Paediatric Management of Diabetic Ketoacidosis (DKA)
Guideline No: 13

IMMEDIATE ASSESSMENT

Clinical History
Polyuria / enuresis
Polydipsia
Weight loss (Weigh)
Abdominal pain
Tiredness
Vomiting
Confusion

Clinical Signs
Dehydration
Deep sighing respiration (Kussmaul)
Smell of ketones
Lethargy/drowsiness ± vomiting

Biochemical Signs
Ketones in urine
Elevated blood glucose (>11mmol/l)
Acidaemia (pH <7.3)
Take urgent blood for blood gases, glucose, electrolytes & urea
Other investigations as indicated

DIAGNOSIS CONFIRMED
DIABETIC KETOACIDOSIS
Contact Senior Staff

SHOCK
Reduced peripheral pulses
Reduced conscious level
Coma

Dehydration > 5%
Clinically acidotic (hyperventilation)
Not in shock
Vomiting

Clinically well
Tolerating fluid orally

Resuscitation
Airway ± NG tube
Breathing (100% O_2)
Circulation (Saline 0.9% 10-20 ml/kg) repeated until periph. circulation restored: max 3 doses

IV Therapy
Calculate fluid requirements
Correct over 48 hours
Saline 0.9%
ECG for elevated T-waves
If OK start KCl 40 mmol per litre

Therapy
Start with SC insulin
Continue oral hydration

No improvement

Low-dose continuous INSULIN INFUSION
0.1 unit / kg / hour

Critical Observations
Hourly blood glucose
Hourly fluid input & output
Neurological status at least hourly
Electrolytes 2 hourly after start of IV therapy
Monitor ECG for T-wave changes

Acidosis not improving

when blood glucose falls to 15 mmol/l
OR
Blood glucose falls > 5 mmol/hour

Neurological deterioration
WARNING SIGNS
headache, slowing heart rate, irritability, decreased conscious level, incontinence, specific Neurological signs

Re-evaluate
IV fluid calculations
Insulin delivery systems & consider more glucose & insulin
Need for additional resuscitation fluid
Consider sepsis

IV Therapy
Change to Saline 0.45% + Glucose 5%
Monitor BG & sodium
Adjust glucose, insulin & sodium infusion to maintain BG & promote rise in sodium

Clinically well & tolerating oral fluids

Transition to SC Insulin
Start SC Insulin as per protocol
Stop IV insulin 30 mins later

Exclude hypoglycaemia
Is it
CEREBRAL OEDEMA ?

Management
Move to CICU
Inform Paed Consultant On-call
Give Mannitol 1 g/kg or Hypertonic Saline 2-4 mls/kg
Restrict IV fluids by 1/3
Liaise with CICU Consultant re: intubation
Consider Cranial imaging **only** after patient stabilised

DIABETIC KETOACIDOSIS (DKA)

◊ Severe DKA is a grave illness and is the commonest cause of diabetes-related deaths in children and adolescents
◊ Most deaths in DKA occur in young people as a result of cerebral oedema
◊ Treatment is distinctly different from adults because of the threat of cerebral oedema
◊ Deaths should be avoidable by

(a) Reducing the incidence of DKA by
- earlier diagnosis at onset, immediate referral and urgent treatment
- appropriate management of diabetes during intercurrent illness
- recognition that recurrent DKA is often caused by insulin omission

(b) Optimal management of DKA.

1. No protocol for DKA has been shown to eliminate the risk of cerebral oedema and this guideline is based on internationally agreed Consensus Guidelines.
2. The Consultant on call must be informed of children with DKA
3. Drs Greening/Shenoy and Diabetes Specialist Nurses and Dietician like to be informed as soon as possible about all diabetic admissions

Definition

These DKA guidelines are recommended for children with

- Heavy glycosuria (> 55mmol/l) and ketonuria
- Hyperglycemia (BG >11 mmol/l)
- pH < 7.3
- Bicarbonate < 15 mmol/l and who are

5% or more dehydrated
± vomiting
± drowsy

NB Children less than 5% dehydrated and not clinically unwell (even with ketonuria) usually tolerate oral rehydration and subcutaneous insulin (see Protocol 15 a)

Children and adolescents who develop DKA as defined above should be managed either on CICU or Ward 11/12 where the nurses have experience of specialist treatment and where vital signs, neurological status and laboratory results can be monitored and evaluated frequently

Emergency assessment

Confirm the diagnosis

- Characteristic history – polydipsia, polyuria, nocturia, enuresis
- Biochemical confirmation – glycosuria, ketonuria, Blood Glucose (BG >11), pH <7.3 and Bicarbonate <15
- Clinical assessment – full examination

◊ Severity of dehydration
- 3 % just detectable
- 5 % dry mucous membranes, reduced skin turgor
- 8 % capillary return 3 seconds or more, sunken eyes
- 10 %+ shock, poor peripheral pulses

NB Clinical assessment of dehydration may be difficult especially in young children. Severity of dehydration is often overestimated.

◊ Evidence of moderately severe acidosis – hyperventilation, pH <7.2, HCO_3 <10
or severe acidosis – hyperventilation, pH <7.1, $HC0_3$ <5

◊ Assessment of conscious level, GCS score (and examine pupils & retinal fundi)

Glasgow Coma Scale						
	1	2	3	4	5	6
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Verbal	Makes no sounds	Incomprehensible sounds	Utters inappropriate words	Confused, disoriented	Oriented, converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli	Abnormal flexion to painful stimuli	Flexion / Withdrawal to painful stimuli	Localizes painful stimuli	Obeys Commands
Paediatric Glasgow Coma Scale						
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Verbal	No verbal response	Infant moans to pain	Infant cries to pain	Infant is irritable and continually cries	Infant coos or babbles (normal activity)	N/A
Motor	No motor response	Extension to pain	Abnormal flexion to pain for an infant	Infant withdraws from pain	Infant withdraws from touch	Infant moves spontaneously or purposefully

Consider admitting direct to CICU if there is
(a) severe acidosis pH<7.1 with marked hyperventilation
(b) severe dehydration with shock (see below)
(c) depressed sensorium with risk of aspiration from vomiting

Immediate investigations

- Weigh child whenever possible (or obtain recordings from recent OPD visits which gives a pre-morbid weight from which you can accurately calculate the % dehydration)
- Capillary BG (often inaccurate in the presence of poor peripheral circulation and severe acidosis when it under-reads)
- Capillary, venous or arterial blood gases
- Venous BG, electrolytes and urea, FBC (leucocytosis is a common feature of DKA), blood culture
- Please also take blood for HbA1c, thyroid function, thyroid antibodies, coeliac screen, GAD antibodies, Islet cell antibodies, and insulin antibodies if newly diagnosed.
- As indicated: urine culture, throat swab, chest X-ray.

Height measurement or estimation is of value if calculation of Body Surface Area is required. Retrospectively a fluid input of > 4 litre/m²/24h has been suggested as a risk factor in cerebral oedema

Resuscitation

Airway

- Ensure airway patent; in coma or severe vomiting - insert airway and drain stomach with NG tube

Breathing

- Oxygen 100% by face mask

Circulation

- Insert Cannula and take blood samples

  Normal Saline 0.9% 10ml/kg as a bolus usually over 10-15mins and may be repeated if still in shock to a total of 30 mls/kg (further resuscitation fluid may be required if peripheral pulses remain poor but additional rapid fluid input should be discussed with consultant).
  (There is no evidence to support the use of colloids or other volume expanders in preference to crystalloids)

- Attach ECG monitor to assess T-waves

NB: In most DKA protocols the fluid for resuscitation up to 20 mls/kg is not included in the calculations for later deficit dehydration

Fluid Replacement

To be commenced if resuscitation is not required or has been completed.
IV fluid administration alone results in substantial falls in blood glucose, ECF osmolality and improves GFR before insulin is given

The cause of CEREBRAL OEDEMA during treatment remains unclear. However, too rapid reduction in intravascular/extracellular osmolality may aggravate the process. It seems prudent therefore that rehydration should occur more slowly in children with DKA than in other causes of dehydration.

PROCEED WITH URGENCY BUT WITH CAUTION.

Fluid calculation

Requirements = Deficit + 48hr Maintenance

- Calculate DEFICIT = estimated % dehydration x body weight (kg) X 10 (amount in mls)
  (Not to exceed 10% in deficit calculation)
- Calculate MAINTENANCE as below

Age (years)	Weight (kg)	Maintenance Fluid (ml/kg/24 hrs)
<1	3 – 9	80
1 – 5	10 – 19	70
6 – 9	20 – 29	60
10 – 14	30 – 50	50
>15	>50	35

- Then add DEFICIT to 48 HOURS MAINTENANCE and replace this volume evenly over 48 hours as Normal Saline 0.9% initially

Example: 20 kg child 10% dehydrated.
Deficit = 10 x 20kg x10 = 2000mls
Maintenance = 20 x 60 = 1200 mls/24 or 2400 mls/48h
Total fluid steadily over 48 h = 2000 + 2400 = 4400 mls or 4400/48 = 91 mls per hour

These calculations will usually cover ongoing losses which in most cases do not need additional replacement but excessive continuing fluid losses in urine and /or vomiting might need replacing if the severity of dehydration is not improving

Potassium

◊ Total body potassium is always depleted in DKA (probably by 3-6mmol/kg)
◊ Initial serum potassium may be low, normal or high
◊ If serum potassium is not available before the completion of resuscitation, check ECG monitor to before potassium is added to the infusion fluid

- Potassium replacement should **not** be started until shock has been successfully reversed, the ECG does not show elevated T waves (or if serum potassium is not elevated) but is best commenced before the insulin infusion is started
- **Potassium chloride 40 mmol** is usually added to each litre of Saline infusion
  (Rate is approximately 3 mmol / kg / 24h)

Insulin

DKA is caused by insulin deficiency, either relative or absolute.

- Insulin should only be given when shock has been successfully reversed by emergency resuscitation and Saline/potassium rehydration regimen has already begun (this avoids sudden influx of potassium from plasma into cells with danger of cardiac arrhythmia). Commence 1-2 hours after starting fluid replacement therapy.
- **Insulin by continuous low-dose intravenous infusion is the optimal method**
  [There is evidence that bolus insulin is unnecessary, but may be used when treatment is very delayed]

- A solution of **Soluble (Actrapid) Insulin 1.0 unit / ml made up in Normal Saline** should be given by electronic syringe pump

(make up solution by drawing up 50mls Normal saline into a 50ml syringe and then injecting exactly 50 units of Actrapid insulin into the saline in the syringe, mix well and use syringe pump via extension tubing to 3-way tap and into the main infusion line)

- Recommended initial insulin dose = 0.1 units / kg / hour (to the nearest round figure)

BG monitoring and further IV infusion

During rehydration the typical rate of fall of BG is 4 –5 mmol / hour

- If the BG does not fall by at least 3mmol/l/hr over the first 4 hours of insulin administration, **increase the insulin infusion to** 0.125 units/kg/hr and increase to 0.15 units/kg/hr if the fall is less than 3mmol/hr in the subsequent 4 hours

- **When BG falls below 15 mmol/l or falls at more than 5 mmol/hr** change to a glucose solution namely **Half Normal Saline 0.45% + Glucose 5% infusion** to maintain BG in the desired range of 8 – 15 mmol/l
- From now on if the BG rises again above 15 mmol/l., increase insulin infusion by 0.025units/kg/hr (ie from 0.1u/kg/hr to 0.125u/kg/hr). Do not revert back to 0.9% Saline

If BG falls to < 8 mmol/l or falls more rapidly than 5 mmol/hr., increase the concentration of Glucose infusion to 10% with added Saline 0.45%*. If BG should then continue to fall at more than 5mmol/hr reduce insulin infusion by 0.025u/kg/hr, and again by 0.025u/kg/hr if BG is still <8 mmol/l, or still falling more than 5 mmol/l/hr.

NB only decrease the insulin infusion if acidosis improving with ph> 7.3, bicarbonate > 15mmol/l and serum ketones decreasing – otherwise discuss with consultant to increase glucose concentration to 12.5% - also re-evaluate fluid quantities.

(*this solution is supplied as special DKA fluid in glass bottles on the ward. If unavailable mix 250ml 20% glucose with 250ml N.Saline by withdrawing 250ml from each 500ml bag & mixing the residual amounts with each other)

Do not stop insulin infusion during the rehydration process because a continuous supply of both insulin and glucose substrate is needed to promote anabolism and reduce ketosis. The insulin infusion rate should only be decreased to less than 0.05 units/kg/hr if the BG level remains below 5 mmol/l despite glucose supplementation.

- If sufficient clinical and biochemical improvement occurs in the first 24 hours, the need for IV infusions should be reviewed with consideration of starting s/c insulin and oral fluids

Clinical observations and monitoring

Careful frequent documented clinical monitoring to detect warning signs of complications is of paramount importance

- Hourly pulse rate, respiratory rate, BP
  accurate fluid input and output (when level of consciousness is impaired a urinary catheter may be necessary). Test urine for glucose and ketones
- Hourly or more frequent neurological observations
- ECG monitoring may be helpful in the initial assessment of severe DKA for T-wave measurement
  (There is no evidence but it would seem logical after resuscitation to nurse patients with the head of the bed raised in an attempt to reduce CSF pressure)

Bicarbonate in DKA

There is evidence that BICARBONATE confers no clinical benefit and it may be unsafe in childhood onset DKA.
Acute resuscitation protocols no longer include bolus bicarbonate administration.
Fluid and insulin replacement without bicarbonate corrects ketoacidosis.

- Potential hazards of bicarbonate therapy
  - ◊ Exacerbation of CNS acidosis
  - ◊ Hypokalaemia and altered calcium ionisation
  - ◊ Excessive osmolar load
  - ◊ Tissue hypoxia
- Persistent acidosis is likely to be caused by inadequate resuscitation, inadequate insulin effect or sepsis. If you are sure the calculated volume of fluid replacement is correct, consider increasing insulin to 0.125 units/kg/hr. Bicarbonate should only be considered for treatment of impaired cardiac contractility in persistent severe shock but always discuss this with a member of the Consultant staff

  (If bicarbonate is considered, proceed with caution giving 1-2 mmol / kg bicarbonate over 60 minutes. A 4.2% Bicarbonate solution contains 0.5mmol / ml)

Oral fluids

- In severe dehydration, impaired consciousness & acidosis, only allow sips of cold water or ice to suck.
- Oral fluids (eg fruit juice/oral rehydration solution) should only be offered after substantial clinical improvement and no vomiting
- When good clinical improvement occurs before the 48hr rehydration calculations have been completed, oral intake may proceed and the need for IV infusions reduced to take account of the oral intake.
- If oral intake includes carbohydrate and the BG rises DO NOT stop the oral intake but increase the insulin infusion or insulin doses to improve anabolism and further reduce ketone production

Monitoring progress

Serum ketones – bedside with optium xeed

Ketones <0.6mmol/l = neg	Ketones 0.6 – 1.5mmol/l = mildly elevated
Ketones 1.5 – 3mmol/l = moderately elevated	Ketones >3mmol/l = severely elevated

Capillary blood glucose – monitored hourly (cross-checked 2 or 4 hourly against laboratory venous glucose because of the inaccuracies of capillary measurements in conditions of dehydration and acidosis) and should fall in a steady controlled manner

Laboratory tests - electrolytes, urea, blood glucose and blood gases should be repeated 2-4 hourly until acidosis is reversed

Sodium and Osmolality - despite the depletion of total body sodium in DKA, the elevated osmolality in the hyperglycaemic state results in a dilutional effect on the measured sodium (ie artefactual hyponatraemia exaggerated by hyper triglyceridaemia)

◊ Serum sodium often rises as the blood glucose falls. Theoretically sodium should rise by 2 mmol for every 5.5 mmol fall in BG, resulting in a slower fall in osmolality

A fall in serum sodium has been noted in a number of studies as one of the laboratory correlates of impending cerebral oedema

- If serum sodium fails to rise and particularly if it falls, a careful re-evaluation of the fluid replacement is required. Consider increasing the concentration of sodium chloride and observe with increased vigilance for signs of cerebral oedema (see later)
- An initial serum sodium >150 mmol/l might prompt slower rehydration rate than 48 hours

Potassium -The potassium infusion should be titrated to maintain serum potassium within the laboratory normal range

Urine output – if this is inadequate the cause must be sought (eg. acute renal failure, continuing shock, urinary obstruction, bladder retention). If fluid retention is occurring there is some evidence that a single dose of a loop diuretic might be helpful in promoting a water diuresis

Complications

Cerebral oedema

◊ Approximately 0.4-1% of children with DKA develop cerebral oedema with a high mortality/morbidity

◊ Cerebral oedema most commonly occurs in the first 24 hours, often secondary to vigorous rehydration. It is advisable to avoid more than 30 mls/kg fluid bolus. Vigilant observations throughout the 24 hours must not diminish

◊ In many cases warning signs/symptoms occur which should prompt the emergency administration of Mannitol

Warning signs/symptoms of cerebral oedema

- Headache & slowing of heart rate
- Change in neurological status (restlessness, irritability, increased drowsiness, incontinence) specific neurological signs (eg. cranial nerve palsies)
- Rising BP, decreased O_2 saturation

◊ More dramatic changes such as convulsions, papilloedema, respiratory arrest are late signs associated with extremely poor prognosis

Action – These children should be transferred to CICU as soon as possible for further management. Please inform the General Paediatric Consultant on call and CICU team

- Exclude hypoglycaemia
- If warning signs occur at any time day or night, give
  Immediate IV Mannitol 1 g/kg over 20 minutes (ie. 5ml / kg 20% solution) or 2-4 mls/kg of Hypertonic (3%) Sodium Chloride to maintain serum Na > 150 mmol/l
- Halve rehydration infusion rate until situation is improved but it is important to maintain insulin infusion to switch off ketotic process
- Nurse with child's head elevated
- Avoid intubation unless absolutely necessary. Decision for intubation and advice on optimal pCO2 levels if intubated should be discussed with CICU consultant. pCO2 should be kept >3.5kPa – very poor outcome associated when pCO2 falls <2.9kPa
- Consider continuation of Mannitol infusion 0.25 g/kg/hour to prevent rebound increase in intracranial pressure (or repeat bolus doses every 4-6 hours).
  Hypertonic 3% saline may be an alternative to mannitol
- Cranial imaging should only be considered after child has been stabilised. Intracranial events other than oedema may occur e.g.haemorrhage, thrombosis, infarction

Hypoglycaemia and hypokalaemia – avoid by careful monitoring and adjustment of infusion rates
Systemic Infections – Antibiotics are not given as a routine unless a severe bacterial infection is suspected
Aspiration pneumonia – avoid by nasogastric tube in vomiting child with impaired consciousness

Other associations with DKA require specific management e.g. continuing abdominal pain (due to liver swelling/gastritis/bladder retention but beware appendicitis), pneumothorax ± pneumomediastinum, interstitial pulmonary oedema, unusual infections (eg TB, fungal infections), hyperosmolar hyperglycaemic non - ketotic coma, ketosis in type 2 diabetes.

Transition to subcutaneous insulin injections

- Oral fluids should be introduced only when substantial clinical improvement has occurred (mild acidosis / ketosis may still be present)
- Insulin infusion may be continued with adjustments to cover carbohydrate intake. Do not restrict carbohydrate intake at this stage. If BG rises increase insulin infusion.
- Insulin by subcutaneous injection may be started when oral intake is tolerated
- Stop both the IV fluid and insulin infusion simultaneously 30 minutes after the first subcutaneous injection is given and child has had a meal.

Give their normal dose of subcutaneous insulin.
If newly diagnosed:
Weight < 30kg - 0.2 u/kg/dose Insulatard am, 0.1 u/kg/dose Insulatard pm
Weight > 30kg – 0.4 u/kg/dose Mixtard 30/70 am, 0.2 u/kg/dose Mixtard 30/70 pm
subcutaneously and let the child have a meal. Wait for 30 minutes and then stop the IV insulin and IV fluids simultaneously.

If the child is on multiple daily insulin regimen with once daily basal insulin (Glargine/Levemir) and Novorapid with meals, give normal dose of basal insulin and Novorapid with meal and stop the IV insulin and fluids simultaneously at this time. Instead if the normal dose of basal insulin is more than 8 hours away, give half the normal dose of basal insulin with regular dose of Novorapid.

Eg: If a child is normally on 20 units Glargine at 6pm, give 20 units Glargine and Novorapid with evening meal. If changing to subcut insulin at 8 am, give 10 units Glargine at 8 am and further 20 units at 6pm that evening.

- Do not be worried by continuing mild ketonuria or considerable fluctuations of glycaemia in the first day or two following DKA so long as the child is clinically improving or well. Adjustments of insulin dose can be made according the premeal BG levels with additional doses of quick or rapid acting insulin (see protocol 15 a & b)

Diet

- The dietitian will advise on this according to the child's usual food intake. In the recovery period the child's appetite is likely to be enormous. Do not restrict this. The child must however receive starchy carbohydrate food every 2-3 hours with emphasis given to bedtime snack to avoid nocturnal hypoglycaemia.

RECURRENT DKA

◊ Associated with inadequate insulin levels
◊ Commonly due to insulin omission

- In Leicester we try to teach parents and young people that they must treat severe hyperglycaemia with additional doses of rapid acting insulin (such as Novorapid) and in this way prevent progression to DKA especially during episodes of intercurrent infections (see protocol 15 b). Novorapid doses can be repeated every 2 hours in the event of persistent hyperglycaemia.
- Parents are given access to 24 hour emergency phone numbers for advice and treatment

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