

Managing diabetic ketoacidosis in adults: New national guidance from the JBDS

Article points

1. Diabetic ketoacidosis (DKA) is a metabolic abnormality associated with type 1 diabetes.
2. The Joint British Diabetes Societies (JBDS) have developed updated guidelines on the management of DKA and first recommend involvement of a diabetes specialist team.
3. A fixed-rate intravenous insulin infusion is recommended with bedside measurement of blood levels of ketones and glucose.
4. Continuation of long-acting insulin analogues is advised to avoid rebound hyperglycaemia.

Key words

- Diabetic ketoacidosis
- Inpatient care
- Joint British Diabetes Societies
- Ketone

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Diabetic ketoacidosis (DKA) is a life-threatening metabolic abnormality associated with type 1 diabetes. It results from absolute or relative insulin deficiency, with an associated increase in counter-regulatory hormones which increase hepatic glucose production, inducing severe hyperglycaemia. Despite improvements in diabetes care, it remains a significant clinical problem. As a result, the Joint British Diabetes Societies (JBDS) has produced updated guidance for the management of DKA to reflect developments in technology and new practice in the UK. A number of new recommendations have been introduced, including prompt referral to the diabetes specialist team and the use of ketone meters. This article summarises the JBDS guideline and discusses the implications of standardised treatment in departments admitting people with DKA.

Diabetic ketoacidosis (DKA) is the classic metabolic abnormality associated with type 1 diabetes. Although preventable, DKA is a frequent and life-threatening complication, and is associated with significant morbidity and mortality (Hamblin et al, 1989). Despite improvements in diabetes care (Fishbein and Palumbo, 1995; Umpierrez et al, 1997) it remains a significant clinical problem, and although mortality rates have fallen significantly in the past 20 years, from 7.96% in 1982 to 0.67% in 2002 (Lin et al, 2005), early diagnosis and effective management of the condition is vital.

The main causes of mortality in the adult population with DKA include severe

hypokalaemia (low blood potassium levels), adult respiratory distress syndrome and comorbid states such as pneumonia, acute myocardial infarction and sepsis (Hamblin et al, 1989).

The true incidence of DKA is difficult to establish, although population-based studies report rates that range from 4.6 to 8 episodes per 1000 people with diabetes (Johnson et al, 1980; Faich et al, 1983).

To address these issues, the Joint British Diabetes Societies (JBDS), with support from NHS Diabetes, has developed up-to-date guidance for the management of DKA in adults. This article explores the key recommendations made by the guideline and

discusses the implications both for people with DKA and for nurses charged with their care.

Purpose of the guideline

The guideline, *The Management of Diabetic Ketoacidosis in Adults* (Savage et al, 2010), is intended for use by clinicians and service commissioners in delivering high-quality care for people admitted to hospital with DKA.

There are several currently available national and international guidelines for the management of DKA both in adults and children (Savage et al, 2006; McGeoch et al, 2007; British Society for Paediatric Endocrinology and Diabetes [BSPED], 2009; International Society for Pediatric and Adolescent Diabetes [ISPAD], 2009; Kitabchi et al, 2009).

In the past decade, however, there has been a change in the way that people with DKA present clinically, with partially treated DKA and consequently lower blood glucose levels. In addition, there has been rapid development of near-patient testing technology, which is now readily available for monitoring blood ketone levels, allowing for a shift away from the dependence on blood glucose levels to drive treatment decisions in the management of DKA.

The guideline discussed in this article (Savage et al, 2010) updates the currently available UK-based guidelines, and has been endorsed by the JBDS. It has been developed to reflect the advances in technology and new practice in the UK. They are evidence based, where possible, but are also drawn from pooled multiprofessional knowledge and consensus agreement.

Pathophysiology

DKA occurs as a result of absolute or relative insulin deficiency accompanied by an increase in counter-regulatory hormones. This hormonal imbalance increases hepatic glucose production, resulting in severe hyperglycaemia.

Enhanced fat breakdown increases serum-free fatty acids, which are then metabolised, producing large quantities of ketone bodies and consequently results in metabolic acidosis.

Osmotic diuresis due to hyperglycaemia, as well as other factors, can lead to serious problems such as fluid deprivation, and is also related to electrolyte shifts and depletion, resulting in hyper- and hypokalaemia.

Diagnosis

Absolute diagnostic criteria for DKA do not exist, however the following are proposed in the guideline (Savage et al, 2010): ketonaemia >3 mmol/L or significant ketonuria (more than 2+ on standard urine sticks); blood glucose >11 mmol/L or known diabetes; and venous bicarbonate (HCO_3^-) <15 mmol/L and/or venous pH <7.3 . It is not necessary to measure arterial pH as this is not significantly different from venous pH (Kelly, 2006). *Table 1* outlines the signs and symptoms of DKA.

Developments in management

Diabetes teams have been using ketone meters with increasing regularity to manage outpatients with type 1 diabetes. Until recently, the management of DKA has focused on addressing hyperglycaemia with fluids and insulin, and using arterial pH and serum bicarbonate to assess metabolic

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Table 1. Signs and symptoms of diabetic ketoacidosis.

Signs	<ul style="list-style-type: none"> ● Deep, rapid breathing. ● Dry skin and mouth. ● Flushed face. ● Fruity breath (fruit drop odour). ● Nausea and vomiting. ● Stomach pain.
Symptoms	<ul style="list-style-type: none"> ● Fatigue. ● Frequent urination or thirst for 1 day or more. ● Mental stupor that may progress to coma. ● Muscle stiffness or aching. ● Shortness of breath. ● Abdominal pain. ● Decreased appetite. ● Decreased consciousness. ● Headache.

Page points

1. The guideline recommends that the management of people with diabetic ketoacidosis is based on bedside monitoring.
2. All people admitted to hospital should be reviewed by a member of the diabetes specialist team prior to discharge to maintain safety and optimise care.
3. The main aims of fluid replacement are to restore circulatory volume, clear ketones and correct electrolyte imbalance.
4. In people with kidney or heart failure, as well as older people and adolescents, there may be a need to modify the rate and volume of fluid replacement.

improvement based on the assumption that this would suppress ketogenesis and reverse the process of acidosis.

It is now possible, however, to focus on the underlying metabolic abnormality – ketonaemia – which simplifies treatment of people who present with modest hyperglycaemia but with acidosis secondary to ketonaemia, a condition known as “euglycaemic diabetic ketoacidosis” (Munro et al, 1973; Johnson et al, 1980; Jenkins et al, 1993). This clinical presentation is being encountered more frequently.

The guideline recommends that the management of people with DKA is based on bedside monitoring. Blood glucose is routinely checked at the bedside, but portable ketone meters now also allow bedside measurement of 3-beta-hydroxybutyrate, which is an important advance in DKA management (Vanelli et al, 2003; Bektas et al, 2004; Khan et al, 2004; Wallace and Matthews, 2004; Naunheim et al, 2006; Sheikh-Ali et al, 2008). The treatment of DKA depends on the suppression of ketonaemia, therefore measurement of blood ketones now represents best practice in monitoring the response to DKA treatment (Wiggam et al, 1997).

The majority of blood-gas analysers currently available provide measurements of blood gas and electrolytes at the bedside within a few minutes of blood being taken. The guideline therefore recommends that glucose, ketones and electrolytes, including bicarbonate and venous pH, should be assessed at or near the bedside.

The guideline recognises that not all units have access to ketone meters, therefore recommendations are also given on monitoring treatment using the rate of rise of bicarbonate and fall in blood glucose as alternative measures.

Involvement of diabetes specialist teams

Evidence has consistently shown that diabetes specialist teams, particularly with diabetes inpatient specialist nurse (DISN)

involvement, shorten inpatient stay and improve safety (Levitan et al, 1995; Cavan et al, 2001; Davies et al, 2001). The present guideline recommends that diabetes specialist team involvement should occur “as soon as possible” during the acute phase, pointing out that the practice of admitting, treating and discharging people admitted to hospital with DKA without the involvement of the diabetes specialist teams is unsafe and likely to compromise safe patient care.

DISNs are pivotal in reviewing people with DKA, establishing the cause and educating the individuals around treatment and sick-day rules. All people admitted to hospital should be reviewed by a member of the diabetes specialist team prior to discharge to maintain safety and optimise care (Clement et al, 2004). *Box 1* gives a case study highlighting some common issues related to the management of people admitted with DKA.

General management issues

There is common agreement that the most important initial therapeutic intervention in people with DKA is appropriate fluid replacement followed by insulin administration (Savage et al, 2006; Kitabchi et al, 2009). The main aims of fluid replacement are to restore circulatory volume, clear ketones and correct electrolyte imbalance. For example, an adult weighing 70 kg presenting with DKA may be up to 7 litres in fluid deficit, with associated electrolyte deficits.

In people with kidney or heart failure, as well as older people and adolescents, there may be a need to modify the rate and volume of fluid replacement. The aim of the first few litres of fluid is to correct any hypotension, address the intravascular deficit and offset the effects of the osmotic diuresis with correction of electrolyte disturbance.

Assessment of severity

The presence of one or more of the following may indicate severe DKA:

- Blood ketones over 6 mmol/L.
- Bicarbonate level below 5 mmol/L.

- Blood pH below 7.1.
- Hypokalaemia on admission (less than 3.5 mmol/L).
- Glasgow Coma Scale less than 12 or obtunded patient.
- Oxygen saturation less than 92% on air (assuming normal baseline respiratory function).
- Systolic blood pressure below 90 mmHg.
- Pulse over 100 or below 60 beats per minute.

Admission to a level 2 high-dependency unit environment, insertion of a central line and immediate senior review should be considered.

Insulin therapy and metabolic treatment targets

The guideline recommends a fixed-rate intravenous insulin infusion (FRIVII) calculated on 0.1 units/kg. As global obesity continues to escalate, people with DKA are now more likely to be overweight or obese, or presenting with other insulin-resistant states such as pregnancy. This has led to the re-emergence of FRIVII in adults in the USA and international paediatric practice (BSPED, 2009; ISPAD, 2009; Kitabchi et al, 2009).

Fixed dose(s) per kilogram of body weight enable rapid blood ketone clearance, but it requires close monitoring and may need to be adjusted if the target (shown below) is not met. The recommended target is a reduction of the blood ketone concentration by 0.5 mmol/L/hour; however, if a ketone meter is not available the venous bicarbonate should rise by 3 mmol/L/hour and capillary blood glucose fall by 3 mmol/L/hour. Potassium should be maintained between 4.0 and 5.0 mmol/L.

Intravenous glucose concentration

It is recommended that the management of DKA should be focused on clearing ketones as well as normalising glycaemia. Administration of an intravenous infusion of 10% glucose via an intravenous pump is often required to avoid hypoglycaemia and permit the continuation of a FRIVII to suppress ketogenesis.

The guideline recommends the administration of 10% glucose when blood

glucose levels fall below 14 mmol/L. It is important to continue 0.9% sodium chloride solution concurrently via an intravenous pump. Glucose should not be discontinued until the person is eating and drinking normally (Savage et al, 2010).

Continuation of long-acting analogue insulin

For the initial management of DKA, continuation of long-acting analogue insulin is recommended to provide background insulin when the intravenous insulin is discontinued. This avoids rebound hyperglycaemia when

Box 1. Case study.

Narrative

A 19-year-old woman was admitted to hospital at 17:00 hours with a 2-day history of flu-like symptoms. She had been diagnosed with type 1 diabetes 3 months earlier. As she was unable to eat her normal food she had felt it best to stop taking her fast-acting pre-meal insulin, although she had continued her long-acting bedtime analogue insulin. She was polyuric and polydipsic and her breath smelt of nail varnish remover (ketones).

The on-call medical staff checked her oxygen saturations on air (99%) and proceeded to take blood samples. Venous pH and bicarbonate levels measured on the ward blood-gas analyser confirmed acidosis with a pH of 7.1 and a bicarbonate of 6 mmol/L. Serum potassium was 4.9 mmol/L. Finger-prick testing for ketones and glucose showed 4.7 and 34.3 mmol/L, respectively.

Discussion

Her weight was 9 stones ($9 \times 14 = 126$ lb divided by 2.2 = 57 kg); a fixed-rate intravenous insulin infusion at 0.6 units/hr of fast-acting intravenous insulin was set up along with 1 litre of 0.9% sodium chloride solution with no potassium in the first bag.

Over the next 6 hours her blood ketone level returned to 0 mmol/L but her blood glucose fell to below 14 mmol/L and 10% glucose infusion had to be infused alongside the 0.9% sodium chloride infusion.

She felt symptomatically better the next day and was able to eat breakfast with her normal fast-acting insulin injected after she had eaten, and the intravenous glucose and 0.9% sodium chloride solutions were stopped afterwards. The emergency unit had contacted the diabetes inpatient specialist nurse and, after some further advice on sick-day rules, she was provided with a home ketone-measuring device, referred for a 5-day education package and given contact details for the community diabetes nursing service. She was in hospital for fewer than 24 hours.

Page points

1. Hypokalaemia and hyperkalaemia are the two most serious acute metabolic complications that can arise during the management of diabetic ketoacidosis (DKA).
2. The guideline recommends that if the serum potassium level remains above 5.5 mmol/L, no additional potassium should be prescribed.
3. As ketoacidosis is treated, blood glucose levels can drop very quickly. A common mistake is to allow the blood glucose to drop to hypoglycaemic levels, which can result in rebound ketosis driven by counter-regulatory hormones.

intravenous insulin is discontinued, which should result in a reduced length of hospital stay. This only applies to long-acting analogue insulins, however, and short-acting insulin must still be administered before discontinuing the intravenous insulin infusion.

Serious complications of DKA and its treatment

Hypokalaemia and hyperkalaemia are the two most serious acute metabolic complications that can arise during the management of DKA. There is a risk of acute renal failure as a result of severe dehydration, and it is therefore recommended that no potassium is administered during initial fluid resuscitation. Furthermore, the guideline recommends that if the serum potassium level remains above 5.5 mmol/L, no additional potassium should be prescribed. However, since potassium levels will almost always drop as insulin is administered for the treatment of DKA, it is recommended that 0.9% sodium chloride solution with potassium 40 mmol/L (ready mixed) is prescribed, as long as the serum potassium level is below 5.5 mmol/L and the person is passing urine (Savage et al, 2010).

The guideline states that review of the potassium regimen is required if the serum potassium level falls below 3.5 mmol/L. It is essential that all aspects of potassium use comply with local and national guidance (National Patient Safety Agency, 2002),

and trusts must ensure that local protocols that allow for the safe administration of concentrated potassium injectable (this may require transfer to a higher care environment). The majority of modern blood analysers measure electrolyte levels, and should be used to monitor sodium, potassium and bicarbonate levels at the bedside.

Hypoglycaemia

As ketoacidosis is treated, blood glucose levels can drop very quickly. A common mistake is to allow the blood glucose to drop to hypoglycaemic levels, which can result in rebound ketosis driven by counter-regulatory hormones. Severe hypoglycaemia (defined as requiring third-party assistance) is also associated with cardiac arrhythmias, acute brain injury and death. It is partly for this reason that 10% glucose is recommended.

Implications of guidelines for nurses

DISNs will be involved in education and, increasingly, with hands-on treatment of people being admitted with DKA. However, unless there is a diabetes specialist team on-call rota covering 24 hours it is more likely that nurses working in emergency admission units and other acute or semi-acute settings will be treating people with the condition. Thus, nurses will need to be familiar with hand-held ketone meters. Modern meters for ward use also have bar-coding technology to permit the downloading of data to the hospital laboratory and so full training will need to be implemented.

Conclusion

DKA is a medical emergency associated with significant morbidity and mortality. It should be diagnosed promptly and managed intensively.

The JBDS, in association with NHS Diabetes, has produced new guidance for the management of this condition. The guideline recommends that FRIVII be used with bedside measurement of metabolic parameters; the diabetes specialist team should always be involved as soon as possible and ideally within 24 hours as this has

Further information.

- Full guidance, including a 1-page pdf summary chart, is available at: <http://tinyurl.com/octswq>. For young people under the age of 18 years, contact your paediatric diabetes service and use the British Society for Paediatric Endocrinology and Diabetes diabetic ketoacidosis guidelines, which can be found at: <http://tinyurl.com/32w8dph>.
- Joint British Diabetes Societies consists of: Association of British Clinical Diabetologists; British Society for Paediatric Endocrinology and Diabetes and Association of Children's Diabetes Clinicians; Diabetes Inpatient Specialist Nurse UK Group; Diabetes UK; NHS Diabetes (England); Northern Irish Diabetologists; Scottish Diabetes Group; Society of Acute Medicine; Welsh Endocrine and Diabetes Society.

been demonstrated to be associated with a better patient experience and reduced length of stay.

Diabetes nurses are likely to become key players in training nursing colleagues in the management of DKA as well as being the key professionals in the assessment of people presenting with the condition.

Healthcare professionals must, however, implement the guideline in accordance with the statutory obligations of the person admitted to hospital and of the organisation, and also with local protocol. Professionals delivering care remain individually responsible for making appropriate decisions regarding the specific medical circumstances of every person with DKA admitted to hospital. ■

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“Diabetes nurses are likely to become key players in training nursing colleagues in the management of diabetic ketoacidosis as well as being the key healthcare professionals in the assessment of people presenting with the condition.”