HHS care pathway

The Hyperglycaemic Hyperosmolar State (HHS) is a medical emergency. In the UK it is less common than diabetic ketoacidosis (DKA), though in areas with a high proportion of patients of African origin this may not be the case. HHS is associated with a significant morbidity and higher mortality than DKA and must be diagnosed promptly and managed intensively. The diabetes specialist team should be involved as soon as possible after admission.

For young people under the age of 16 years contact your paediatric diabetes service and refer to published paediatric guidelines for the management of HHS such as those by Zeitler (2011).

Diagnosis

The characteristic features of a person with HHS are:

- Hypovolaemia
- Marked hyperglycaemia (30 mmol/L or more) **without** significant hyperketonaemia (less than 3 mmol/L), ketonuria (2+ or less) or acidosis (pH greater than 7.3, bicarbonate greater than 15 mmol/L)
- Osmolality usually 320 mosmol/kg or more

N.B. A mixed picture of HHS and DKA may occur

Assessment of severity

Patients with HHS are complex and often have multiple co-morbidities so require intensive monitoring. Consider the need for admission to a high-dependency unit / level 2 environment, when one or more of the following are present:

- osmolality greater than 350 mosmol/kg
- sodium above 160 mmol/L
- venous / arterial pH below 7.1
- hypokalaemia (less than 3.5 mmol/L) or hyperkalaemia (greater than 6 mmol/L) on admission
- Glasgow Coma Scale (GCS) less than 12 or abnormal
- AVPU (Alert, Voice, Pain, Unresponsive) scale
- oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- systolic blood pressure below 90 mmHg
- pulse over 100 or below 60 bpm
- urine output less than 0.5 ml/kg/hr
- serum creatinine >200 µmol/L
- hypothermia
- macrovascular event such as myocardial infarction or stroke
- other serious co-morbidity.

Goals of treatment

The goals of treatment of HHS are to treat the underlying cause and to gradually and safely:

- normalise the osmolality
- replace fluid and electrolyte losses
- normalise blood glucose.

Other goals include prevention of:

- arterial or venous thrombosis
- other potential complications e.g. cerebral oedema/ central pontine myelinolysis
- foot ulceration.

New principles

- ***Measure or calculate osmolality ($2Na^+$ + glucose + urea) frequently to monitor treatment response.***
- ***Use IV 0.9% sodium chloride solution as the principle fluid to restore circulating volume and reverse dehydration. Only switch to 0.45% sodium chloride solution if the osmolality is not declining despite adequate positive fluid balance.***
- ***An initial rise in sodium is expected and is not in itself an indication for hypotonic fluids. Thereafter, the rate of fall of plasma sodium should not exceed 10 mmol/L in 24 hours.***
- ***The fall in blood glucose should be no more than 5 mmol/L/hr. Low dose IV insulin (0.05 units/kg/hr) should be commenced once the blood glucose is no longer falling with IV fluids alone OR immediately if there is significant ketonaemia (3β-hydroxy butyrate greater than 1 mmol/L).***
- ***Assess foot risk score on admission.***

A. Hour 1: Immediate management upon diagnosis: 0 to 60 minutes

T=0 at time intravenous fluids are commenced. If there is a problem with intravenous access critical care support should be requested immediately.

- Commence IV 0.9% sodium chloride – 1 litre to run over 1 hour
    - Consider more rapid replacement if SBP below 90 mmHg
    - Caution in the elderly where too rapid rehydration may precipitate heart failure but insufficient may fail to reverse acute kidney injury
- Only commence insulin infusion (0.05 units/kg/hr) **IF** there is significant ketonaemia (3β-hydroxy butyrate greater than 1 mmol/L) or ketonuria 2+ or more (i.e. mixed DKA and HHS)
- Clinical assessment of the patient:
    - Does the history suggest sepsis/vascular event or a recent change in medication?
    - Assess the degree of dehydration
    - Examine for a source of sepsis or evidence of vascular event
    - Mental state assessment

- Assess foot risk score – assume high risk if patient obtunded or uncooperative
    - Ensure heels are off-loaded
    - Ensure daily foot checks
- Investigations
    - Capillary BG
    - Venous plasma BG
    - Urea and electrolytes
    - Measured or calculated osmolality ($2Na^+$ + glucose + urea)
    - Venous blood gas
    - Blood ketones and lactate
    - Full blood count
    - Blood cultures
    - ECG
    - CXR
    - Urinalysis and culture
    - CRP (if indicated)
- Establish monitoring regime appropriate to patient – generally hourly blood glucose (BG), Na^+, K+, urea and calculated osmolality ($2Na^+$ + glucose + urea) for the first 6 hours then 2 hourly if response satisfactory (a fall of 3-8 mosmol/kg/hr).
    - Chart osmolality / glucose / sodium
    - Continuous pulse oximetry
    - Consider continuous cardiac monitoring
- Insert urinary catheter to monitor hourly urine output and calculate fluid balance.
- Ensure early senior review and/or inform specialist diabetes team
- Commence prophylactic LMWH
- Consider IV antibiotics if sepsis identified or suspected

B. 60 minutes to 6 hours

Aims

- To achieve a gradual decline in osmolality (3-8 mosmol/kg/hr)
    - Using 0.9% normal saline aim to give a further 0.5 – 1 L/hr depending on clinical assessment of dehydration / risk of precipitating heart failure and fluid balance (target is to achieve positive fluid balance of 2-3 L by 6 hours)
    - Measure glucose, urea and electrolytes hourly and calculate osmolality ($2Na^+$ + glucose + urea)
        - If plasma Na^+ increasing but osmolality declining at appropriate rate, continue 0.9% sodium chloride

        - If plasma Na^+ increasing AND osmolality increasing (or declining at less than 3 mosmol/kg/hr) check fluid balance. If positive balance inadequate increase rate of infusion of 0.9% sodium chloride
        - If osmolality increasing and fluid balance adequate, consider switching to 0.45% sodium chloride at same rate
        - If osmolality falling at rate exceeding 8 mosmol/kg/hr consider reducing infusion rate of IV fluids and/or insulin (if already commenced).
    - If blood glucose falling less than 5 mmol/L per hour check fluid balance.
        - If positive balance inadequate, increase rate of infusion of 0.9% sodium chloride
        - If positive fluid balance adequate, commence low dose IV insulin (0.05 units/kg/hr) or if already running, increase rate to 0.1 units/kg/hr
- To maintain potassium in the normal range
    - Hypokalaemia (less than 3.5 mmol/L) and hyperkalaemia (greater than 6 mmol/L) are life-threatening conditions and warrant senior review. They are less common in HHS than DKA but monitoring and replacement are essential

Potassium level in first 24 hr (mmol/L)	**Potassium replacement in infusion solution**
Over 5.5	Nil
3.5 - 5.5	40 mmol/L
Below 3.5	Senior review as additional potassium required

- Avoidance of hypoglycaemia
    - Aim to keep blood glucose 10-15 mmol/L in first 24 hours
    - If blood glucose falls below 14 mmol/L commence 5% or 10% glucose at 125 ml/hr AND CONTINUE 0.9% sodium chloride solution
- Monitor vital signs and chart Early Warning Score (EWS)
- Maintain accurate fluid balance chart (minimum urine output 0.5 ml/kg/hr)

C. 6 to 12 hours

The aim within this time period is to:

- Ensure that clinical and biochemical parameters are improving
    - o Continue charting blood glucose hourly; sodium and calculated osmolality 2 hourly
    - o Take appropriate action (as outlined in time 60 minutes to 6 hours) above
- Continue IV fluid replacement to achieve positive balance of 3-6 litres by 12 hours
    - o Maintain an accurate fluid balance chart
- Assess for complications of treatment e.g. fluid overload, cerebral oedema, extra pontine myelinolysis (e.g. deteriorating conscious level)
- Continue treatment of any underlying precipitant
    - o If patient not improving seek senior advice
- Avoid hypoglycaemia
    - o Aim to keep blood glucose 10-15 mmol/L in first 24 hours
    - o If blood glucose falls below 14 mmol/L commence 5% or 10% glucose at 125 ml/hr AND CONTINUE 0.9% sodium chloride solution
- Ensure referral has been made to diabetes team

D. 12 to 24 hours

Aim:

- Ensure continuing improvement of clinical and biochemical parameters
    - o Continue charting blood glucose hourly. Measurement of sodium and calculated osmolality can be reduced to 4 hourly if improvement maintained (if not continue 2 hourly)
    - o Do not expect biochemistry to have normalised by 24 hr (sodium and osmolality are likely to be raised)
    - o Take appropriate action (as outlined in time 60 minutes to 6 hours) as outlined above depending on results
- Continue IV fluid replacement to achieve remaining replacement of estimated fluid losses within next 12 hours – this will be dependent on factors such as initial degree of dehydration / body weight etc and MOST IMPORTANTLY the response to treatment so far. Therefore:
    - o Continue maintaining accurate fluid balance chart, plotting osmolality and make appropriate adjustments to fluid replacement rates
- Continue IV insulin with or without 5 or 10% glucose solution to maintain blood glucose 10-15 mmol/L
    - o Adjust insulin infusion rate hourly by 1 unit/hr increments or decrements to achieve desired BG
- Assess for complications of treatment e.g. fluid overload, cerebral oedema, extra pontine myelinolysis (e.g. deteriorating conscious level)
- Continue treatment of any underlying precipitant
    - o If patient not improving seek senior advice

E. 24 hours to Day 3

Expectation: patient should be steadily recovering, beginning to eat and drink, biochemistry back to normal.

- Ensure that clinical and biochemical parameters are improving or have normalised
    - o Continue IV fluids until eating and drinking normally
    - o Variable rate insulin if not eating and drinking
    - o Convert to appropriate subcutaneous regime when biochemically stable
    - o Encourage early mobilisation
    - o Daily urea and electrolytes
    - o Remove catheter when clinically appropriate
- Assess for signs of fluid overload or cerebral oedema
- Assess for evidence of continuing sepsis
- Daily foot checks
- Continue LMWH until day of discharge (consider extended treatment in very high risk patients)
- Ensure patient has been reviewed by diabetes team

After care

Most patients should go home on subcutaneous insulin (the regime being determined by their circumstances). For patients with previously undiagnosed diabetes or well controlled on oral agents, switching from insulin to the appropriate oral hypoglycaemic agent should be considered after a period of stability (weeks or months). Ensure patient has appropriate diabetes education prior to discharge and arrange follow-up by diabetes team.