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Diabetes UK Position Statements and Care Recommendations

Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis

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Abstract

The Joint British Diabetes Societies guidelines for the management of diabetic ketoacidosis (these do not cover Hyperosmolar Hyperglycaemic Syndrome) are available in full at:

(i) http://www.diabetes.org.uk/About_us/Our_Views/Care_recommendations/The-Management-of-Diabetic-Ketoacidosis-in-Adults;
(ii) http://www.diabetes.nhs.uk/publications_and_resources/reports_and_guidance;
(iii) http://www.diabetologists-abcd.org.uk/JBDS_DKA_Management.pdf.

This article summarizes the main changes from previous guidelines and discusses the rationale for the new recommendations.

The key points are:

Monitoring of the response to treatment

(i) The method of choice for monitoring the response to treatment is bedside measurement of capillary blood ketones using a ketone meter.
(ii) If blood ketone measurement is not available, venous pH and bicarbonate should be used in conjunction with bedside blood glucose monitoring to assess treatment response.
(iii) Venous blood should be used rather than arterial (unless respiratory problems dictate otherwise) in blood gas analysers.
(iv) Intermittent laboratory confirmation of pH, bicarbonate and electrolytes only.

Insulin administration

(i) Insulin should be infused intravenously at a weight-based fixed rate until the ketosis has resolved.
(ii) When the blood glucose falls below 14 mmol/l, 10% glucose should be added to allow the fixed-rate insulin to be continued.
(iii) If already taking, long-acting insulin analogues such as insulin glargine (Lantus®, Sanofi Aventis, Guildford, Surry, UK) or insulin detemir (Levemir®, Novo Nordisk, Crawley, West Sussex, UK.) should be continued in usual doses.

Delivery of care

(i) The diabetes specialist team should be involved as soon as possible.
(ii) Patients should be nursed in areas where staff are experienced in the management of ketoacidosis.

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Keywords diabetic ketoacidosis guidelines, ketone meter

Introduction

Diabetic ketoacidosis is defined by the biochemical triad of ketonaemia, hyperglycaemia and acidaemia. The incidence is difficult to establish, ranging from 4.6 to 8 episodes per 1000 patients with diabetes in population-based studies from the USA [1]. In England, more than 11% of people with Type 1 diabetes had an episode of diabetic ketoacidosis in the years between 2004 and 2009 [2]. It remains a life-threatening condition despite improvements in diabetes care [3,4]. Mortality in the UK from

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[1]*The Joint British Diabetes Societies consists of: the Association of British Clinical Diabetologists; the British Society for Paediatric Endocrinology and Diabetes and the Association of Children's Diabetes Clinicians; the Diabetes Inpatient Specialist Nurse (DISN) Group; Diabetes UK; NHS Diabetes (England); the Northern Ireland Diabetologist's Group; the Society of Acute Medicine; the Scottish Diabetes Group; and the Welsh Endocrine and Diabetes Society.*

diabetic ketoacidosis is low at approximately 2% [5], but each death is potentially avoidable. There is a need to improve patient education and attendance at clinics and to raise awareness of diabetic ketoacidosis and its management amongst healthcare professionals. The mortality rate remains high in developing countries and among non-hospitalized patients [6]. This illustrates the importance of early diagnosis and implementation of effective prevention programmes.

Cerebral oedema remains the most common cause of mortality, particularly in young children and adolescents. In the adult population, hypokalaemia, adult respiratory distress syndrome/acute lung injury and co-morbid states such as pneumonia, acute myocardial infarction and sepsis are all associated with increased mortality [7].

There are several existing national and international guidelines for the management of diabetic ketoacidosis in both adults and children [8–12]. The Joint British Diabetes Societies guidelines take into account developments in technology and changes in the presentation of diabetic ketoacidosis over the last few years. In the last decade, the development of technology for near patient testing of ketones has allowed monitoring of 3-beta-hydroxybutyrate at the bedside. As a result, the focus of monitoring has shifted from the blood glucose to the blood ketone level, which is a more accurate marker of the resolution of the acidosis.

These guidelines are evidence based wherever possible, but are also drawn from accumulated professional knowledge and consensus agreement. They are intended for use by any healthcare professional managing diabetic ketoacidosis in adults. They are not meant to be the definitive guideline on the management of diabetic ketoacidosis. It is clear that there are gaps in the published evidence and that these guidelines should be audited and results of these audits and of research should lead to revisions as necessary.

Pathophysiology

Diabetic ketoacidosis occurs as a consequence of absolute or relative insulin deficiency, usually accompanied by an increase in counter-regulatory hormones such as glucagon, cortisol and epinephrine. This hormonal imbalance leads to hepatic gluconeogenesis and glycogenolysis, resulting in severe hyperglycaemia. Enhanced lipolysis increases serum free fatty acids with production of large quantities of ketone bodies (acetone, acetoacetate and 3-beta-hydroxybutyrate) and consequent metabolic acidosis. The osmotic diuresis induced by hyperglycaemia combined with ketone-induced nausea and vomiting leads to severe fluid depletion and life-threatening electrolyte imbalance.

Diagnosis

The diagnostic criteria for diabetic ketoacidosis are:

(i) ketonaemia 3 mmol/l and over or significant ketonuria (more than 2 + on standard urine sticks);
(ii) blood glucose over 11 mmol/l or known diabetes mellitus;
(iii) venous bicarbonate (HCO_3^-) below 15 mmol/l and/or venous pH less than 7.3.

Note: this excludes Hyperosmolar Hyperglycaemic Syndrome which occurs in Type 2 diabetes and is generally not associated with acidosis caused by ketonaemia.

Developments in management

Until recently, the management of diabetic ketoacidosis has focused on lowering the elevated blood glucose with fluids and insulin, on the assumption that this would suppress ketogenesis and reverse the acidosis. Metabolic improvement was assessed using arterial pH and serum bicarbonate. The development of blood ketone meters allows us to focus on the underlying metabolic abnormality (ketonaemia). This simplifies treatment of patients who present with only modest elevation of blood glucose, but with acidosis secondary to ketonaemia–'euglycaemic diabetic ketoacidosis' [1,13,14]. This clinical presentation is encountered more frequently as improved patient education with increased blood glucose and ketone monitoring has led to partial treatment of diabetic ketoacidosis prior to admission and lower blood glucose levels at presentation.

The facility to monitor blood ketones and blood glucose is an important advance in the management of diabetic ketoacidosis [15–21]. Portable blood ketone analysers that are compliant with approved laboratory protocols are now available with in-built quality assessment and calibration; these also have computerized links to the laboratory and bar code scanning of patients' identification labels. Bedside monitoring has been shown to be helpful in the clinical situation of diabetic ketoacidosis (17). Access to analysers for blood gas and electrolyte measurement is now therefore relatively easy and results are available within a few minutes rather than hours. Therefore, glucose, ketones and electrolytes, including bicarbonate and venous pH, should be assessed at or near the bedside. This recommendation raises important issues:

(i) Staff must be trained in the use of blood glucose and blood ketone meters (note: those used in hospital units are not the same as used by patients).
(ii) Meters should be subject to rigorous quality assurance and under the control of the Near Patient Testing Coordinator, or equivalent.
(iii) Laboratory measurement will be required in certain circumstances, such as when blood glucose or ketone meters are 'out of range'.
(iv) Blood gas analysers must be readily available to admitting teams.

It is recognized that not all units have access to ketone meters and that there is a lead-in time to getting the appropriate meters that are laboratory approved. Thus, management guidance is also given based on the rate of rise of bicarbonate and fall in blood glucose.

The involvement of Diabetes Specialist Teams

The Diabetes Specialist Team must always be involved in the care of those admitted to hospital with diabetic ketoacidosis. Their involvement shortens patient stay and improves safety [22–25]. The Diabetes Specialist Team should be informed as soon as possible during the acute phase, but this will depend on local circumstances. Specialists should be involved in the assessment of the precipitating cause of diabetic ketoacidosis, management, discharge, provision of hand-held ketone meters to appropriate patients and follow-up. This will include assessment of the patient's understanding of diabetes, their attitudes and beliefs. Diabetes Specialist Team involvement is essential to ensure regular audit and continuous quality improvement in the implementation of diabetic ketoacidosis guidelines. The practice of admitting, treating and discharging patients with diabetic ketoacidosis without the involvement of the diabetes specialist team is unsafe and likely to compromise safe patient care and is a governance issue [26].

General management issues

Patients should be treated in a clinical area experienced in the management of patients with diabetic ketoacidosis. Criteria for high-dependency unit admission are specified in the full guideline.

Fluid replacement

The most important initial therapeutic intervention is fluid replacement followed by insulin administration. The main aims for the first few litres of fluid replacement are to:

(i) correct hypotension by restoration of circulatory volume;
(ii) clear ketones;
(iii) correct electrolyte imbalance.

An adult weighing 70 kg presenting with diabetic ketoacidosis may be up to 7 litres in fluid deficit with associated electrolyte disturbances. Fluid should be replaced as crystalloid rather than colloid and 0.9% sodium chloride is recommended as the initial replacement fluid (see Controversial areas below). The rate and volume of fluid replacement may need to be modified for patients with kidney or heart failure, the elderly and adolescents.

Insulin therapy and metabolic treatment targets

A fixed-rate intravenous insulin infusion calculated on 0.1 units/kg is recommended. It may be necessary to estimate the weight of the patient as one does for other medications. The rationales for this recommendation are:

(i) the change in patient demographics, with increasing prevalence of obesity and other insulin-resistant states including pregnancy;
(ii) the need to engender conformity of practice across healthcare systems, which will also permit a robust evolutionary approach to future guideline modifications.

These have already led to the re-emergence of the use of fixed-rate intravenous insulin infusions in adults in the USA and international paediatric practice [8,11,12]. It is, however, recognized that the fixed rate may need to be increased in insulin-resistant states if metabolic targets are not being met.

The metabolic targets suggested by the writing group, arrived at by consensus of the group and the constituent societies, based on metabolic changes during treatment in published papers [18] are:

(i) reduction of the blood ketone concentration by at least 0.5 mmol l^{-1} h^{-1};
(ii) in the absence of blood ketone monitoring, the venous bicarbonate should rise by 3 mmol l^{-1} h^{-1} and capillary blood glucose fall by 3 mmol l^{-1} h^{-1}.

If these targets are not achieved, the rate of the insulin infusion should be increased.

However, as a safety measure, particularly for those unfamiliar with insulin doses, even for the morbidly obese, an infusion of 15 units of insulin per hour is likely to be sufficient. There should be senior input and careful consideration before giving more than this.

Potassium should be monitored regularly and maintained between 4.0 and 5.0 mmol/l.

Intravenous glucose infusion

Management should be focused on clearing ketones as well as normalizing blood glucose. Introduction of 10% glucose is recommended when the blood glucose falls below 14 mmol/l in order to avoid hypoglycaemia, while continuing the fixed-rate intravenous insulin infusion to suppress ketogenesis. It is important to continue 0.9% sodium chloride solution concurrently to correct circulatory volume if the fluid deficit has not been corrected. Glucose should not be discontinued until the patient is eating and drinking normally.

Special patient groups

The following groups of patients need specialist input as soon as possible and special attention needs to be paid to fluid balance:

(i) elderly;
(ii) pregnant;
(iii) young people 18–25 years of age;
(iv) heart or kidney failure;
(v) other serious co-morbidities.

Precipitating factors and patient education

Patients with diabetes who are admitted with diabetic ketoacidosis should be counselled about the precipitating cause

and early warning symptoms. Failure to do so is a missed educational opportunity. Things to consider include:

(i) identification of precipitating factors such as infection or omission of insulin injections;
(ii) education to prevent recurrence; for example, provision of written sick day rules;
(iii) warning about potential insulin ineffectiveness; for example, the patient's insulin may be expired or denatured;
(iv) provision of hand-held ketone meters with education on management of ketonaemia.

Controversial areas

The clinical assessment and aims of treatment in the management of diabetic ketoacidosis are not controversial. However, there is disagreement about the optimum treatment regimen and, where the evidence base is not strong; recommendations are based on consensus and experience. Some of the controversial points will be considered and good practice recommendations are made.

Arterial or venous pH and bicarbonate measurements?

Recent evidence shows that the difference between venous and arterial pH is 0.02–0.15 pH units and the difference between arterial and venous bicarbonate is 1.88 mmol/l [27,28]. This difference will not influence either diagnosis or management of diabetic ketoacidosis and it is not necessary to use arterial blood to measure acid base status [29]. Venous blood can be used in portable and fixed blood gas analysers and therefore venous measurements (bicarbonate, pH and potassium) are easily obtained in most admitting units. Arterial line insertion should only be performed if frequent arterial oxygen level measurements or blood pressure monitoring is required in the critically unwell patient.

Colloid vs. crystalloid?

Many guidelines recommend initial fluid resuscitation with colloid in hypotensive patients. However, the hypotension results from a loss of electrolyte solution and it is more physiological to replace with crystalloid. A recent Cochrane review did not support the use of colloid in preference to crystalloid fluid [30].

Rate of fluid replacement?

There is concern that rapid fluid replacement may lead to cerebral oedema in children and young adults. National and international paediatric guidelines recommend cautious fluid replacement over 48 h. Existing adult guidelines [9,10,12] all recommend rapid initial fluid replacement in the first few hours. No randomized controlled trials exist to guide decision making in this area. Therefore, cautious fluid replacement is recommended in small young adults who are not shocked at presentation.

Solution of 0.9% sodium chloride vs. Hartmann's solution for fluid replacement?

There has been much debate recently about the relative merits of these two solutions [31].

Advantages of 0.9% sodium chloride: decades of clinical experience; readily available in clinical areas; commercially available ready mixed with potassium at required concentrations; compliant with National Safety Patient Agency advice regarding safe practice with injectable potassium [32].

Disadvantages: use of large volumes can lead to hyperchloraemic metabolic acidosis, which may cause renal arteriolar vasoconstriction, oliguria and delayed resolution of acidosis.

Advantages of compound sodium (Hartmann's): balanced crystalloid with minimal tendency to hyperchloraemic metabolic acidosis.

Disadvantages: insufficient potassium if used alone; not commercially available with adequate premixed potassium and not compliant with National Safety Patient Agency guidance for safe use of potassium in general clinical areas [32]; unfamiliar and not routinely kept on medical wards.

Therefore, 0.9% sodium chloride solution is recommended as the fluid of choice for resuscitation in all clinical areas as it supports safe practice and is available, ready to use, with adequate ready-mixed potassium.

Continuation of long-acting insulin analogues?

In the last few years, the use of long-acting basal insulin analogues (Levemir®, Lantus®) has become widespread and others may be launched on the market soon. Continuation of long-acting analogues during the initial management of diabetic ketoacidosis provides background insulin when the intravenous insulin is discontinued. Although there is no evidence on which to base recommendations about the continuation of long-acting insulin analogues during the acute episode, maintaining the normal daily dose of these insulins is unlikely to adversely affect the blood glucose response to the intravenous infusion and should facilitate a smoother transition from the intravenous insulin infusion to subcutaneous insulin. This avoids rebound hyperglycaemia and ketogenesis when intravenous insulin is stopped and may avoid excess length of stay. This advice only applies to long-acting analogues and does not obviate the need to give short-acting insulin before discontinuing the intravenous insulin infusion. If the patient is not taking a long-acting analogue, background insulin (isophane) should be reintroduced before the intravenous infusion is discontinued.

Use of a priming dose (bolus) of insulin?

It has been demonstrated that a priming dose of insulin is not necessary, provided that the insulin infusion is started promptly at a dose of 0.14 unit $kg^{-1} h^{-1}$ [33]. Although the insulin infusion

dose recommended in these guidelines is lower than that quoted above, immediate commencement of intravenous fluids and an insulin infusion is considered to be the most important step. The additional task of administering a bolus insulin dose introduces more scope for error and may detract from getting the fluids and insulin infusion correct.

Intravenous bicarbonate?

Adequate fluid and insulin therapy will resolve the acidosis in diabetic ketoacidosis and the use of bicarbonate is not indicated [34,35]. The acidosis may be an adaptive response as it improves oxygen delivery to the tissues by causing a right shift of the oxygen dissociation curve. Excessive bicarbonate may cause a rise in the carbon dioxide (CO_2) partial pressure in the cerebrospinal fluid and may lead to a paradoxical increase in cerebrospinal fluid acidosis [36.37]. In addition, the use of bicarbonate in diabetic ketoacidosis may delay the fall in blood lactate:pyruvate ratio and ketones when compared with intravenous 0.9% sodium chloride infusion [35]. There is some evidence to suggest that bicarbonate treatment may be implicated in the development of cerebral oedema in children and young adults [38].

Use of intravenous phosphate?

Whole-body phosphate deficits in diabetic ketoacidosis are substantial, averaging 1 mmol/kg of body weight. There is no evidence of benefit of phosphate replacement [39] and the routine measurement or replacement of phosphate is not recommended. However, in the presence of respiratory and skeletal muscle weakness, phosphate measurement and replacement should be considered [40].

Admission to high-dependency unit or equivalent

This is of course somewhat subjective, the Joint British Diabetes Societies suggest that the presence of one or more of the following may indicate severe diabetic ketoacidosis and admission to a Level 2 / high-dependency unit environment. Insertion of a central line and immediate senior review should be considered:

(i) blood ketones over 6 mmol/l;
(ii) bicarbonate level below 5 mmol/l;
(iii) venous/arterial pH below 7.1;
(iv) hypokalaemia on admission (under 3.5 mmol/l);
(v) Glasgow Coma Scale (GCS) less than 12 or abnormal AVPU (Alert, Voice, Pain, Unresponsive) scale;
(vi) oxygen saturation below 92% on air (assuming normal baseline respiratory function);
(vii) systolic blood pressure below 90 mmHg;
(viii) pulse over 100 or below 60 b min^{-1};
(ix) anion gap above16 [anion gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$].

Serious complications of diabetic ketoacidosis and its treatment

Hypokalaemia and hyperkalaemia

These are potentially life-threatening conditions and careful management of potassium during treatment of DKA diabetic ketoacidosis is essential. Severe dehydration may lead to acute pre-renal failure and it is recommended that potassium should not be prescribed with the initial litre of fluid or if the serum potassium level remains above 5.5 mmol/l. Treatment with fluid and insulin will almost always lead to a fall in potassium and 0.9% sodium chloride solution with potassium 40 mmol/l (ready-mixed) is recommended if the serum potassium level is below 5.5 mmol/l and the patient is passing urine. If the serum potassium level falls below 3.5 mmol/l, the potassium regimen needs review. Where fluid balance permits, an increase in rate of 0.9% sodium chloride solution with potassium 40 mmol/l infusion is possible. Otherwise, a more concentrated potassium infusion will be needed and, to ensure safe practice, all aspects of its use must comply with local and national guidance [32]. Trusts need to ensure that they have local protocols in place which allow for the safe administration of concentrated potassium injectables. This may require transfer to a higher care environment. Electrolyte measurements can be obtained from most modern blood gas analysers and should be used to monitor sodium, potassium and bicarbonate levels.

Hypoglycaemia

The blood glucose may fall very rapidly as ketoacidosis is corrected and a common mistake is to allow the blood glucose to drop to hypoglycaemic levels. This may result in a rebound ketosis driven by counter-regulatory hormones, which can lengthen duration of treatment. Severe hypoglycaemia is associated with cardiac arrhythmias, acute brain injury and death. Once the blood glucose falls to 14 mmol/l, intravenous glucose 10% should be commenced alongside the 0.9% sodium chloride solution in order to prevent hypoglycaemia.

Cerebral oedema

Symptomatic cerebral oedema is relatively uncommon in adults treated for diabetic ketoacidosis, although asymptomatic cerebral oedema may be a relatively common occurrence [41]. The observation that cerebral oedema usually occurs within a few hours of initiation of treatment has led to the speculation that it is iatrogenic [42]. However, there is evidence that subclinical cerebral oedema may be present before treatment is started [43]. The exact cause of this phenomenon is unknown; recent studies suggest that cerebral hypoperfusion with subsequent re-perfusion may be the mechanism operating [38,44,45].

The Management of Diabetic Ketoacidosis in Adults

For young people under the age of 18 years use British Society of Paediatric Endocrinology and Diabetes (BSPED) guidelines: http://www.bsped.org.uk/professional/guidelines/docs/DKAGuideline.pdf

Diagnostic criteria: all three of the following must be present
- capillary blood glucose above 11 mmol/L
- capillary ketones above 3 mmol/L or urine ketones ++ or more
- venous pH less than 7.3 and/or bicarbonate less than 15 mmol/L

BOX 1: Immediate management: time 0 to 60 minutes

(T=0 at time intravenous fluids are commenced)

If intravenous access cannot be obtained request critical care support immediately

Action 1: Commence 0.9% sodium chloride solution (use large bore cannula) via infusion pump.
See Box 2 for rate of fluid replacement

Action 2: Commence a fixed rate intravenous insulin infusion (IVII). (0.1unit/kg/hr based on estimate of weight) 50 units human soluble insulin (Actrapid® or Humulin S®) made up to 50ml with 0.9% sodium chloride solution. If patient normally takes long acting insulin analogue (Lantus®, Levemir®) continue at usual dose and time

Action 3: Assess patient
- o Respiratory rate; temperature; blood pressure; pulse; oxygen saturation
- o Glasgow Coma Scale
- o Full clinical examination

Action 4: Further investigations
- Capillary and laboratory glucose
- Venous BG
- U & E
- FBC
- Blood cultures
- ECG
- CXR
- MSU

Action 5: Establish monitoring regimen
- Hourly capillary blood glucose
- Hourly capillary ketone measurement if available
- Venous bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter
- 4 hourly plasma electrolytes
- Continuous cardiac monitoring if required
- Continuous pulse oximetry if required

Action 6: Consider and precipitating causes and treat appropriately

HDU/level 2 facility and/or insertion of central line may be required in following circumstances (request urgent senior review)

- Young people aged 18-25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities
- Severe DKA by following criteria
  - Blood ketones above 6 mmol/L
  - Venous bicarbonate below 5 mmol/L
- Venous pH below 7.1
- Hypokalaemia on admission (below 3.5 mmol/L)
- GCS less than 12
- Oxygen saturation below 92% on air (Arterial blood gases required)
- Systolic BP below 90 mmHg
- Pulse over 100 or below 60 bpm
- Anion gap above16 [Anion Gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$]

BOX 2: Initial fluid replacement

Restoration of circulating volume is priority

Systolic BP (SBP) below 90mmHg

Likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.
- Give 500ml of 0.9% sodium chloride solution over 10-15 minutes. If SBP remains below 90mmHg repeat whilst requesting senior input. Most patients require between 500 to 1000ml given rapidly.
- Consider involving the ITU/critical care team.
- Once SBP above 90mmHg give 1000ml 0.9% sodium chloride over next 60 minutes. Addition of potassium likely to be required in this second litre of fluid

Systolic BP on admission 90 mmHg and over
- Give 1000ml 0.9% sodium chloride over first 60 minutes

Potassium replacement

Potassium level (mmol/L)	Potassium replacement mmol/L of infusion solution
> 5.5	Nil
3.5-5.5	40 mmol/L
< 3.5	senior review – additional potassium required

BOX 3: 60 minutes to 6 hours

Aims of treatment:
- Rate of fall of ketones of at least 0.5 mmol/L/hr OR bicarbonate rise 3 mmol/L/hr and blood glucose fall 3 mmol/L/hr
- Maintain serum potassium in normal range
- Avoid hypoglycaemia

Action 1: Re-assess patient, monitor vital signs
- Hourly blood glucose (lab blood glucose if meter reading 'HI')
- Hourly blood ketones if meter available
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter.
- If potassium is outside normal range, re-assess potassium replacement and check hourly. If abnormal after further hour seek immediate senior medical advice

Action 2: Continue fluid replacement via infusion pump as follows:
- 0.9% sodium chloride 1L with potassium chloride over next 2 hours
- 0.9% sodium chloride 1L with potassium chloride over next 2 hours
- 0.9% sodium chloride 1L with potassium chloride over next 4 hours
- Add 10% glucose 125ml/hr if blood glucose falls below 14 mmol/L

More cautious fluid replacement in young people aged 18-25 years, elderly, pregnant, heart or renal failure. (Consider HDU and/or central line)

Action 3: Assess response to treatment

Insulin infusion rate may need review if
- Capillary ketones not falling by at least 0.5 mmol/L/hr
- Venous bicarbonate not rising by at least 3 mmol/L/hr
- Plasma glucose not falling by at least 3 mmol/L/hr
- Continue fixed rate IVII until ketones less than 0.3 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/L.

If ketones and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin residual volume is present (to check for pump malfunction).

If equipment working but response to treatment inadequate, increase insulin infusion rate by 1 unit/hr increments hourly until targets achieved.

Additional measures
- Regular observations and Early Warning Score (EWS)
- Accurate fluid balance chart, minimum urine output 0.5ml/kg/hr
- Consider urinary catheterisation if incontinent or anuric (not passed urine by 60 minutes)
- Nasogastric tube with airway protection if patient obtunded or persistently vomiting
- Measure arterial blood gases and repeat chest radiograph if oxygen saturation less than 92%
- Thromboprophylaxis with low molecular weight heparin
- Consider ECG monitoring if potassium abnormal or concerns about cardiac status

BOX 4: 6 to 12 hours

Aims:
- Ensure clinical and biochemical parameters improving
- Continue iv fluid replacement
- Avoid hypoglycaemia
- Assess for complications of treatment e.g. fluid overload, cerebral oedema
- Treat precipitating factors as necessary

Action 1: Re-assess patient, monitor vital signs
- If patient not improving by criteria in Box 3 seek senior advice
- Continue iv fluid via infusion pump at reduced rate
  - o 0.9% sodium chloride 1L with potassium chloride over 4 hours
  - o 0.9% sodium chloride 1L with potassium chloride over 6 hours
- Add 10% glucose 125ml/hr if blood glucose falls below 14 mmol/L

Reassess cardiovascular status at 12 hours; further fluid may be required.

Check for fluid overload

Action 2 – Review biochemical and metabolic parameters
- At 6 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose
- Resolution is defined as ketones less than 0.3 mmol/L, venous pH over 7.3 (do not use bicarbonate as a surrogate at this stage).
- Ensure referral has been made to diabetes team

If DKA not resolved review insulin infusion (see BOX 3 Action 3)
If DKA resolved go to BOX 6

BOX 5: 12 to 24 HOURS

Expectation: By 24 hours the ketonaemia and acidosis should have resolved. Request senior review if not improving

Aim:
- Ensure that clinical and biochemical parameters are continuing to improve or are normal
- Continue iv fluid replacement if not eating and drinking.
- If ketonaemia cleared and patient is not eating and drinking move to a variable rate IVII as per local guidelines
- Re-assess for complications of treatment e.g. fluid overload, cerebral oedema
- Continue to treat precipitating factors
- Transfer to subcutaneous insulin if patient is eating and drinking normally.

Action 1 – Re-assess patient, monitor vital signs
Action 2 – Review biochemical and metabolic parameters
- At 12 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose
- Resolution is defined as ketones <0.3 mmol/L, venous pH>7.3
- If not resolved review fluid **Box 4 Action 1** and insulin infusion **Box 3 Action 3**

If DKA resolved go to Box 6

BOX 6: Resolution of DKA

Expectation: Patient should be eating and drinking and back on normal insulin.
If DKA not resolved identify and treat the reasons for failure to respond.
This situation is unusual and requires senior and specialist input.

Transfer to subcutaneous insulin

Convert to subcutaneous regime when biochemically stable (capillary ketones less than 0.3 mmol/L, pH over 7.3) and the patient is ready and able to eat. **Do not discontinue intravenous insulin infusion until 30 minutes after subcutaneous short acting insulin has been given**
Conversion to subcutaneous insulin should be managed by the Specialist Diabetes Team. If the team is not available use local guidelines. If the patient is newly diagnosed it is essential they are seen by a member of the specialist team prior to discharge.
Arrange follow up with specialist team.

Groups represented: Association of British Clinical Diabetologists; British Society for Endocrinology and Diabetes and Association of Children's Diabetes Clinicians; Diabetes Inpatient Specialist Nurse (DISN) Group; Diabetes UK; NHS Diabetes (England); Northern Irish Diabetologists; Society of Acute Medicine; Welsh Endocrine and Diabetes Society, Scottish Diabetes Group.

FIGURE 1 The management of diabetic ketoacidosis in adults. Summary of the guidelines. Reproduced from NHS Diabetes (2010), with permission of Joint British Diabetes Societies.

Cerebral oedema associated with diabetic ketoacidosis is more common in children than in adults. In the UK, approximately 70–80% of diabetes-related deaths in children under 12 years of age are caused as a result of cerebral oedema [46]. The UK case–control study of cerebral oedema complicating diabetic ketoacidosis showed that children who developed cerebral oedema were more acidotic and, after severity of acidosis was corrected for, insulin administration in the first hour and volume of fluid administered over the first 4 h were associated with increased risk [47].

Pulmonary oedema

This has only been reported rarely as a complication of diabetic ketoacidosis. As with cerebral oedema, the observation that pulmonary oedema usually occurs within a few hours of initiation of treatment has led to the speculation that the complication is iatrogenic and that rapid infusion of crystalloids over a short period of time increases the likelihood of this complication [48]. Elderly patients and those with impaired cardiac function are at particular risk and monitoring of central venous pressure should be considered.

Summary

Figure 1 shows a summary of the guidelines in boxed format; this is also available from the Association of British Clinical Diabetologists (http://www.diabetologists-abcd.org.uk/Shared_Documents/notice_board/meeting_flyers_etc/DKA%20pathway%20poster%20March%202010.pdf).

Diabetic ketoacidosis is a medical emergency with a significant morbidity and mortality. It should be diagnosed promptly and managed intensively by experienced staff. A fixed-rate, weight-based intravenous insulin infusion should be used with bedside measurement of metabolic changes. The specialist diabetes team should be involved as soon as possible and ideally within 24 h; this has been demonstrated to be associated with a better patient experience and reduced length of stay. Full guidance is available from: Diabetes UK; NHS Diabetes (England); and the Association of British Clinical Diabetologists (http://www.diabetes.org.uk/About_us/Our_Views/Care_recommendations/The-Management-of-Diabetic-Ketoacidosis-in-Adults/; http://www.diabetes.nhs.uk/publications_and_resources/reports_and_guidance/; http://www.diabetologists-abcd.org.uk/JBDS_DKA_Management.pdf).

For young people under the age of 18 years, contact your paediatric diabetes service and use the BSPED diabetic ketoacidosis guidelines (http://www.bsped.org.uk/professional/guidelines/docs/DKAGuideline.pdf).

Competing interests

Nothing to declare.

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