients can eventually be managed with oral hypoglycaemic agents and diet, but recovery of insulin secretion may take time

and insulin may be required for a few weeks.

Conflict of interest statement

The authors have not received any pharmaceutical funding to assist in the preparation of these guidelines.

References

1. Levetan CS, Passaro MD, Jablonski KA, *et al.* Effect of physician specialty on outcomes in DKA. *Diabetes Care* 1999; **22**: 1790–1795.
2. Thompson CJ, Cummings F, Chalmers J, *et al.* Abnormal insulin treatment behaviour: A major cause of ketoacidosis in the young adult. *Diabetic Med* 1995; **12**: 429–432.
3. Guerci B, Benichou M, Floriot M, *et al.* Accuracy of an electrochemical sensor for measuring capillary blood ketones by fingerstick samples during metabolic deterioration after continuous subcutaneous insulin infusion interruption in type 1 diabetic patients. *Diabetes Care* 2003; **26**: 1137–1141.
4. Glaser N, Barnett P, McCaslin I, *et al.* Risk factors for cerebral edema in children with diabetic ketoacidosis. *N Engl J Med* 2001; **344**: 264–269.
5. Page MM, Alberti KG, Greenwood R, *et al.* Treatment of diabetic coma with continuous low-dose infusion of insulin. *BMJ* 1974; **2**(921): 687–690.
6. Sonksen P, Sonksen J. Insulin: understanding its action in health and disease. *Br J Anaesth* 2000; **85**: 69–79.
7. Kitabchi AE, Fisher JN. Insulin therapy of diabetic ketoacidosis: physiological *versus* pharmacological doses of insulin and their routes of administration. In *Diabetes Mellitus*. Brownlee M (ed). Chichester: Wiley, 1981; s95–149.
8. Morris LR, Murphy MB, Kitabchi AE. Bicarbonate therapy in severe diabetic ketoacidosis. *Ann Intern Med* 1986; **105**: 836–840.
9. Butler A, Talbot N. Metabolic studies in diabetic coma. *Trans Assoc Am Physicians* 1947; **60**: 102–109.
10. Keller U, Berger W. Prevention of hypophosphataemia by phosphate infusion during treatment of diabetic ketoacidosis and hyperosmolar coma. *Diabetes* 1980; **29**: 87–95.
11. Pinies JA, Cairo G, Gaztambide S, *et al.* Course and prognosis of 132 patients with diabetic non ketotic hyperosmolar state. *Diabete Metab* 1994; **20**: 43–48.