A survey of the implementation of the NHS diabetes guidelines for management of diabetic ketoacidosis in the intensive care units of the East of England 3C00

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For patients with insulin-treated diabetes, diabetic ketoacidosis (DKA) is a serious acute complication that often leads to intensive care admission. To overcome perceived shortcomings in care, the Joint British Diabetes Societies (JBDS) published national guidelines for the management of DKA in adults in March 2010. A telephone survey of the 13 general adult intensive care units in the East of England during November 2011 examined how widely four key steps of the guidelines had been adopted in the region. The survey demonstrated that while most units had guidelines for the management of DKA, the majority had not adopted the JBDS guidelines. We recommend that future national guidelines for DKA are developed with the participation of the intensive care community and are disseminated to all intensivists.

Keywords: *diabetes; diabetic ketoacidosis; guidelines*

Introduction

Diabetic ketoacidosis (DKA) is a severe and frequent life-threatening complication of type 1 diabetes. In England in 2010, there were 14,375 admissions to acute NHS hospitals where DKA was the primary diagnosis.[1] It was perceived by the Joint British Diabetes Societies (JBDS) that the lack of consistent and current guidance may contribute to the morbidity and mortality associated with DKA.[2] To overcome these concerns, in March 2010 the JBDS published guidelines for the management of DKA in adults.[2]

The key points in the JBDS guidelines include:

- Use of a weight-based fixed-rate intravenous insulin infusion (FRIII). The FRIII should be administered at a rate of 0.1 units of short-acting human soluble insulin (Actrapid® or Humulin S®)/kg/hour until resolution of ketosis.
- Use of bedside measurement of capillary ketones using a hand-held meter to monitor response to treatment.
- Use of 0.9% saline as the main resuscitation fluid, adding 10% glucose when the blood glucose falls below 14 mmol/L in order to allow the FRIII to be continued.
- Continuation of long-acting insulin analogues such as insulin glargine and insulin detemir if the patient is already taking these.
- Referral for consideration of intensive care if the patient has any of the following criteria:
  - Capillary ketones over 6 mmol/L
  - Bicarbonate level below 5 mmol/L
  - Venous/arterial pH below 7.1
  - Hypokalaemia on admission (under 3.5 mmol/L)
  - Glasgow coma score less than 12 or abnormal AVPU scale
  - Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
  - Systolic blood pressure (BP) below 90 mm Hg
  - Pulse over 100 or below 60 bpm
  - Anion gap above 16.[2]

The aim of the survey was to audit the 13 general adult intensive care units (ICUs) in the East of England region and elucidate whether they had changed their DKA guidelines and adopted the recent JBDS DKA recommendations, particularly focusing on the use of weight-based fixed rate intravenous insulin infusions; use of ketone meters; choice of resuscitation fluid; and continuation of basal long-acting insulin analogues. The referral criteria were not studied.

Methods

The 13 general ICUs in the East of England were identified and contacted by telephone in November 2011 (**Table 1**). The following data was obtained from the senior nurse or duty doctor from each ICU:

- The presence of a DKA guideline.
- The use of a hospital-wide guideline or one specific to the intensive care unit.
- Whether the guideline had been updated since March 2010.
- Whether the unit used a variable rate intravenous insulin infusion or a weight-based fixed-rate intravenous insulin infusion.
- Whether ketone meters were used routinely to monitor capillary ketone levels during treatment.
- The standard resuscitation fluid used (0.9% sodium chloride solution or Hartmann's solution).
- Continuation of long-acting basal insulin analogues during treatment.

Name of hospital (type of hospital)	Level of care provided by intensive care unit
Bedford Hospital (DGH)	Level 2 and 3
Colchester Hospital (DGH), Essex	Level 2 and 3
Ipswich Hospital (DGH), Suffolk	Level 2 and 3
James Paget Hospital, Great Yarmouth, Norfolk	Level 2 and 3
Addenbrookes University Teaching Hospital, Cambridge	Level 2 and 3
Lister Hospital (DGH), Stevenage, Hertfordshire	Level 2 and 3
Luton Hospital (DGH), Bedfordshire	Level 2 and 3
Norfolk and Norwich University Teaching Hospital	Level 2 and 3
Peterborough Hospital, Cambridgeshire	Level 2 and 3
Princess Alexandra Hospital, Harlow, Essex	Level 2 and 3
Queen Elizabeth Hospital (DGH), Kings Lynn, Norfolk	Level 2 and 3
Queen Elizabeth II Hospital (DGH), Welwyn Garden City, Hertfordshire	Level 2 and 3
West Suffolk Hospital (DGH), Bury St Edmunds, Suffolk	Level 2 and 3

Table 1 The units studied in this survey.

Data from these 13 ICUs were also extracted from the Case Mix Programme Database (CMPD), in order to assess the incidence of DKA in intensive care. The Case Mix Programme (CMP) is the national comparative audit of adult, general ICUs in England, Wales and Northern Ireland, co-ordinated by the Intensive Care National Audit & Research Centre (ICNARC). The CMPD has been independently assessed to be of high quality[3] and contains pooled case mix and outcome data on consecutive admissions to participating units, which have undergone extensive local and central validation.[4] Support for the collection and use of patient-identifiable data without consent in the CMP has been obtained under Section 251 of the NHS Act 2006 (approval number PIAG 2-10(f)/2005).

Admissions of patients with DKA to ICU were identified using the ICNARC Coding Method (ICM), which is a 5-tier hierarchical method specifically designed for coding reasons for admission to ICU.[5] The total number of admissions from 1 April 2010 to 31 March 2011 and the number of those with DKA recorded as the primary or secondary reason for admission to the ICU were reported for the 13 ICUs in the East of England, for all CMP participating units in England and for all adult general ICUs in England. The latter was calculated by extrapolating the figures obtained for CMP participating units to the total number of ICUs in England based on the level of coverage of the database.

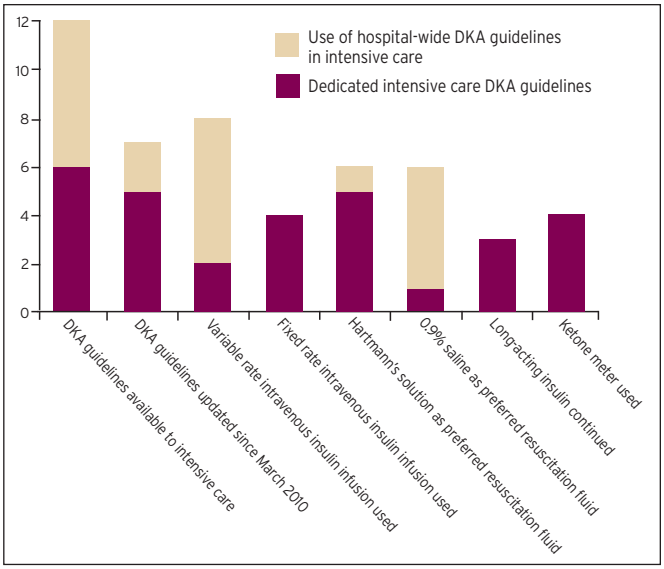

Figure 1 Summary of the management of DKA within the 13 general adult ICUs of the East of England.

Results

The 13 units recruited to this study are all the adult general ICUs located in the East of England (**Table 1**). All units provide level 2 as well as level 3 care.

Of the 13 ICUs studied, all but one had DKA guidelines. Of the twelve ICUs that had guidelines, six units were using an intensive care-specific guideline; the others were using hospital-wide guidelines. Seven ICUs were using guidelines that had been updated since March 2010. Two further ICUs stated that their guidelines were in the process of being updated at the time of the survey.

Eight ICUs were using a variable rate intravenous insulin infusion, four units used a fixed-rate intravenous insulin infusion. Only those units with a dedicated ICU DKA guideline were using a fixed-rate intravenous insulin infusion (see **Figure 1**). Hand-held capillary ketone meters were available in four ICUs; however, only one unit used them routinely to monitor ketone levels.

Six ICUs used 0.9% sodium chloride solution as their standard resuscitation fluid and six used Hartmann's solution. Units with an intensive care-specific protocol were more likely to be using Hartmann's solution as their fluid of choice.

Three units continued long-acting basal insulin analogues. These results are summarised in **Table 2** and **Figure 1**.

Results of the CMPD analyses are summarised in **Table 3**. Of the 13 ICUs in the East of England, complete data for the year were available for nine units, data for part of the year for three units, and no data for one unit. Overall, these units admitted 103 patients with DKA (1.7% of all admissions). Nationally there were 1,439 admissions to ICU with DKA, which extrapolates to approximately 1,800 admissions with DKA per year to all adult general ICUs in England.

Discussion

In the period from 1 April 2010 to 31 March 2011 there were 14,375 admissions to acute hospitals in England where DKA was the primary diagnosis.[1] The CMPD analyses indicated that

ICU	DGH/Teaching hospital	DKA guideline available to intensive care	Dedicated ICU guideline or hospital-wide guideline	Updated since March 2010	Variable rate (VRIII) or fixed rate (FRIII) intravenous insulin infusion	Hartmann's solution or 0.9% sodium chloride as preferred resuscitation fluid	Long-acting basal insulin analogues continued	Ketone meter used
1	DGH	Yes	Hospital	No	Variable rate	0.9% NaCl	No	No
2	DGH	Yes	Hospital	Unknown	Variable rate	0.9% NaCl	No	No
3	DGH	Yes	ICU	Yes	Variable rate	Hartmann's	No	No
4	DGH	Yes	ICU	Yes	Variable rate	Hartmann's	No	No
5	DGH	Yes	Hospital	Yes	Variable rate	Hartmann's	No	No
6	Teaching hospital	Yes	ICU	No	Fixed rate	0.9% NaCl	Yes	AV
7	DGH	No	NA	NA	NA	NA	NA	NA
8	DGH	Yes	ICU	Yes	Fixed rate	Hartmann's	Yes	Yes
9	DGH	Yes	Hospital	No	Variable rate	0.9% NaCl	No	No
10	Teaching hospital	Yes	ICU	Yes	Fixed rate	Hartmann's	No	AV
11	DGH	Yes	Hospital	Yes	Variable rate	0.9% NaCl	No	No
12	DGH	Yes	Hospital	No	Variable rate	0.9% NaCl	No	No
13	DGH	Yes	ICU	Yes	Fixed rate	Hartmann's	Yes	AV

Table 2 The management of DKA within individual ICUs of the East of England. NA=not applicable. AV=available, but not routinely used.

	All available CMP data from the 13 adult, general ICUs which participated in the survey	All CMP participating adult, general ICUs in England	All adult, general ICUs in England
Number of ICUs	12	175	204
Total number of admissions	6,146	101,845	125,500
Admissions with diabetic ketoacidosis, n (%)	103 (1.7)	1,439 (1.4)	1,800 (1.4)

†Extrapolation to all adult, general ICUs in England based on those units participating in the Case Mix Programme

Table 3 Number of admissions with diabetic ketoacidosis in adult, general ICUs participating in the Case Mix Programme, 1 April 2010 to 31 March 2011.

almost 2% of the admissions to general ICUs in the East of England had a diagnosis of DKA. Extrapolating from the available data to all units in England would mean about 1,800 annual admissions to ICU with a diagnosis of DKA. Furthermore, this suggests that approximately 13% of the patients admitted with DKA to acute hospitals in England are subsequently admitted to ICU. Thus DKA is a common condition that frequently necessitates intensive care intervention.

The JBDS guidelines recommend the use of FRIII, and monitoring the response to treatment with bedside, hand-held meters measuring capillary ketone levels.[2] In this study, only four of the ICUs used a FRIII and only one unit routinely measured capillary ketone levels. A FRIII is thought to decrease ketones faster and is potentially more appropriate in insulin-resistant states such as pregnancy and obesity.[2] The FRIII used with ketone meters, uses ketone clearance as the endpoint of successful treatment, thus ensuring that sufficient insulin has been administered to stop ketogenesis. It is the clearance of ketones in this condition that is crucial to determining outcome, with the plasma glucose only being a surrogate marker. In the past, it was only possible to measure this surrogate, but with the advent of better technology, it has become possible to measure the compound responsible for most of the morbidity and mortality associated with DKA, β-hydroxybutyrate. The move towards measuring ketones is designed to prevent the practice of stopping the insulin infusion once the blood glucose has returned to normal level, but before the ketotic process has been terminated. The JBDS guidelines recommend the additional administration of 10% glucose at 125 mL/hr should the capillary glucose fall below 14 mmol/L and the capillary ketones still be greater than 0.3 mmol/L. The use of a FRIII with capillary ketone

- Obtain the patient's weight in kg.
- If patient's weight is not available, estimate patient's weight (in kg).
- If pregnant, use present weight and consider calling for senior obstetric help as well.
- Start continuous FRIII via an infusion pump, 50 units human soluble insulin (Actrapid®, Humulin S®) made up to 50 mL with 0.9% sodium chloride solution. Ideally this should be provided as a ready-made infusion.
- Infuse at a fixed rate of 0.1 unit/kg/hr (ie 7 mL/hr if weight is 70 kg).
- If the patient normally takes insulin Lantus® or Levemir® subcutaneously, continue this at the usual dose and usual time.
- Measure capillary ketones and capillary glucose hourly.
- Continue FRIII until ketones are less than 0.3 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/L.
- If glucose falls below 14 mmol/L, commence 10% glucose given at 125 mL/h alongside the resuscitation fluid.
- Continue the FRIII until ketones are less than 0.3 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/L.
- Once the ketonaemia and acidosis have resolved, either move to a variable rate intravenous insulin infusion (more commonly referred to as an insulin sliding scale) as per local guidelines if the patient is not eating and drinking. If the patient is eating and drinking, recommence normal insulin regime.

Table 4 Use of a fixed rate intravenous insulin infusion (FRIII) as recommended by the JBDS DKA guidelines.

monitoring is based on expert diabetology opinion and consensus.[2] **Table 4** summarises the use of a FRIII.

The preferred resuscitation fluid in the ICUs surveyed was evenly balanced between the use of Hartmann's solution and 0.9% sodium chloride solution. While the fluid of choice advised in the JBDS guidelines is 0.9% sodium chloride solution, some units prefer to use Hartmann's solution. This occurred more commonly in those units with a unit-specific DKA guideline, suggesting that protocols may have been adapted to allow the use of Hartmann's in areas where its major disadvantage (insufficient potassium) can be overcome.

The JBDS guidelines discuss the debate around resuscitation fluid choice in DKA. In 2007, the *British Medical Journal* published an editorial that suggested the use of Hartmann's solution should be avoided in the treatment of DKA.[6] This was due to the belief that:

- the lactate would be poorly metabolised
- the potassium content may constitute an unacceptable risk in a hyperkalaemic patient
- cerebral oedema may be precipitated due to the hypotonicity of Hartmann's solution.

This editorial generated multiple responses,[7] with the majority of intensivists supporting the use of Hartmann's solution to treat DKA. A recent prospective randomised double-blinded study in the *American Journal of Emergency Medicine* suggested that Hartmann's solution is superior to 0.9% saline in treating DKA, as it results in a lower serum chloride and higher serum bicarbonate post-resuscitation.[8]

The choice of resuscitation fluid advised in the JBDS guidelines is 0.9% sodium chloride solution as it is readily available and can be readily obtained with pre-mixed potassium, unlike Hartmann's solution. This ensures that it is compliant with the recommendations from the National Patient Safety Agency (NPSA) not to allow potassium to be added to solutions on the general ward.[9] The JBDS guidelines do acknowledge that Hartmann's is a more physiological solution and its administration is less likely to result in hyperchloraemic metabolic acidosis. While potassium cannot be added to bags of Hartmann's solution on general wards, ICUs are an exception in the NPSA guidance on storage of potassium.[9] It is thus possible to administer Hartmann's with appropriate addition of potassium on the ICU, overcoming its disadvantage when used on the general ward.

Among specialist diabetic teams, the idea that the long-acting basal insulin analogues (detemir and glargine) should be continued at the same time as the intravenous insulin infusion is now well established.[10] While no studies have been carried out, the rationale for this is that the continuation of long-acting analogues during the initial management of DKA provides background insulin when the intravenous insulin is discontinued. This avoids rebound hyperglycaemia when intravenous insulin is stopped. It is designed to help reduce the length of stay in patients admitted with DKA. This only applies to long-acting insulin analogues, and does not mean that short acting insulin should not be given before the intravenous infusion has been stopped.[10]

The results from the current survey show that only a minority (three) of the ICUs' guidelines advocate continuation of the long-acting insulin analogues. Possible reasons for this are:

- The patients were so ill that there was little point in addressing measures that would reduce length of stay until they were back on a general medical ward.
- The intensive care teams did not know that continuing long-acting insulin analogues was (among specialist diabetes teams) the standard of care for those individuals not admitted to a ICU.

At the time of this survey, the JBDS DKA recommendations had not been widely implemented in ICUs in the East of England, despite two of the leading authors of the JBDS guidelines working in two different centres here. It is therefore unlikely that the JBDS guidelines have been widely adopted by the intensive care community across the UK.

The JBDS guidelines were produced without the involvement of the Intensive Care Society (ICS), or any other formal representative from the intensive care community. This lack of engagement with the intensive care community may have hindered the dissemination and subsequent widespread adoption of the JBDS recommendations within intensive care. Not all of the recommendations in the document are pertinent to intensive care; however, the main treatment aims should be the same wherever the patient is cared for. These include:

- Administration of a weight-based fixed rate intravenous insulin infusion until the ketotic process is terminated, as defined by capillary ketone testing.

- Fluid and electrolyte resuscitation.
- Administration of additional glucose as required, to prevent hypoglycaemia whilst facilitating the FRIII.
- Administration of the normal long-acting insulin analogue.
- Identification of the precipitating cause of the DKA.

In the light of our results, we recommend that the JBDS work with the intensive care community (and other applicable specialties, eg emergency medicine) to produce national DKA guidance that is endorsed and disseminated to all relevant medical practitioners.

Conflict of Interests

Dr Dhatariya was one of the authors of the JBDS DKA guidelines[2] and wrote the *BMJ* editorial[6] advocating the use of 0.9% saline as the fluid of choice in the resuscitation of patients with DKA. Dr Levy contributed to the fluid section within the JBDS DKA guidelines.[2]

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