Diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome – clinical guidelines

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ABSTRACT
Background: The aim of this study was to establish a standardized approach to the initial care of patients with diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar syndrome (HHS). DKA and HHS are metabolic emergencies. Effective and efficient management is the responsibility of the multidisciplinary team. The admission of patients to the intensive care unit (ICU) with DKA and HHS is rare, and management of patients’ diverse problems is prone to error because of a lack of familiarity.
Aim: The paper’s aim is to set the developmental process of a clinical guideline following a review of the literature.
Discussion: This clinical guideline is based on a review of the evidence available within the literature in the early phase of resuscitation. Collaborative working among the multidisciplinary team through clinical practice group was the method adopted. Management of DKA and HHS is divided into three main areas: intravenous fluid replacement, insulin therapy and electrolyte management. The controversy associated with the administration of sodium bicarbonate is discussed.
Conclusion: Effective treatment requires a rapid initial assessment of the patient based on current medical history and clinical presentation. To this end, a quick reference algorithm and guide to management were also developed. Key criteria for evaluating the effectiveness of treatment are provided and complications of treatment are addressed. The formation of the practice development group that led to this innovation is outlined, and in conclusion, the success of the group is reflected upon.
Key words: Clinical guidelines • Diabetic ketoacidosis • Hyperglycaemic hyperosmolar syndrome

PROBLEM IDENTIFICATION
Admission to hospital for the treatment of diabetic ketoacidotic coma has been estimated at 26–44 per million people living in the UK (Williams, 1989). These are the most recent figures available. Current methods of coding for admission are confusing as similar codes are used to identify admission for hypoglycaemic coma (Home et al., 1999). Therefore, the true incidence of diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar syndrome (HHS) is unknown in the UK.

The admission of patients to the intensive care unit (ICU) for the management of DKA is rare. The total number of patients admitted over the past year to our ICU was two. The incidence of HHS (previously hyperosmolar non-ketotic coma) is even more infrequent. This entails considerable risk because the multidisciplinary team cannot gain in-depth experience, and competence is difficult to maintain. Specific areas of concern identified by members of the ICU team were associated with the safety of commencing an insulin infusion when the potassium level was low, the speed at which the blood glucose should be lowered, when point of care (POC) testing was safe and laboratory analysis was no longer required, and the appropriate concentration of saline in treating dehydration.

CLINICAL GUIDELINE DEVELOPMENT – THE PROCESS
As a result of these concerns, the practice development group decided to produce clinical guidelines. The
practice development group is formed from a team of nurses who then choose if they wish to participate in the development of a chosen topic. This self selection results in the formation of the group which will take the topic area forward. It also prevents the same people always being responsible for practice development. The ICU pharmacist is a permanent member of the group. Other members of the multidisciplinary team are co-opted as appropriate. On completion of the project, the clinical guidelines are presented to senior nurses and consultant medical staff for approval. They are then revised as appropriate. Once agreed, the clinical guideline is added to the bedside clinical practice folder and placed on the local ICU intranet for easy reference and support.

Each member of the group chose a particular dimension to work on. For example, pathophysiology was reviewed by the pharmacist and a nurse, fluid and electrolyte management by individual members of the group with special responsibility being taken for identification of current algorithms for the management of DKA and HHS. The group then met on a regular basis over a 6-month period to review the work undertaken and guide the development of the guideline. A maximum of 10 h is made available to group members to work on the project, which can then be claimed back from the succeeding on-duty rotas.

The aim of the practice development group in this case was to provide a clinical guideline for the initial management of DKA and HSS at the bedside (Figure 1 and Table 1) and supply an in-depth explanation of the rationale supporting this for general reference within the ICU.

THE CLINICAL GUIDELINE – THE EVIDENCE BASE

Assessment

This may require two members of the ICU team. It is important to identify the recent occurrence of prodromal illness, infection or non-compliance with the insulin regime. However, in this emergency situation, a rapid physical assessment is required using an ABCDE approach familiar to all members of the ICU team. Particular attention should be given to any difficulty the patient may have in maintaining their airway and the presence of Kussmaul breathing. Intubation and ventilation may be required. Hypotension (<90 mmHg) and tachycardia (>125 b/min), cool peripheries and a reduced level of consciousness all indicate the presence of hypovolaemic shock. The restoration of these to normal values can aid the evaluation of treatment delivered. Exposure of the patient

![Diagram](image1.png)

**Figure 1** Management of adult diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome. Complete initial assessment: start i.v. fluids and full monitoring. Measure blood sugar hourly until within range of 10–12 mmol/L.
is necessary to identify dehydration and potential causes of DKA or HSS such as infection.

Management of DKA and HHS

**Intravenous fluid replacement**

Dehydration and sodium depletion develop as a result of the osmotic diuresis. There would be an estimated fluid loss of 6–10 L in a patient with DKA (Hand, 2000) and 9 L in a patient with HHS (Kitabchi et al., 2001) with an associated raised serum osmolality of 320–340 mOsmol/L (English and Williams, 2004). The dominant feature of HHS is hyperosmolarity (>320 mmol/L) (Kitabchi et al., 2001). Electrolyte deficits of 500–700 mmol of sodium, 200–500 mmol of potassium, 350–500 mmol of phosphate and 200–350 mmol of chloride are likely in DKA (English and Williams, 2004). Larger deficits of especially sodium, potassium and chloride can also be expected in HHS (Kitabchi et al., 2001). An estimate of true sodium should be made because of the degree of hyperglycaemia. Glucose induces water movement from the intracellular to extracellular space and dilutes the sodium concentration (Miller, 1999) (Appendix).

The main objective in the treatment of DKA and HHS is to correct water and electrolyte deficits over the first 24–48 h to replete extracellular fluid volume and restore intravascular volume (Kitabchi et al., 2001). The choice of replacement fluid should consider factors such as age, degree of hydration and patient history, e.g. cardiac disease (Hand, 2000).

Isotonic saline (0.9% NaCl) is seen as the initial fluid of choice by most authors (Charalambos, 1999; Miller, 1999; Savage et al., 2004). If hypovolaemic shock is present (systolic blood pressure <100 mmHg) (English and Williams, 2004), then intravenous colloid should be considered (Savage et al., 2004).

The recommended volume of 0·9% NaCl by Kitabchi et al. (2001) is 10–20 mL/kg/h and the American Diabetes Association (2003) is 15–20 mL/kg/h. In mild to moderate depletion, rates of 7 mL/kg/h have also shown the desired effect (Kitabchi and Wall, 1999). The goal is to replace half of the fluid deficit over the first 8 h and the remaining fluid should be replaced over the next 16 h (Brenner, 2006). The American Diabetes Association (2003) suggests that the serum osmolality should not decrease by >3 mOsmol/kg H2O/h (Appendix).

Incorrect use of resuscitation fluid can cause an increase in plasma sodium levels and further increase plasma osmolality, which has been associated with pontine myelinolysis (Keays, 2003). Sudden falls in serum sodium can cause cerebral oedema. A reduced rate of intravenous fluid replacement is recommended in the elderly, those with cardiac disease and mild DKA (Savage et al., 2004). Frequent assessment of cardiac, renal and mental status is advised by the American Diabetes Association (2003) to avoid iatrogenic fluid
overload. Caution should be taken if blood pressure stability is not achieved after 2 h of intravenous fluid administration (Kitabchi et al., 2001; Savage et al., 2004).

If the corrected serum sodium rises above 155 mmol/L, 0.9% NaCl should be replaced with 0.45% NaCl if the corrected sodium is normal or elevated. The administration of hypotonic saline (0.45% NaCl) is similar to the fluid loss during osmotic diuresis and would gradually replenish both intracellular and extracellular compartments (Kitabchi and Wall, 1999). The initial fluid choice of 0.9% or 0.45% saline is followed by 5% glucose or glucose saline once the blood glucose levels decrease below 13 mmol/L (Kitabchi et al., 2001). Authors disagree on the absolute blood glucose value (Table 2).

Savage et al. (2004) recommended 1 L of 5% glucose over 8 h. A similar suggestion was made by English and Williams (2004) and 5% glucose can be started at 100–125 mL/h. Ten percent glucose can be given if less fluid is required (English, 2004). NaCl 0.9% can be continued at a slower rate to complete rehydration and electrolyte replacement. Administration of 5% glucose can be continued until ketonaemia is controlled and iatrogenic hypoglycaemia is avoided (Kitabchi and Wall, 1999).

**Insulin therapy**

It is essential to obtain a serum potassium level before insulin is started. Some patients with DKA initially present with hypokalaemia and insulin administration may decrease potassium levels even further, resulting in muscular weakness. If the potassium level is below 3.3 mmol/L, insulin should not be commenced.

Insulin administration seeks to restore normal glucose uptake by cells. However, excessive insulin administration and associated hypokalaemia and hypophosphataemia must be avoided. Literature strongly suggests that intravenous infusion is the best method of delivery in the acute management of DKA (Miller, 1999), although subcutaneous methods are now cited in the management of uncomplicated DKA (Umpierrez et al., 2004a, 2004b). However, these studies often involve small sample sizes (e.g. n = 40) and intermediate care units are not always available in the UK. Chiasson et al. (2003) claim that continuous intravenous infusion is the most effective as all other routes are unreliable in the volume-depleted patient where erratic absorption can occur with intramuscular or subcutaneous administration. Currently, there are no data to support any advantage in giving an initial bolus. The initial recommended starting dose is 0.1 unit insulin/kg/h (Kitabchi et al., 2001).

Chiasson et al. (2003) suggest that the aim should be to reduce blood glucose by 2–3 mmol/L/h. If this is not achieved, the insulin dose should be doubled every hour until a decrease of 3–4 mmol/L/h is achieved. It is important that the serum glucose is not lowered too rapidly, thus avoiding complications such as cerebral oedema (Brenner, 2006). Patients with HHS are very sensitive to insulin, but obese patients with type 2 diabetes might require larger doses to reduce hyperglycaemia. When the blood glucose reaches 12–14 mmol/L, the insulin rate may be reduced by half and 5% glucose or glucose saline replaces 0.9% or 0.45% NaCl.

**Management of electrolytes**

**Potassium**

Hyperosmolality causes a shift of potassium from within the cells to the extracellular space. This is then lost because of the osmotic diuresis. This depletion can be more severe in HHS than in DKA. As the cells are rehydrated and insulin therapy is commenced, this shift is reversed. The serum potassium should be corrected to 3.5 mmol/L before insulin is commenced (Keays, 2003) as the use of insulin and saline will further decrease extracellular potassium levels (Morton et al., 2006). Electrocardiograph monitoring is essential at this time.

Initial potassium levels may vary according to the individual. Patients with an initially low serum potassium (<3.3 mmol/L) are at risk of cardiac arrhythmias and muscle weakness. English and Williams (2003) recommend 40 mmol potassium/L of saline until the serum potassium reaches 3.5 mmol/L. Serum potassium levels may also be high and potassium therapy should be omitted if blood levels exceed 5.5 mmol/L (Keays, 2003). Starting potassium with an unknown level and compromised renal function can be fatal (Morton et al., 2006).

If levels are between 3.5 and 5.5 mmol/L, 20–40 mmol of potassium can be given initially in the first hour of treatment, but this is not generally exceeded (English and Williams, 2004). Further decisions should then be based on the patient’s potassium levels and urine output. Potassium levels may decline as

<table>
<thead>
<tr>
<th>Blood glucose</th>
<th>Author</th>
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<tbody>
<tr>
<td>13.9 mmol/L</td>
<td>Kitabchi and Wall (1999)</td>
</tr>
<tr>
<td>&lt;14 mmol/L</td>
<td>English (2004)</td>
</tr>
<tr>
<td>&lt;15 mmol/L</td>
<td>Savage et al. (2004)</td>
</tr>
<tr>
<td>12–14 mmol/L</td>
<td>Chiasson et al. (2003)</td>
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potassium returns to the intracellular space when insulin is administered and hydration is restored. The aim was to maintain serum potassium >4 mmol/L, thus if serum potassium is >3.5–5.0 mmol/L, 20–30 mmol of potassium could be given in each litre of intravenous fluid (English and Williams, 2003).

**Phosphate**

Phosphate levels are normal or elevated on initial presentation of DKA (American Diabetes Association, 2003). Insulin therapy lowers serum phosphate levels. Hypophosphataemia should be carefully corrected as it can result in muscular weakness and neurological dysfunction. Excessive replacement of phosphate can lead to hypocalcaemia; therefore, serum calcium levels should be also monitored (Keays, 2003).

**Magnesium**

Chronic magnesium depletion can be present in uncontrolled diabetes and can contribute to insulin resistance. However, research has yet to show any benefits in the administration of magnesium in diabetic emergencies (Keays, 2003).

**Sodium bicarbonate**

The use of sodium bicarbonate has been the subject of controversy. Research has found no benefit in the administration of sodium bicarbonate in DKA (Gehlbach and Schmidt, 2004). The administration of sodium bicarbonate is associated with side effects that may preclude any potential benefits. These include increased CO2 production, acidosis of cerebrospinal fluid, hypokalaemia, rebound alkalosis, volume overload and altered tissue oxygenation (Keays, 2003).

Below a pH of 6.9, most authorities would recommend the use of bicarbonate to correct the pH to a threshold of 6.9–7.15, although this threshold has been disputed. However, life-threatening hyperkalaemia is an undisputed indication for bicarbonate therapy (Keays, 2003).

**Obtaining glucose levels – biochemistry procedures**

POC testing is inaccurate above 27 mmol/L. Therefore, the blood gas analyser should not be used to monitor blood glucose levels until the level has fallen below this figure. This may differ according to POC testing in different ICUs; therefore, this should be clarified at an individual hospital level.

**Evaluating the effectiveness of treatment**

The aims of treatment are to attain normal biochemical values as soon as possible in a safe and effective manner. In the initial resuscitation period, blood glucose should be monitored hourly via biochemistry until levels can be accurately analysed by the blood gas analyser. To precipitate a fall in blood glucose may result in fluid shifts between the intravascular and extravascular space and further electrolyte disturbance, particularly potassium. Once the blood glucose reaches 12–14 mmol/L, fluid replacement may change from saline to 5% glucose or glucose/saline. The insulin rate should be halved at this point to avoid potential hypoglycaemia. The final aim of management was to attain a blood glucose level of 10 mmol/L. On an hourly basis, assessment should be made of the corrected sodium level in order to ascertain the need for hypotonic saline. The same is also necessary for the measurement of potassium levels, pH and serum osmolality. Phosphate, magnesium and calcium levels should also be assessed four hourly together with urinary ketones. Urinary ketones may be raised for up to 2 days after correction of the acidosis. Renal function should be assessed on a daily basis to ensure renal function returns to normal (Table 3). The clinical guideline developed for use at the bedside, based on the evidence above, is given in Figure 1 and Table 1.

**Implementation and evaluation**

**Reflection on the process of practice development for DKA and HHS**

This method of practice development worked well. The enthusiasm of the group was maintained because...
members had self-selected and the guidelines were completed on time, although there was some delay in achieving the goals set for completion during an exceptionally busy period on the ICU. Areas that were the cause of most discussion were the rate at which the blood glucose level should fall and the calculation of corrected sodium. Each bedside has a clinical resource file to aid the multidisciplinary team in the management of critically ill patients and the DKA-HHS clinical guidelines have been added to this and placed on the local ICU intranet. The clinical resource file is particularly useful to junior medical staff and agency nurses. The utilization of consultant nurse and matron-led ward rounds also aids the implementation and maintenance of the clinical guidelines, which have been developed for the ICU.

The clinical guideline
The clinical guideline was introduced in November 2006. Since that time it has been used twice, on both occasions at the weekend when the number of senior staff available for consultation is reduced. The process was evaluated by the consultant intensive care doctor. The evaluation indicated that the ICU team responsible for managing the patient utilized the clinical guideline immediately to prescribe treatment and monitor its effectiveness. Blood glucose levels and normal pH were established in a timely manner with the complete absence of adverse events, e.g. precipitate reduction in blood sugar, insulin administration prior to correction of potassium levels. Of most note was the ability of nursing staff to maintain treatment goals when the ICU registrar had to attend a prolonged trauma call. One deficit was identified in one patient. This related to the reduction in fluid replacement as near normal blood glucose levels were achieved and as a result the serum lactate level failed to resolve. This led to the amendment of the clinical guideline to include fluid replacement to titrate against serum lactate level (Figure 1).

CONCLUSION
This method of practice development has thus far proved successful in the development and acceptance of clinical guidelines and innovations to practice on the ICU. The specific benefit to patients is the reduction of risk in relation to the management of forms of critical illness seen infrequently in our ICU and the promotion of best practice to which all members of the multidisciplinary team adhere.

ACKNOWLEDGEMENTS
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WHAT IS KNOW ABOUT THIS TOPIC
- Most recent figures available indicate 26–44 per million people in the UK will be admitted to hospital for the treatment of DKA.
- The incidence of admission to ICU is unknown.

WHAT THIS PAPER ADDS
- DKA and HHS rarely require admission to the ICU. In this lies considerable clinical risk as the multidisciplinary team may have little experience of the complex management required by this patient population.
- To reduce this risk, we developed a set of clinical guidelines based on the pathophysiology of these abnormalities. The aim of this study was to both inform staff of the reasons why management was so multi-faceted, and potentially hazardous, and produce a set of rapid review bedside guidelines to promote safe and effective management.

REFERENCES
APPENDIX – CALCULATIONS

Calculation 1: Corrected sodium calculation

Calculate the true sodium by dividing the blood glucose by three and add this to the measured sodium

Calculation 2

\[ 2 \left( \text{Na}^+ + \text{K}^+ \right) + \text{glucose} + \text{urea} = \text{serum osmolality} \]
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