Hyperglycaemic Hyperosmolar States in Diabetes:

Guidelines on Diabetic Ketoacidosis (DKA) and Hyperosmolar Non-ketotic Hyperglycaemia (HONK)

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Introduction

Diabetic ketoacidosis (DKA) and Hyperosmolar non-ketotic hyperglycaemia (HONK) are hyperglycaemic Hyperosmolar states and represent the acute hyperglycaemic complications of diabetes.

DKA is caused by absolute insulin deficiency and is usually seen in the context of type 1 diabetes. Insulin deficiency leads to hyperglycaemia and a metabolic shift to alternative energy sources. Free fatty acids are metabolised to the ketone bodies beta-hydroxybutyrate and acetoacetate. Ketone bodies are weak acids and, in high concentrations can cause a significant acidosis and severe illness. DKA accounts for 14% of diabetes related hospital admissions.

HONK is associated with insulin resistance and is most commonly seen in type 2 diabetes. It is characterised by very high glucose concentrations and renal impairment with absent ketones.

DKA is the classic decompensation state in type 1 diabetes but insulin deficient type 2 diabetes patients may also present with ketoacidosis, particularly African Caribbean patients. This is termed ketosis-prone type 2 diabetes or Flatbush diabetes, named after the area in New York where it was first described.

DKA and HONK are both hyperglycaemic states of decompensation in diabetes and may overlap. However, they require different management and are therefore considered separately in this guideline.

Diabetic Ketoacidosis

It is critical to exclude DKA in *any* unwell patient with diabetes. It is important to note that the magnitude of hyperglycaemia does not correlate with acidosis in DKA.

Precipitants of DKA are:

- Infection 30-40%
- Non-compliance 25%
- Inappropriate dose alteration 13%
- Newly diagnosed diabetes 10-20%
- Myocardial Infarction 1%

The mortality of DKA is 2-5% (higher in euglycaemic ketoacidosis), rising up to 50% in elderly patients.

The majority of mortality and morbidity in DKA is attributable to delays in presentation and initiation of treatment. Rapid recognition and treatment of DKA is critical.

DKA occurs due to insulin deficiency but it is not always associated with hyperglycaemia. DKA with a normal or near-normal glucose concentration is termed euglycaemic ketoacidosis. It is precipitated in circumstances where glycogen stores are exhausted such as protracted vomiting, alcohol use, malnourishment and pregnancy. Euglycaemic ketoacidosis has a higher mortality than DKA with elevated glucose concentrations.

Presentation

History

Patients with DKA may complain of:

- Nausea
- Vomiting
- Dehydration/ thirst
- Polyuria
- Abdominal pain
- Headache
- Blurred vision
- Weight loss
- Leg cramps
- Symptoms of any precipitant

Examination

- Kussmaul respiration, Ketotic breath
- Dehydrated, hypotensive
- Abdominal tenderness (DKA may mimic an acute abdomen)
- Gastric stasis
- Decreased conscious level, confusion
- Features of the precipitant

Immediate Investigations

Establish Diagnosis

- Laboratory glucose
 - Usually > 11mmol/L
- Blood gas (venous unless O₂ saturations low)
 - pH < 7.3
 - Bicarbonate <20mmol/L
- Urine dip
 - Ketones +++ or above

Others

- Urgent potassium, venous blood gas is acceptable
- Urea and electrolytes
- ECG

Further Investigations

- Chest X-ray (abdominal X-ray if tender or profuse vomiting)
- Full blood count
- CRP
- Liver function
- Capillary blood ketone estimation (if available)
- Blood cultures
- Urine microscopy
- Pregnancy test
- Troponin

DKA Diagnosis:

Laboratory Glucose >11mmol/L pH<7.3 or Bicarbonate <20mmol/L Urine Ketones ++++

(Capillary blood ketones > 1mmol/L)

Immediate Management

- Ensure airway, breathing and circulation are intact and support as appropriate
- Contact ITU early if severe DKA (pH<7.1 or HCO₃<8mmol/L) or patient obtunded
- The central management of DKA is ensuring adequate fluid and insulin

Intravenous fluids

- Patients with DKA may have a fluid deficit of over 6-8 litres
- Fluid status should be assessed clinically, biochemically and, if necessary, with central venous monitoring and a urinary catheter
- The initial fluid of choice is 0.9% Saline with no potassium in 1st bag
- Rate of administration is dependent on hydration
- If serum sodium > 150mmol/L, consider 0.45% Saline
- Once capillary blood glucose <12mmol/L, switch to 5% Dextrose. Do not switch back to saline. If glucose concentration exceeds 12mmol/L, increase insulin sliding scale infusion rates
- If hypoglycaemia occurs, **do not** stop insulin infusion, switch to 10% dextrose and continue insulin as per sliding scale.

Potassium

- Patients with DKA are usually 200-700 mEq deplete due to renal losses
- Despite overall deficit, the blood compartment may be hyperkalaemic due to insulin deficiency
- An urgent assessment of potassium is required (venous blood gas is acceptable) during the first 1litre bag of 0.9% Saline
- Potassium usually starts in 2nd or 3rd litre of fluid and should be given in every bag thereafter
- Electrolytes must be checked a minimum of every 4 hours in the first 24 hours (venous blood gas electrolyte values may be used)
- Ready-mixed IV infusion solutions should be prescribed and administered where possible

Approximate guidance for fluid and potassium replacement in first 4 hours of DKA.

Time (Minutes)	Fluid	Potassium
30	1 litre 0.9% Saline	Nil
60	1 litre 0.9% Saline	Nil/ 20 mEq
120	1 litre 0.9% Saline	20 mEq
240	1 litre 0.9% Saline/	20/ 40 mEq
	5% Dextrose if glucose <12mmol/L	

This guidance must be adjusted according to clinical and biochemical status

Intravenous insulin

- An intravenous sliding scale should be instituted immediately
- If any delay occurs in giving insulin sliding scale, 10 units of Actrapid may be given intramuscularly
- DKA is an insulin resistant state and patients may require large doses of insulin
- Sliding scale insulin should be continued until ketonuria has resolved and patient can eat and drink

If the patient normally takes insulin glargine (Lantus) or detemir (Levemir) subcutaneously continue this at the usual dose and usual time. Continuation of long acting analogues during the initial management of DKA provides background insulin when the IV insulin is discontinued. This avoids rebound hyperglycaemia when IV insulin is stopped and should avoid excess length of stay. This only applies to long acting analogues and does not obviate the need to give short acting insulin before discontinuing the intravenous insulin infusion.

Insulin sliding scale

50 units of Actrapid (soluble insulin) in 50mls 0.9% Saline (1 unit Actrapid in 1ml Normal Saline). Note that patients with a high BMI may have a large insulin requirement, sliding scales should be frequently reviewed and adjusted accordingly.

Capillary Blood Glucose (mmol/L)	Infusion rate (ml/hr)
0-3.9	0.5
4-7.9	1
8-11.9	2
12-15.9	3
16-19.9	4
≥20	6-8

Initial infusion rates for DKA:

Nursing Care

- 1. Set up 2 IV lines through a 3-way tap consisting of a non-return valve:
 - 1st line: Make up 50 units Actrapid (soluble insulin) in 50ml 0.9% normal saline in a syringe driver
 - 2nd line: Commence 1litre IV fluids (with or without KCI) through another pump
- 2. Check infusions against prescription with another trained nurse.
- 3. Document start of infusions on input/output chart and prescription chart
- **4.** Explain need for infusions to patient and reassure that it is a temporary way to control glucose
- Monitor capillary blood glucose levels 1 hourly until stable (capillary glucose 5– 10mmol/L for 3 consecutive hours) and 2 hourly subsequently. If hypoglycaemia occurs or capillary glucose greater than 15mmol/L, revert to 1 hourly monitoring.
- 6. Check any rate changes with another trained nurse and document
- **7.** Aim for blood glucose levels of 5-10 mmol/L. Discuss with medical staff if this is not being achieved as rates of insulin may need to be amended

If the glucose is greater than 20mmol/L for 2 hours please contact medical staff

Infusion rates should be reviewed daily and altered according to glycaemic control.

Acid/ Base Balance Monitoring Venous blood gases should be assessed a minimum of every 4 hours until pH and bicarbonate are normal.

Capillary Blood Ketone Monitoring Capillary blood ketone monitoring is not available on all Imperial trust sites.

Blood ketone monitoring does not alter the treatment of DKA but may be useful in clarifying the source of a metabolic acidosis as pH, bicarbonate and anion gap are all non-specific. Capillary ketone monitoring may also be useful in oligo-anuric patients with suspected DKA. Capillary ketone monitoring may be useful in documenting clearance of blood ketones and therefore guiding the changeover to SC insulin (as below).

Further management

- Thromboprophylaxis with low molecular weight heparin and TED stockings
- Broad spectrum antibiotic therapy or antibiotic regime appropriate to underlying infection. Consult Trust Adult Treatment of Infection Policy or contact microbiology/infectious diseases if appropriate
- Nasogastric tube if vomiting or decreased conscious level
- Consider central venous access
- Treat precipitant as appropriate

Bicarbonate

Sodium bicarbonate infusions should not be used in DKA without specialist advice. Studies of administration of bicarbonate to patients with advanced diabetic ketoacidosis (pH 6.9–7.1), have shown no improvement in morbidity or mortality rates, nor an increase in the frequency of adverse outcomes. Therefore, its use is only advocated if the pH is less than 6.9 with no improvement in the metabolic parameters during insulin and fluid therapy. Failure to improve acidosis despite adequate management is usually related to an unidentified source of sepsis or tissue necrosis (e.g., intra-abdominal abscess, foot sepsis, bowel infarction, pancreatitis).

Continuing Care

All patients with DKA should be referred to the diabetes team within 24 hours of admission, except at weekends.

All patients with DKA should have daily urine dipstick analysis and electrolytes Sliding scale insulin should be continued until:

- Urine ketones have resolved or capillary blood ketones <1mmol/L
- Plasma glucose <12mmol/L
- Patient is eating and drinking

Discontinuing Intravenous Insulin The discontinuation of the intravenous infusion of insulin depends on tolerance of nutritional intake by the patient. Once the patient resumes adequate dietary intake without the risk of nausea or vomiting, the IV infusion can be discontinued and patient resumed on premorbid treatment.

The usual dose of subcutaneous insulin should be given before the meal, depending on patient's regime. IV insulin can then be discontinued 30 - 45 minutes later. This is necessary to prevent any gap in insulin coverage which could lead to loss of metabolic control; IV insulin remains active for 10 - 15 minutes.

HONK

HONK has a mortality of 50%. This is partly because HONK has an insidious, gradual onset but is also because 60% of cases occur in newly diagnosed type 2 diabetes, affecting an older population with more significant co-morbidities.

HONK rarely occurs in isolation and glucose management must be considered in the context of any other acute presenting conditions which may include sepsis (particularly related to diabetic foot disease), ischaemic heart disease, cerebrovascular disease and electrolyte and other metabolic abnormalities.

HONK is characterised by:

- Severe hyperglycaemia
- dehydration and renal failure and,
- mild/ absent ketonuria

The mortality of HONK accrues from the complications of the hyperosmolar state which leads to hyperviscosity and arterial and venous thrombosis. Complications include:

- Rhabdomyolysis
- Venous thromboembolism
- Lactic acidosis
- Hypertriglyceridaemia
- Renal failure
- Stroke
- Cerebral oedema

The precipitants of HONK are:

- New diagnosis of T2DM
- Infection
- High dose steroids
- Myocardial Infarction
- Vomiting
- Stroke
- Thromboembolism
- Poor treatment compliance

Presentation

History

Patients with HONK may present with:

- Confusion
- Coma
- Seizures
- Vomiting
- Features of precipitant

Onset is usually insidious

HONK Diagnosis:

Lab glucose > 40mmol/L Serum osmolality > 320mOsm Urine ketone -/trace/+

Examination

- Dehydration
- Hypotension
- Decreased conscious level
- Coma
- Confusion
- Focal neurology
- Features of the precipitant

Immediate Investigations Establish Diagnosis

- Laboratory glucose
- Urea, electrolytes and creatinine
- Blood gas (venous unless O₂ saturations low)
- Urine dip

The diagnostic criteria for HONK are:

- Serum osmolality >320mOsm/kg
- Urine ketones -/tr/+
- Plasma glucose >40

If laboratory osmolality is difficult to obtain rapidly, osmolality should be estimated as:

Osmolality = 2 x (Na + K) + Glucose

Bicarbonate is usually >15mmol/L but may be lower in the case of acute renal failure or lactacidosis.

Capillary blood ketone monitoring may be useful to exclude ketoacidosis. A value of <1.0mmol/L excludes ketoacidosis.

Further Investigation

- Chest X-ray
- ECG
- Full blood count
- Liver function, CRP, Troponin
- Blood cultures, Urine microscopy, culture and sensitivity
- Amylase, CK
- Consider CT head if obtunded

Immediate management

- Ensure airway, breathing and circulation are intact and support as appropriate
- Cardiac monitoring
- Oxygen
- Urinary catheter
- Consider central venous access and nasogastric tube
- HONK should be managed in a high dependency environment, contact ITU early to review airway, need for inotropic support, and consideration of renal replacement therapy
- The central management of HONK is supportive care and *slow* metabolic resolution

Intravenous Fluids

- Patients with HONK often have a deficit of over 8 litres
- Extreme caution should be exercised with rapid replacement; rapid osmolar shifts outside of the blood-brain barrier cannot be matched intracerebrally and cerebral oedema occurs. This can be fatal, symptoms include decreased GCS, headache and confusion.
- The initial fluid of choice is 0.9% Saline with no potassium
- Once capillary blood glucose <12mmol/L, ensure 5% Dextrose is given. This may be given concurrently with 0.9% Saline to ensure hydration and prevent hyponatraemia
- Rate of fluid administration should be titrated to clinical status, CVP, cardiac status, renal function and osmolality
- A guide is 4 litres maximum in first 24 hours
- 0.45% Saline may be used in significant hypernatraemia (>150mmol/L). Aliquots of 100-250mL should be given and serum sodium checked after each aliquot

• Try not to reduce osmolality by more than 5mOsm/kg per hour

Insulin

- An intravenous sliding scale should be instituted immediately
- Aim for slow correction of hyperglycaemia
- Do not use more than 3units/hour
- Once capillary blood glucose <15mmol/L, switch to 5% dextrose

Insulin sliding scale

50 units of Actrapid (soluble insulin) in 50mls 0.9% Saline (1 unit Actrapid in 1ml Normal Saline).

Initial infusion rates for HONK:

Capillary Blood Glucose (mmol/L)	Infusion rate (ml/hr)
0-3.9	0.5
4-7.9	0.5
8-11.9	1
12-15.9	2
16-19.9	2.5
≥20	3

Do not exceed 3mls/hr infusion rate

Nursing Care

- 1. Set up 2 IV lines through a 3-way tap consisting of a non-return valve:
 - 1st line: Make up 50 units Actrapid (soluble insulin) in 50ml 0.9% normal saline in a syringe driver
 - 2nd line: Commence 1litre IV fluids (with or without KCL) through another pump
- 2. Check infusions against prescription with another trained nurse.
- 3. Document start of infusions on input/output chart and prescription chart

- **4.** Explain need for infusions to patient and reassure that it is a temporary way to control glucose
- Monitor capillary blood glucose levels 1 hourly until stable (capillary glucose 5– 10mmol/L for 3 consecutive hours) and 2 hourly subsequently. If hypoglycaemia occurs or capillary glucose greater than 15mmol/L, revert to 1 hourly monitoring.
- 6. Check any rate changes with another trained nurse and document
- **7.** Aim for blood glucose levels of 5-10 mmol/L. Discuss with medical staff if this is not being achieved as rates of insulin may need to be amended

If the glucose is greater than 20mmol/L for 2 hours please contact medical staff

Infusion rates should be reviewed daily and altered according to glycaemic control.

Potassium

- Await lab potassium result before replacmement
- HONK is often accompanied by acute renal impairment. Care should therefore be taken with potassium replacement
- Electrolytes must be checked a minimum of every 4 hours in the first 24 hours (venous blood gas electrolyte values may be used).
- Ready-mixed IV infusion solutions should be prescribed and administered where possible

Further management

- Full anticoagulation with low molecular weight heparin and TED stockings
- Broad spectrum antibiotic therapy or antibiotic regime appropriate to underlying infection. Consult Trust Adult Treatment of Infection Policy or contact microbiology/infectious diseases if appropriate
- Treat precipitant as appropriate

Continuing Care

All patients with HONK should be referred to the diabetes team within 24 hours of admission, except at weekends.

All patients with HONK should have daily urine dipstick analysis, renal function and electrolytes as a minimum

Sliding scale insulin should be continued until:

- Plasma glucose <12mmol/L
- Patient is eating and drinking

Discontinuing Intravenous Insulin The discontinuation of the intravenous infusion of insulin depends on tolerance of nutritional intake by the patient. Once the patient resumes adequate dietary intake without the risk of nausea or vomiting, the IV infusion can be discontinued and patient resumed on premorbid treatment or a treatment appropriate to the patient. Following HONK, patients usually require conversion to regular subcutaneous insulin (although ultimately it may be possible to convert to oral hypoglycaemic agents).

Contacting the Team

ALL PATIENTS WITH DKA OR HONK <u>MUST</u> BE REVIEWED BY THE DIABETES TEAM AS SOON AS POSSIBLE AFTER ADMISSION.

The diabetes inpatient teams are available to review patients on all sites and should be contacted on:

St Mary's Campus

Diabetes Specialist Nurse: Diabetes SpR:	Bleep 1224 Bleep 1622	Extension 21073	Fax 26150
Charing Cross Campus Diabetes Specialist Nurse: Diabetes SpR:	Bleep 5302 Bleep 1061	Extension 11062	Fax 11080
Hammersmith Campus Diabetes Specialist Nurse: Diabetes SpR:	Bleep 6749 Bleep 9050/9051	Extension 34693	Fax 32348

DKA Summary

	Insulin	Fluids	Potassium	Other
1st Hour	 Institute sliding scale Intramuscular soluble insulin 	• 1 to 2 litres 0.9% saline	• 0 to 20 mEq	 DVT prophylaxis Antibiotics Monitoring Consider CVP line Treat precipitant
2 to 6 Hours	 Continue sliding scale Adjust as appropriate to achieve target glucose 	 Continue rehydration Regularly assess clinical, physiological and metabolic markers and titrate accordingly Up to 3-4 litres 0.9% Saline Switch to 5% dextrose when capillary glucose <12mmol/L Consider 0.45% saline if hypernatraemic 	 Total deficiency may be 200-700 mEq Continue K⁺ replacement up to 80 mEq Monitor serum potassium a minimum of 4 hourly 	 Glucose, capillary ketone, acid/base monitoring Continued clinical monitoring Contact ITU/ HDU as required
> 6 Hours	 Continue sliding scale Adjust as appropriate to achieve target glucose Discontinue when appropriate 	 Continue rehydration Regularly assess clinical, physiological and metabolic markers and titrate accordingly Switch to 5% dextrose when capillary glucose <12mmol/L Consider 0.45% saline if hypernatraemic 	 Continue K⁺ replacement Monitor serum potassium a minimum of 4 hourly 	 Glucose, capillary ketone, acid/base monitoring Continued clinical monitoring Contact diabetes team Daily urine dipstick Manage precipitant as required Diabetes education

*Ready-mixed IV infusion solutions should be prescribed and administered where possible

POTENTIAL PROBLEM	NURSING ACTION	RATIONALE
Impaired consciousness	 Observations of vital signs Administer oxygen and monitor oxygen saturations Nurse in an upright position or lateral position Neurovascular observations Administration of anti-emetics Monitor, report and document all laboratory results 	To assess clinical status To correct hypoxia To prevent risk of aspiration of secretions or vomitus To detect changes in conscious level To prevent risk of aspiration To assess clinical status and liaise with medical staff promptly
Hyperglycaemia and Ketonaemia	 Maintain IV sliding scale insulin Blood glucose monitoring Urinary ketone testing in DKA Safe transition from IV insulin to S/C insulin 	To reduce blood glucose levels and ketonaemia To change rate of IV insulin and monitor glycaemic control To monitor ketosis To prevent recurrence
Fluid replacement	 Administration of IV fluids Monitor CVP if patient is severely unwell Catheter care Fluid balance chart 	To correct hypovolaemia and electrolyte imbalance To assess effects of fluid replacement To ensure that urine is passed if patient is semi-conscious or oliguric To monitor renal function
Electrolyte imbalance	 Administer IV fluids and potassium replacement Cardiac monitoring due to potassium replacement report any ECG changes to medical staff Administer IV NaCI as prescribed Monitor arterial blood gases 	To prevent hypokalaemia and potential cardiac arrhythmias To monitor risk of cardiac arrhythmias To correct electrolyte imbalance To assess pH of blood
Infection: probable or current	 Administration of antibiotics Take bloods for MC & S 	To treat underlying cause of DKA or HONK or use prophylactically To detect presence of infection and treat with appropriate antibiotics
Hygiene needs	Assist in personal care – body wash, mouth care and pressure area care if patient is unable to self-care	To provide general comfort, well-being and reduce risk of infection
Other Possible Clinical Considerations	 Administration of low molecular weight heparin Patient requires a chest x-ray Care of nasogastric tube if appropriate 	To reduce risk of DVT To detect presence of infection To reduce nausea and vomiting and reduce risk of aspiration pneumonia
Psychological needs	Explain plan of care and reassure patient and relatives at all times	DKA or HONK may be first presentation of diabetes and are potentially life-threatening conditions which may be frightening
Education	 Refer to the Diabetes Team Refer to dietician Commence education about insulin injections and blood glucose targets 	To facilitate a planned programme of education for self- management, discharge planning, reduced length of stay and prevent recurrence To commence educational support

Hyperglycaemic Hyperosmolar State Nursing Summary - The intensity of care depends on severity of DKA or HONK

The following sections are compulsory and <u>must</u> be completed

6) IMPLEMENTATION

Training required for staff	No
If yes, who will provide training	N/A
When will training be provided?	N/A
Date for implementation of guideline	

7) MONITORING / AUDIT

When will this guideline be audited?	1/1/2011
Who will be responsible for auditing this guideline?	Dr. Jonathan Valabhji, Clinical Lead, Diabetes
Are there any other specific recommendations for audit?	

8) REVIEW

When will this guideline be reviewed?	June 2013 Nick Oliver
Please indicate frequency of review:	3 yearly
As a guide:	
 Drug related guidance should be reviewed every 2 years 	
 Therapy related guidance should be reviewed every 5 years 	
 Clinical treatment guidance should be reviewed every 3 – 5 years 	
Date of next review	June 2013

10) ADMIN DETAIL

Start Date:	
(date of final approval by CPG)	
Dates approved by:	Divisional Guidelines Group (if applicable)
	CPG1 Guidelines Committee
Have all relevant stakeholders (Trust sites, CPGs and departments) been included in the development of this guideline?	Imperial College Healthcare NHS Trust Diabetes Team Professor D Johnston Dr A Dornhorst Dr J Valabhji Dr E Hatfield Dr N Martin Dr T Tan Dr D Gable Dr M Yee Dr N Oliver Sarah Allen Carol Jairam Mary Joyce Barbara Muzenda Clare Poulter Jo Reed Carmel Ryan Anna Sackey Inez Walkes Sarah Menezes Nicola Bandaranayake Louisa Fearnley
Who will you be notifying of the existence of this guidance?	Please give names/depts
Related documents:	If applicable
Author/further information:	Nick Oliver / Carol Jairam Diabetes Dept CPG1 – Medicine St. Mary's Hospital 0203 312 1073
Document review history:	v. 1.2
Next review due	2013
THIS GUIDELINE REPLACES:	Management Of Hyperosmolar Non-Ketotic Coma (HONK)
	Guidelines for Management of DKA

11) INTRANET HOUSEKEEPING

Key words	Diabetes, Ketoacidosis, hyperosmolar, DKA, HONK, Hyperglycaemia, endocrinology
Which CPG does this belong to?	Medicine
Which subdivision of the guidelines spine should this belong to?	Diabetes and Endocrinology
Title for the intranet if different from the document (<i>please note that documents sit alphabetically so should not start with "guideline for…")</i>	Diabetes - Hyperglycaemic Hyperosmolar States - Diabetic Ketoacidosis (DKA) and Hyperosmolar Non-ketotic Hyperglycaemia (HONK)