Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

PAEDIATRICS

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

NATIONAL CLINICAL GUIDELINE

TITLE: Management of Paediatric Diabetic Ketoacidosis

Clinical Strategy and Programmes Office
Health Service Executive

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1.0 Aim of Guideline

The aim of this guideline is to provide clear and standardised guidelines for all staff caring for paediatric patients with type 1 diabetes in relation to the recognition and management of diabetic ketoacidosis.

2.0 Purpose and Scope

2.1 The purpose of this guideline is to improve the management of paediatric diabetic ketoacidosis (DKA). These DKA guidelines are intended for use in children with :

- Hyperglycaemia - plasma glucose > 11 mmol/L, glycosuria
- Ketonuria / ketosis (> 3 mmol/L)
- Acidosis - pH < 7.3, Std Bicarbonate < 18mmol/l
- > 5% dehydration
- ± vomiting
- ± drowsy

2.2 This guideline is intended for healthcare professionals, particularly those in training, who are working in HSE-funded paediatric and neonatal services. It is designed to guide clinical judgement but not replace it.

2.3 In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the child.

3.0 Background and Introduction

Severe DKA 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 risk of cerebral oedema. Prevention of DKA by earlier diagnosis at onset of diabetes, immediate referral and support for those challenged by diabetes self- care is the goal. Optimal management of established DKA is key to reducing morbidity and mortality.

4.0 Legislation/Other Related Policies

4.1 Model of Care for All Children and Young People with Type 1 Diabetes (2015)
http://www.hse.ie/eng/about/Who/clinical/natclinprog/paediatricsandneonatology/paedsmoc.pdf

5.0 Glossary of Terms and Definitions

DKA Diabetic ketoacidosis
GCS Glasgow Coma Scale
KCL Potassium Chloride
NaCL Sodium chloride

6.0 Roles & Responsibilities

6.1 This guideline should be reviewed by each hospital's senior management team to appropriately plan implementation. This will ensure that the inpatient care of children/neonates admitted to their facility is optimised irrespective of location**.**

6.2 Each unit requires clear arrangements that identify the resources and area where a child with DKA is safely managed. This should be communicated to all staff that care for paediatric patients.

7.0 Clinical Guideline

The goals of therapy in DKA are to:

- Correct acidosis and reverse ketosis
- Correct dehydration
- Restore blood glucose to near normal
- Monitor for complications of DKA and its treatment
- Identify and treat any precipitating event

7.1 General Resuscitation

7.1.1 **A**irway - ensure that airway is patent and secure airway if child is comatose. Pass N/G tube, on free drainage, if comatose or persistent vomiting.

7.1.2 **B**reathing - 100% Oxygen via face mask

7.1.3 **C**irculation - 2 large bore IV cannulae, take baseline bloods (see 7.2.3)

- If child is volume depleted but not shocked, give 10mls/kg 0.9% saline over 30 mins (as a bolus)
- Reassess capillary refill time and heart rate
- +/- repeat bolus 10mls/kg 0.9% saline
- Senior input is required if considering need for a third bolus of 10mls/kg 0.9% saline

(See appendix 2)

Remember - children can die from DKA. Always discuss these children with the Consultant Paediatrician/Consultant Paediatric Endocrinologist on call. Paediatric Endocrinology should also be consulted for management advice for a child with hyperosmolar, non-ketotic acidosis.

7.2 Confirm Diagnosis

7.2.1 ***History****:* polydipsia, polyuria, weight loss, vomiting, abdominal pain, drowsiness, hyperventilation (note what fluids the child has been drinking as if large volumes of very sweet fluids (e.g. sugar-sweetened beverage) have been consumed, initial glucose may be very high and may fall rapidly once insulin is commenced)

7.2.2 ***Clinical assessment (needs to be reviewed at regular intervals):*** acidotic respirations, dehydration, drowsiness (record GCS), focus of infection, ileus. DKA does not cause pyrexia. If febrile, look for underlying infection (e.g. urinalysis, CXR, blood cultures etc).

7.2.3 ***Bloods***

7.2.3.1 Venous glucose (>11mmol/L),

7.2.3.2 Fingerprick (point of care) ketones (Use and Interpretation of blood ketone testing Appendix 1)

7.2.3.3 Venous Gas (pH <7.3)

7.2.3.4 Electrolytes (closely monitor potassium, corrected sodium and renal function)

7.2.3.5 FBC (neutrophilia is common as component of stress response).

7.2.3.6 Calculate corrected sodium and effective osmolality (see 7.9)

7.2.3.7 If a new patient, send samples for:

- *HbA1c* (1.2ml EDTA),
- *TFT* (1.2ml serum) and *anti-TPO* (1.2ml serum),
- *anti-GAD, ZnT8* and *anti-IA2 antibodies* (1.2ml serum to Exeter),
- IgA and TTG (1.2 mls serum)

7.2.4 ***Urine***

7.2.4.1 Urinalysis – check for ketones

7.3 Initial Management

7.3.1 **Check weight: It is almost always possible to measure weight of the child in DKA and is much safer for calculating fluid/insulin requirements.**
If not possible (child is unconscious), use recent clinic weight or estimated weight from centile chart. Actual weight should be confirmed as soon as possible.
APLS calculation (weight in kg = 2 (age+4) is valid for pre-pubertal children; Note APLS now provide weight charts and are generally available in Resuscitation areas.

7.3.2 **Record consciousness level** (Use GCS).

7.3.3 **Assess degree of dehydration** - overestimation of dehydration is dangerous. Do not use more than 8% dehydration in calculations.

% Dehydration	Clinical Features
Mild (3%)	Only just clinically detectable
Moderate (5%)	Dry mucous membranes, reduced skin turgor
Severe (8%)	Above, with sunken eyes and poor capillary return.
+SHOCK	May be severely ill with poor perfusion, thready rapid pulse (hypotension is unlikely and a VERY late sign)

7.3.4 **ECG Monitor** (T wave changes). Children require continuous cardiorespiratory monitoring until acidosis is corrected

7.3.5 **Consider ICU admission** if severe DKA (pH< 7.1, hyperventilation, shock, depressed level of consciousness, persistent vomiting, age< 2 years) or if staffing on ward is insufficient to allow adequate monitoring.

7.3.6 **Physical examination** look for evidence of cerebral oedema, infection or Ileus

7.4 Fluid Management

7.4.1 At this stage, circulating volume should have been restored (see Resuscitation 7.1)

7.4.2 Once circulating volume is restored:

Requirements = Maintenance + Deficit

7.4.3 Calculate Maintenance fluids: see table (Neonates generally requires higher fluid rates 100-150ml/kg/day and this is not included in table)

Weight (kg)	Maintenance fluid (ml/kg/24h)
<12.9	80
13-19.9	65
20-34.9	55
35-59.9	45
>60	35

7.4.4 Calculate Deficit (litres) =

% dehydration (Use % for calculations maximum of 8%) **X** Body weight (kg)

Note that 1kg = 1000ml for calculations.

Worked Example
20kg child with 5% dehydration 20 x 0.05 =1 kg = 1000ml deficit

7.4.5 Add 48 hour Maintenance to Deficit and subtract any initial emergency rehydration that may have been administered (e.g. 10ml/kg boluses)

7.4.6 Give total volume evenly over 48 hours.

Worked Example		
25 kg 6year old boy who is 10% dehydrated who has received fluid bolus of 0.9% NaCl 10ml/Kg in E.D		
Maintenance	55ml X 25kg = 1375ml (over 24hrs)	2750ml (over 48h)
Plus		
Deficit	0.08 (max is 8%) X 25kg = 2 (litres)	2000ml
Subtract		
Resuscitation Bolus		-250ml
Total Fluids Required over 48 hours		4500ml
Rate ml per hour		93.7 ml/hr

7.5 Fluid type

7.5.1 Normal saline (0.9%) with 20 mmol KCl/500ml is recommended initial fluid type and fluids may be adjusted depending on patients hydration status, sodium and osmolality. Dextrose may be added to the normal saline as required (see 7.5.4-7.5.5).

7.5.2 Potassium should be added once passing urine or renal profile result confirms not hyperkalaemic.* see also 7.6.1 below.

7.5.3 Aim for gradual decrease in plasma glucose of 4-5mmol/L per hour

7.5.4 **If** blood glucose is dropping at >5mmol/L per hour
OR blood glucose 14 – 17mmol/L**, add 5% dextrose to the 0.9% saline**

Increase dextrose concentration in fluids to 7.5% if:
blood glucose continues to fall at >5mmol/L per hour
OR* blood glucose *is less than 8mmol/L

Increase dextrose concentration in fluids to 10%, if:
blood glucose continues to fall >5mmol/L per hour
OR is less than 8mmol/L

7.5.5 **If blood glucose continues to drop when patient is maintained on 0.9% saline and 10% dextrose, consider reducing insulin infusion rate (see 7.7.5). This normally will not occur until ketones have cleared**

7.5.6 Excessive continuing ongoing losses might need to be replaced if the severity of dehydration is not improving after review and discussion with Consultant Paediatrician/Endocrinologist

7.5.7 **Oral fluids** – Keep nil po. Re-introduce oral fluids gradually after substantial clinical improvement and correction of acidosis and subtract from total fluid required (IV calculations)

7.6 Potassium:

7.6.1 Total body Potassium is always depleted in DKA although initial serum potassium levels may be low, normal or elevated. Potassium levels will fall once insulin is commenced.

7.6.2 Commence Potassium supplements 20mmol KCL per 500 ml of fluid as soon as initial resuscitation is completed (unless anuria is suspected or peaked T-waves on ECG)

7.6.3 Monitor electrolytes 2 hourly twice after start of resuscitation and then 2-4 hourly until DKA corrected and adjust K replacement accordingly

7.6.4 Continue ECG monitoring during resuscitation

7.7 Insulin

7.7.1 Insulin therapy should not be commenced until shock (if present) has been reversed by resuscitation, and should be deferred until iv fluids have been running for 1hour.

7.7.2 Continuous low dose insulin infusion is the optimal method: * Generally dose of 0.1 iu/kg/hour is recommended but consideration can be given to low dose (0.05 iu/kg/hour in toddlers (see controversy 2 below)

Insulin Infusion
• Add 50 units of Actrapid to 49.5 ml normal saline (concentration of 1 unit per ml) deliver via a syringe pump • Connect via a Y connector to the fluids already running. • Run the infusion at 0.1 iu / kg / hour (0.1ml/kg/hr)* • Continue until pH >7.3 (** Appendix 2)

7.7.3 When glucose level 14-17mmol/L continue insulin at 0.1 i.u./kg/hr and commence (if not already running) dextrose containing rehydration fluids (as 7.5.4)

7.7.4 Increase the dextrose concentration (in steps up to 10%-7.5.4) before reducing insulin dose while acidosis correcting.

7.7.5 If glucose level continues to fall rapidly or level is below 8mmol/L when dextrose 10% has been added to normal saline, decrease insulin to 0.05 i.u./kg/hr. Do not stop insulin infusion (until sc insulin commenced)

7.7.6 Continue insulin infusion until child drinking and eating normally. Discontinue insulin infusion 30 minutes after first subcutaneous injection to allow time for the subcutaneous insulin to start working and avoiding rebound hyperglycaemia

If biochemical parameters do not improve, reassess and review fully (sepsis, other diagnosis, errors in insulin preparation, tissued iv line) and restart protocol.

7.8 Bicarbonate

7.8.1 There is no evidence that bicarbonate is either necessary or safe in the management of DKA. It may exacerbate CNS acidosis, tissue hypoxia and osmolar load. Its only purpose is to improve cardiac contractility in severe shock. Persistent acidosis usually reflects insufficient resuscitation, inadequate insulin or sepsis

7.8.2 Bicarbonate should only be considered if pH <6.9 and/or impaired cardiac contractility after discussion with senior medical staff

7.9 Sodium and Osmolality

7.9.1 A rapid fall in effective plasma osmolality and/or fall in sodium during therapy may be associated with cerebral oedema**.**

7.9.2 Where effective plasma osmolality is elevated in DKA, aim for slow correction over 24 hours (by 8 mmol/L/24h)

Effective plasma osmolality = 2X (Na^+ + K^+) + Glucose

7.9.3 Hyperglycaemia causes falsely low plasma sodium levels. Sodium should rise by 2mmol/l for every 5.5mmol/l fall in glucose and corrected sodium should be followed on a flow sheet.

7.9.4 Corrected Sodium can be calculated using link http://www.strs.nhs.uk/resources/pdf/guidelines/correctedNA.pdf

Corrected Na
Measured Na^+ + (2 X (glucose - 5.5)) / 5.5

7.9.5 If serum sodium fails to rise, and in particular if it falls during therapy, a careful re-evaluation of the fluid replacement is required. Consider slowing rate of rehydration, increasing sodium concentration and increase vigilance for signs of cerebral oedema.

7.9.6 An initial serum Na of >150mmol/L might prompt an even slower rehydration rate than 48 hours

7.10 Monitoring during therapy

Continuous	• ECG monitoring
½ Hourly	• neurological observations, including level of consciousness (using the modified Glasgow coma score) and heart rate, in children under the age of 2 • or in children and young people with a pH less than 7.1, because they are at increased risk of cerebral oedema
1 hourly	• Vital signs (or more frequently as indicated) • Neuro observations (escalate immediately headache, change in conscious level or behaviour) • Blood glucose and blood ketone measurements
2 hourly*	• Electrolytes (x2) (and calculate corrected sodium)/VBG/ lab glucose until acidosis reversed • Review fluid composition and rate following each result • May be able to check 4 hourly after substantial clinical improvement
Accurate	• Documentation of fluid input and output.
Twice Daily	• Weights

7.11 Additional Considerations for the Severely Unwell Child in ICU

7.11.1 Consider anticoagulant prophylaxis particularly in children with femoral lines

7.11.2 Urinary catheterisation should be avoided but may be required in the child with impaired consciousness. If urine output is inadequate (<1.5mls/kg/hr), the cause must be sought (e.g. acute renal failure, ongoing shock, bladder outflow obstruction).

7.11.3 If fluid retention is occurring, there is some evidence that a single dose of a loop diuretic is helpful in promoting water diuresis.

7.11.4 If a massive diuresis continues, fluid intake may need to be increased.

7.11.5 If large volume of gastric aspirates continue, these may need to be replaced with 0.45% saline plus 10mmols KCl

7.11.6 If acidosis is not correcting, resuscitation may have been inadequate-consider (in conjunction with senior medical staff) giving a further bolus of normal saline (10mls/kg)

7.12 Cerebral Oedema

THIS IS A LIFE-THREATENING EMERGENCY

The cause of cerebral oedema during therapy of DKA remains unclear. The results of a recent randomised controlled trial demonstrated that neither the rate nor the sodium chloride content of intravenous fluids significantly influenced neurologic outcomes in children presenting in DKA (please see Appendix 2 controversies for further details).

Early insulin administration (in the first hour of fluid management of DKA) has been shown to increase the risk of cerebral oedema so it is recommended that children receive fluids only in the first hour of treatment.

- Incidence 0.5-0.9% episodes of D.K.A. with 21-24 % mortality.
- Most commonly occurs in first 24 hours, usually 4-12 hours after treatment begins but may occur at 24-48 hours.
- More likely in younger children, first presentation, severe dehydration, more acidotic and longer duration of symptoms
- Pathophysiology of cerebral oedema in DKA is still poorly understood but epidemiological studies show greater risk when children are treated with insulin in the first hour of treatment
- Treat as such if any suspicion

When managing children at high risk of cerebral oedema (low CO2, low pH, very high urea) mannitol dose should be calculated, drawn up and left at bedside.

7.12.1 ***Warning Signs/Symptoms***

7.12.1.1 Headache and slowing of heart rate

7.12.1.2 Change in neurological status (restlessness, irritability, increased drowsiness, incontinence (in a previously continent child) or specific neurological signs (e.g. cranial nerve palsies)

7.12.1.3 Rising BP, decreased O2 saturations

7.12.1.4 Late signs such as seizures, papilloedema and respiratory arrest are associated with a very poor prognosis

7.12.2 ***Management***

7.12.2.1 Contact Consultant Paediatrician/Endocrinologist and Anaesthetist immediately

7.12.2.2 Exclude hypoglycaemia as a cause of neurological deterioration

7.12.2.3 Mannitol (20%) **or** Hypertonic Saline (2.7% or 3%) need to be given as soon as possible
Mannitol 20% - 2.5-5ml/kg over 10-15 mins (0.5-1g/kg) or
Hypertonic Saline – 2.5-5 ml/kg over 10-15min

7.12.2.4 A repeated dose of mannitol may be required after 2 hours if no response

7.12.2.5 Reduce maintenance fluid infusion rate by one third **and** also recalculate rehydration to deliver over 72 hours (instead of 48 hours)

7.12.2.6 Nurse at 45 degree angle

7.12.2.7 Transfer to PICU/ICU (if not there already) and consider need for transfer to tertiary PICU and consider need for ventilation (Note that aggressive hyperventilation to pCO_2 <2.9kPa/22mmHg is associated with poorer outcome)

7.12.2.8 Consider either - Mannitol infusion - 0.25gm/kg/hr or Mannitol 20% - 1gm/kg every 6 hours

7.12.2.9 Consider imaging and Neurosurgical consult. CT/MRI is indicated (as other intracerebral pathology e.g. cerebral venous thrombosis, may occur and present in the same way)

8.0 Implementation, revision and audit

8.1 Distribution to the CEO of each Hospital Group for dissemination through line management in all acute hospitals within their group.

8.2 Implementation through Senior Management Teams of each acute hospital.

8.3 Distribution to other interested parties and professional bodies

8.4 The NCPPN Diabetes Working group has agreed that this guideline will be reviewed on a 3 yearly basis.

8.5 Regular audit of implementation and impact of this guideline through outcome and process measures is recommended to support continuous quality improvement. It is the responsibility of each unit providing care for children with diabetes and intercurrent illness to audit the unit practise regularly in order to ensure that care in being provided in line with guidelines and that any deviations are clinically justified. The audit process should be coordinated in each paediatric unit under local paediatric clinical governance and should be taken from a multidisciplinary perspective where appropriate. Where the audit identifies areas for practise improvement, it is the responsibility of each individual unit to implement changes and re-audit to support continuous quality improvement.

9.0 References

Wolfsdorf J, Glaser N et al. (2018). 'ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state.' *Pediatric Diabetes*. 2018 Oct;19 Suppl 27:155-177. doi: 10.1111/pedi.12701.

10.0 Qualifying Statement

10.1 These guidelines have been prepared to promote and facilitate standardisation and consistency of practice.

10.2 Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each child.

10.3 Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

10.4 This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with the child, parents/guardians and in an environment that is appropriate and which enables respectful confidential discussion.
- Advising children, parents/guardians of their choices and ensure informed consent is obtained.
- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.

11.0 Appendices

11.1 Appendix One

Blood Ketone strips measure Beta-hydroxybutyrate levels which account for 75-80% of circulating ketones in DKA are superior and recommended in DKA management; urine ketones measure acetone which is produced in relatively small quantities in DKA.

Urine levels lag some hours behind blood levels.

While the tests are measuring different ketones, the following may be useful:

Blood	Urine
<0.6 mmol/L	**Negative**
0.6-0.9 mmol/L	**Trace**
0.9-1.4 mmol/L	**Small**
1.5-2.4 mmol/L	**Moderate**
≥2.5 mmol/L	**Large**

11.2 Appendix 2 Controversies

Fluids in DKA: Outcome of RCT (2018)

A recent randomized control trial (conducted in 1289 episodes of DKA managed in a 13 paediatric centre network) examined the effects of the rate of administration and the sodium chloride content of IV fluids on neurologic outcomes in children with DKA. DKA episodes included had blood glucose level >16.7 mmol/l and either pH <7.25 or serum bicarbonate <15 mmol/l and presented with essentially intact neurological status (GCS >14). Mean age was 11.6 ± 4 years and all children were > 3 years of age. Children were randomly assigned to one of four groups (0.9% or 0.45% sodium chloride content and rapid or slow rate of administration). No significant differences were observed in GCS score, short term memory testing or clinically apparent brain injury in the 4 groups. While this study is very reassuring that rehydration rate and fluid type does not significantly affect cerebral oedema risk, the caveats are that no toddlers were included in this study and all children had GCS > 14 at recruitment. We therefore recommend maintaining a judicious approach to fluid management in DKA as above.

Kuppermann N, Ghetti S, et al, (2018). 'Clinical Trial of Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis.' *The New England Journal of Medicine*, 2018 Jun 14;378(24):2275-2287. doi: 10.1056/NEJMoa1716816

Increased insulin sensitivity of younger children:

A single study suggested that younger children with DKA are more insulin sensitive and therefore consideration can be given to reducing insulin infusion rate to 0.05 iu/kg/hour in this cohort.

Nallasamy K, Jayashree M, et al. (2014) 'Low-dose vs standard-dose insulin in pediatric diabetic ketoacidosis: a randomized clinical trial'. *JAMA Pediatrics.* 2014;168(11):999-1005. doi:10.1001/jamapediatrics.2014.1211

11.3 Appendix 3

Acknowledgements

This guideline has been developed by the National Clinical Programme for Paediatrics and Neonatology Diabetes Working Group. The members of this group include medical, nursing and dietetic representatives from paediatric diabetes services. The Diabetes Working Group also wish to thank those who provided input and feedback on draft versions of this guideline throughout development, and those who provided valuable input during the consultation process.

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11.4 Appendix 4

Sign Off

Sign off by Paediatric Diabetes Working Group	December 2018
Sign off by Paediatric Clinical Advisory Group	
Sign off by HSE CSPD Senior Management Team	