MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Guidelines for Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults

All patients with HHS must be referred to the Diabetes Specialist Team within 24hrs. Referrals will automatically be submitted once the PowerPlan is launched. Referrals can also be submitted manually via Requests & Prescribing on EPR.

Hyperosmolar Hyperglycaemic State (formerly known as Hyperosmotic Non-Ketotic coma/HONK) is a medical emergency affecting patients with type 2 diabetes (T2DM). It is characterised by marked dehydration, elevated serum osmolality and severe hyperglycaemia in the absence of significant ketosis or acidosis. It can be precipitated by infection or a vascular event, or manifest as a new presentation of diabetes.

In contrast to diabetic ketoacidosis (DKA), HHS develops gradually, over days to weeks, resulting in profound metabolic disturbances and dehydration associated with a high mortality (15-20%) from vascular complications such as stroke, myocardial infarction and peripheral arterial thrombosis, as well as rarer neurological sequelae such as seizures, cerebral oedema and central pontine myelinolysis (CPM).

Confirming Diagnosis

- **Serum osmolality greater than 320 mOsmol/kg**
- **Venous blood glucose greater than 30 mmol/L**
- **Marked hypovolaemia secondary to dehydration**
- **Absence of significant hyperketonaemia (less than 3 mmol/L)**
- **Absence of acidosis (pH greater than 7.3 and bicarbonate greater than 15 mmol/L)**

Serum osmolality is estimated on the blood gas, or using the following formula:

Osmolality (mOsmol/kg) = $2Na^+$ + [Glucose + Urea]

Ketones may be present at low levels (below 3 mmol/L), usually without acidosis, although patients may have a mixed picture of HHS and DKA. Ketone levels above 3 mmol/L in the presence of acidosis (defined as pH less than 7.3 or serum bicarbonate less than 15 mmol/L) should be treated according to the 'Guidelines for Management of DKA in Adults' MIL with early input from the specialist diabetes team.

General Principles of Treatment

Controlled rehydration with intravenous fluids is the mainstay of treatment, which may be enough to normalize osmolality and bring down glucose levels without the use of insulin. Fluid losses in HHS are typically equivalent to 10–20% of total body weight and the following guide aims to gradually and safely rehydrate while normalizing biochemistry over a 72 hour period. Note that fluid prescriptions may need to be adjusted in patients with renal failure or congestive cardiac failure to prevent fluid overload.

There is typically a lesser requirement for insulin than in DKA and unnecessary use of insulin without adequate rehydration risks dangerous fluid shifts and significant hypotension.

Seek the underlying precipitant early (e.g. infection, ACS, stroke) and commence appropriate treatment. Actively protect pressure areas, particularly heels, and commence prophylactic anticoagulation with LMWH in conjunction with the trust VTE risk assessment (providing there is no contraindication). **Refer all patients with HHS to the specialist diabetes team at the earliest opportunity. Referrals will automatically be submitted once the PowerPlan is launched, however referrals may also be manually submitted via Requests & Prescribing on EPR.**

When prescribing in ePMA use the PowerPlan:

Diabetes – Adult management of hyperosmolar hyperglycaemic state (HHS) PowerPlan

See LINK for further guidance on how to make amendments once a PowerPlan is launched

Monitoring

Patients with HHS should be monitored with usual track-and-trigger observations along with GCS and at least 12 hours of cardiac monitoring. Capillary ketone and venous blood gas measurements are performed 1 hourly in the acute phase (0-6 hours), then 2-4 hourly thereafter. Note that point-of-care glucometers are unable to measure glucose levels above 27.8 mmol/L therefore VBG measurements are preferred.

Accurate fluid balance must be recorded at all times and all fluids must be infused using a volumetric fluid pump. Urinary catheterization with hourly urometer measurement is recommended.

Treatment on Presentation

Infuse one liter of 0.9% sodium chloride over one hour, or faster if systolic blood pressure is below 90 mmHg. Subsequent liter bags of 0.9% sodium chloride are infused over 2 hours then 4 hours and supplemented with 40 mmol/L of potassium whenever levels fall below 5 mmol/L (see figure).

Continue any long acting insulin analogues (detemir/Levemir™, degludec/Tresiba™ or glargine/Lantus™, Abasaglar™, Toujeo™).

Start a low-dose fixed rate insulin infusion on presentation ONLY if blood ketones exceed 1 mmol/L (see below for recommended rates of infusion) via the HHS PowerPlan as the rate differs from VRIII.

Acute Phase (up to 12 hours)

Subsequent adjustments to fluid prescriptions are informed by changes in serum osmolality. **Successful initial treatment of HHS will cause sodium concentrations to rise; this is not an indication for hypotonic fluids**. If no rise in sodium is seen then the patient has not been adequately rehydrated. Rapid decreases in sodium can precipitate CPM and levels should **not** fall by more than 10 mmol/L/24hrs.

Aim for a decrease in serum osmolality of 3 – 5 mOsmol/kg per hour;

- **If osmolality falls too slowly** (less than 3 mOsm/kg/hr) despite an adequately positive fluid balance (2-3 litres positive in the first 6 hours) start hypotonic fluids (0.45% sodium chloride).
- **If osmolality falls too quickly** (more than 8 mOsm/kg/hr) reduced the rate of 0.9% sodium chloride and reduce or stop any insulin infusions.

Glucose levels should fall by 5 mmol/hr. Aim for a blood concentration 10-15 mmol/L

- If glucose levels fall too slowly despite adequate hydration (urine output greater than 0.5 ml/kg/hr) start insulin at 0.05 unit/kg/hr (Regimen A) or, if already in place, increase the insulin infusion rate to 0.1 unit/kg/hr (Regimen B).
- If blood glucose falls below 10 mmol/L reduce any insulin infusion by 1 unit/hr and if persistently low commence glucose 5% at 125 ml/hr concurrently with any other fluid prescriptions.
- If blood glucose falls below 7 mmol/L replace glucose 5% with glucose 10% at the same rate (125 ml/hr)

Post-acute phase

Aims to achieve a positive balance of 3-6 litres by 12 hours with the total fluid deficit replaced by 24 hours (typically 100 – 220 ml/kg or 7 – 14 L in a 70 kg patient). Encourage patients to eat and drink whenever safe to do so and aim to maintain glucose in the range of 6-10mmol/L by titrating the HHS IV insulin infusion rate (+/- 1 unit) with added 5% glucose if needed.

If the patient is not eating and drinking by 24 hours and blood ketones are less than 1mmol/L, start a variable rate insulin infusion (see Variable Rate Intravenous Insulin Infusion MIL).

All patients with HHS should be discharged with regular subcutaneous insulin with blood glucose monitoring under guidance from the diabetes specialist team. Oral hypoglycaemic agents may be reintroduced after 4-6 weeks, which should coincide with planned follow-up

Therapeutic Targets

- Fall in serum osmolality of 3-8 mOsm/kg/hr
- Fall in blood glucose of 5 mmol/L/hr
- Urine output more than 0.5 ml/kg/hr
- Fluid balance 2-3 L positive in the first 6 hours and 3-6 L positive by 12 hours
- Blood glucose 10-15 mmol/L
- Maintain potassium in normal range
- Urine output greater than 0.5 ml/kg/hr

Indications for ICU Review

- Venous/arterial pH less than 7.1
- Shock (Systolic Blood Pressure (SBP) less than 90 mmHg and Heart Rate greater than 100 bpm) after 3 liters of initial fluid resuscitation
- Co-morbidities which would make tight control of fluid balance challenging (e.g. heart failure, chronic kidney disease stage 4/5)
- Persistent hypokalaemia despite IV potassium replacement
- GCS less than 10

Contacts (Oxford and Horton sites)

Inpatient Diabetes Nursing Team:
Tel: 01865 (2)22866 – leave message out of hours
All referrals must be requested via EPR – either via launch of PowerPlan or via Requests & Prescribing
For advice (bleep): JR 4433, CH 6762, NOC 6761, HGH 9912

References:

Joint British Societies Inpatient Care Group. Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults with Diabetes; August 2012. Available from://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_HHS_Adults.pdf

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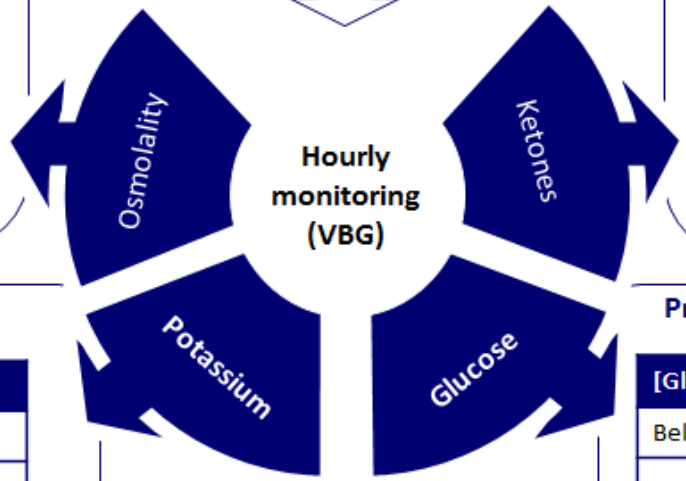
HHS

Serum Osmolality above 320 mOsmol/kg
Glucose above 30 mmol/L
Hypovolaemic

Give 0.9% sodium chloride 1 litre/hr*
*increase rate if systolic below 90 mmHg

Treat underlying precipitant
VTE prophylaxis
Protect pressure areas
Fluid balance
Regular assessment (inc. GCS)



Controlled Rehydration

Ensure **urine output more than 0.5 ml/kg/hr.** Adjust choice and rate of fluid according to decrease in osmolality. Monitor for signs of fluid overload.

Decrease in Osmolality mOsmol/kg/hr	Choice of fluid
Below 3 (despite adequate rehydration)	0.45% sodium chloride
3 – 5	0.9% sodium chloride at suggested rate (see below)
Above 8	0.9% sodium chloride Reduce rate of fluids Reduce insulin (1 unit/hr)

Suggested fluid regime	Infusion Rate
1st litre	Over 1 hour
2nd litre	Over 2 hours
3rd litre	Over 2 hours
4th litre	Over 4 hours
5th litre	Over 4 hours
6th litre	Over 6 hours

Insulin prescribing

On presentation…

[Ketones] mMol/L	Insulin prescription
Below 1	No Insulin (Fluids only)
1 – 3	Insulin **Regime A** (see below)
Above 3 No acidosis (pH above 7.3)	Insulin **Regime B** (see below)
Above 3 With acidosis (pH below 7.3)	Follow DKA MIL

If glucose falls less than 5 mmol/L/hr despite adequate rehydration start insulin **Regime A.** If already receiving insulin via an infusion that is running at the expected rate, start **Regime B.** Continue long-acting insulin analogues.

Weight (kg)	Insulin IV infusion (1 unit/ml) pump settings (ml/hour)	
	Regime A (0.05 unit/kg/hr)	**Regime B (0.1 unit/kg/hr)**
Below 40	1.5	3
40 – 49.9	2	4
50 – 59.9	2.5	5
60 – 69.9	3	6
70 – 79.9	3.5	7
80 – 89.9	4	8
Above 90	4.5	9

Correcting Hypokalaemia

[K^+] mMol/L	Potassium replacement
Below 3.5	Seek Specialist Advice
3.5 – 5	Give K^+ (40 mmol per litre of fluid)
Above 5	No replacement

Max rate of potassium = 20 mmol / hr
K^+ = Potassium

Change Insulin infusion and line every 24 hours and cannula according to Trust guidance and document. Conduct independent verification checks of all insulin prescriptions (see OUH Medicines Policy).

Preventing Hypoglycaemia

[Glucose] mMol/L	Dextrose
Below 7	10% Glucose 500 ml over 4 hrs
7 – 10	Reduce insulin by 1 unit/hr 5% Dextrose 1 L over 8 hrs
Above 10	No replacement

Run glucose concurrently with insulin via a single cannula with "Y" site and dual anti-syphon valves. Run saline via a separate cannula.

Medicines Management and Therapeutics Committee
Oxford University Hospitals

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