PAEDIATRIC AND ADOLESCENT DIABETIC KETOACIDOSIS (DKA) MANAGEMENT GUIDELINES

These guidelines were developed by the New Zealand National clinical network for child and youth diabetes, 2014, and are based on BSPED Endorsed Guidelines by Julie A Edge, Oxford, November 2013

IMPORTANT NOTE: This guideline contains links to a fluid calculator. If you download this calculator for use, it will be a copy only and is valid for that <u>single usage only</u>. Each time you use the calculator, you must download it from the website to ensure that you are using the most up-to-date version.

Background

Diabetic Ketoacidosis (DKA) is an endocrine emergency occurring in new onset and established type 1 diabetic patients due to decreased circulating insulin, insulin resistance and increased counter-regulatory hormones. Management in children highlights the rare but devastating occurrence of cerebral oedema and the over-use of fluid boluses that may/may not be associated with this. Management of DKA in children and adolescents should not follow adult DKA guidelines.

The diagnosis of DKA is based on clinical suspicion followed by biochemical confirmation:

- Diabetes: Hyperglycaemia (blood glucose >11 mmol/L)
- Acidosis : Metabolic acidosis (pH <7.3, Bicarbonate <15 mmol/L)
- Ketosis: Ketonuria and/or ketonaemia

The severity of DKA is categorized by the degree of acidosis (ISPAD definition ²):

| •Mild: | pH <7.3 and/or bicarbonate <15 mmol/L $$ |
|------------|--|
| •Moderate: | pH <7.2 and/or bicarbonate <10 mmol/L |
| •Severe: | pH <7.1 and/or bicarbonate <5 mmol/L |

Life-threatening complications of DKA include:

- Cerebral oedema
- Acute hypokalaemia
- Acute hypoglycaemia (during treatment or as a result of excessive insulin prior)
- Aspiration pneumonia

Key Points

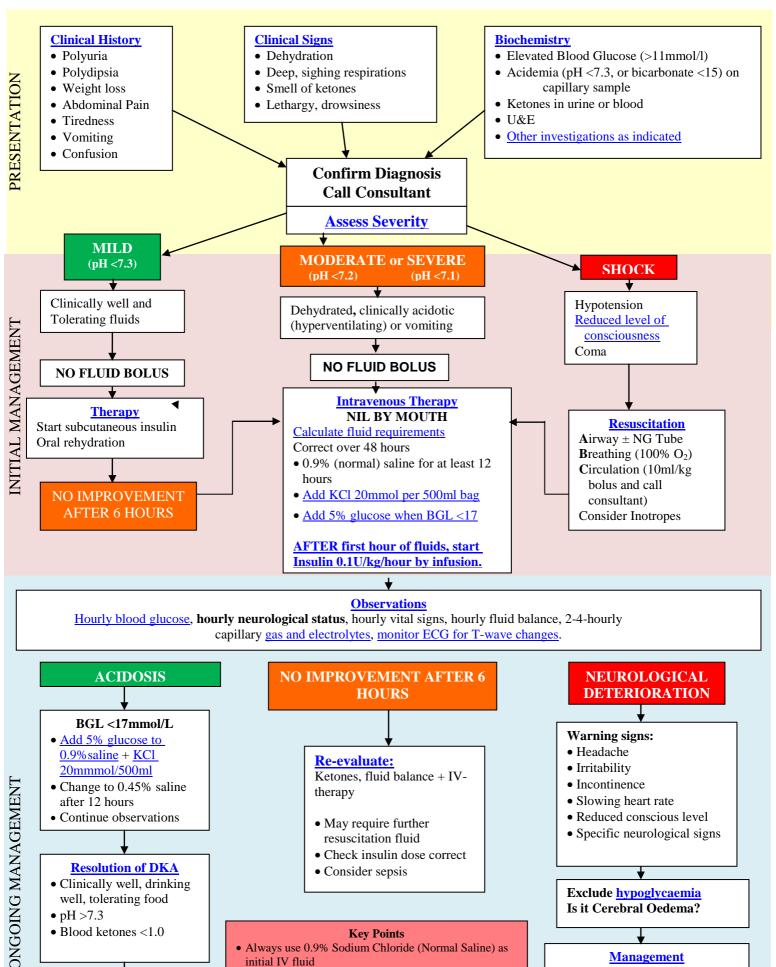
- 1. Always use 0.9% Sodium Chloride (Normal Saline) as initial IV fluid
- 2. Add KCL 20mmol/500mls to all rehydration fluids
- 3. Most (>90%) of patients do NOT need fluid boluses
- 4. Never bolus insulin IV: use low dose IV infusions
- 5. Start insulin infusion 1-2 hours <u>AFTER</u> starting fluid replacement therapy
- 6. Call Paediatrician / Paediatric Endocrinologist for advice early

These GUIDELINES <u>cannot</u> replace careful clinical observation and judgment in treating this potentially fatal condition.

CONTACT NUMBERS:

Outside Auckland: the on-call paediatrician must be contacted via operator Auckland: The Starship Endocrine consultant on call must be contacted via ADHB operator

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• Consider sepsis

initial IV fluid

replacement therapy

advice early

Key Points

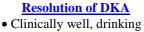
• Add KCL 20mmol/500mls to all rehydration fluids

• Most (>90%) of patients do NOT need fluid boluses

• Start insulin infusion 1-2 hours AFTER starting fluid

• Never bolus insulin IV: use low dose IV infusions

• Call Paediatrician / Paediatric Endocrinologist for



- well, tolerating food • pH >7.3
- Blood ketones <1.0
- Start subcutaneous insulin
- Stop intravenous insulin and fluid after an appropriate interval

Exclude hypoglycaemia Is it Cerebral Oedema?

• Always use 0.9% Sodium Chloride (Normal Saline) as

- Management • Call senior staff
- 3% saline 5 ml/kg/dose OR Mannitol 0.5-1.0g/kg/dose
- Restrict I.V. fluids by 1/2
- Move to PICU/ICU
- Cranial imaging when stabilised

Management

A. Initial Resuscitation (A, B, C):

If possible, weigh the patient and use this weight for all calculations. Alternatively, use recent clinic weight or an estimated weight from centile chart.

- **A.** Ensure airway is patent. Insert airway if child is comatose (<u>Glasgow Coma Scale Score ≤8</u>). If reduced level of consciousness or vomiting insert NGT, aspirate and leave on free drainage.
- **B.** 100% Oxygen by face mask
- C. Insert IV cannula and take blood samples (section C)

Only if shocked (poor peripheral pulses, poor capillary filling with tachycardia, and/or hypotension give 10 ml/kg 0.9% (normal) saline as a bolus. Repeat fluid bolus ONLY if signs of shock remain, and ONLY after discussion with Paediatrician / Paediatric Endocrinologist

Minimum acceptable systolic BP (PICU Guidelines 2009 Shann, F.):

| Age | 6m | 1 | 2 | 4 | 6 | 8 | 10 | 12 | 14 | 16 | 18 |
|-----|----|------|----|---|----|----|----|----|----|----|----|
| BP | 65 | [/() | 15 | | 75 | 80 | 80 | 85 | 90 | 95 | 95 |

B. Confirm Diagnosis

| History | Polydipsia, polyuria |
|-------------|--|
| Clinical | Acidotic (Kussmaul) respiration Dehydration Drowsiness |
| | Abdominal pain/vomiting |
| Biochemical | High blood glucose (>11 mmol/l) Blood pH<7.3 and/or HCO3 <15 mmol/l Glucose and ketones in urine |

C. Initial Investigations

Venous blood gas Blood glucose and ketones Urea and electrolytes (electrolytes on blood gas machine give a guide until accurate results available)

If new onset diabetes – Hba1C, Anti-GAD and anti-IA2 antibodies, TFTS, Coeliac Antibodies, Lipid profile during admission

+ Other investigations only if indicated:

• If infection suspected – consider Full blood count (leucocytosis is common in DKA and does not necessarily indicate sepsis), CXR, CSF, throat swab, blood culture, urine culture and sensitivity etc.

D. Full Clinical Assessment and Observations

Assess and record in the notes, so that comparisons can be made by others later.

1. Degree of Dehydration –

| Mild, <5% | is only just clinically detectable |
|---------------|---|
| Moderate, =5% | dry mucous membranes, reduced skin turgor, |
| Severe, shock | above with sunken eyes, poor capillary return, thready rapid pulse (reduced blood pressure is not likely and is a very late sign) |

Over-estimation of degree of dehydration is common and dangerous. Do not use more than 8% dehydration in calculations without discussing with on-call Paediatric Endocrinologist /Paediatrician^{-6,7}

2. Conscious Level -

Institute hourly neurological observations (including <u>Glasgow Coma Score</u>) whether or not the child is drowsy on admission.

If in coma on admission, or there is any subsequent deterioration,

- Consider transfer to PICU/HDU if available
- Coma is directly related to degree of acidosis, but signs of raised intracranial pressure suggest cerebral oedema
- Consider instituting cerebral oedema management (if high level of suspicion, start treatment prior to transfer)

3. Full Examination - looking particularly for evidence of -

- <u>Cerebral oedema</u>: headache, irritability, slowing pulse, rising blood pressure, reducing conscious level (papilloedema is a late sign).
- Infection
- Ileus

4. Consider ICU/PICU or HDU for the following, and discuss with ICU/ PICU consultant.

- Severe acidosis (ph<7.1) with marked hyperventilation
- Severe dehydration with shock
- Depressed level of consciousness with risk of aspiration from vomiting
- Very young (under 2 years)
- Staffing levels on the wards are insufficient to allow adequate monitoring

Patients in HDU or PICU should have ECG monitoring, which should also be considered for those not in HDU. Consider NG tube.

Where no PICU/HDU facilities are available, transfer to another hospital may not be required unless ventilatory support becomes necessary. However, ALL children with DKA are high-dependency patients and require a high level of nursing care, usually 1:1 even if on general paediatric wards

5. Observations to be carried out by senior nursing staff

- Strict fluid balance with hourly measurement of fluid input and output (urinary catheterisation may be required in young/sick children)
- Hourly capillary blood glucose measurements plus bedside <u>blood ketone testing</u> (if not available -Urine testing for ketones)
- Hourly (or more frequent) blood pressure, heart rate and respiratory rate
- Hourly (or more frequent) neurological observations looking for warning signs of cerebral oedema

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- Reporting immediately to the medical staff, even at night, symptoms of headache, or slowing of pulse rate, or any change in either conscious level or behaviour
- Reporting any changes in the ECG trace, especially T wave changes suggesting hyper- or hypokalaemia

E. Fluid Therapy

Document all fluids carefully, including fluids given in the Emergency Department and on the way to the ward.

1. Volume of fluids

Calculate maintenance fluid rate + deficit, correct over 48hrs (see fluid calculator or <u>appendix</u>). If there is hypernatraemia (<u>corrected Na</u> >150mmols/L) or hyperosmolality (<u>osmolality</u> >310mosmol/L) then consider correcting deficit over 72 hours.

2. Type of fluids

- 0.9% (normal) saline with 20 mmol KCl/500 ml (40mmol/L). Run at the calculated rate for 1 hour <u>before</u> commencing insulin.
- Continue this sodium concentration for at least 6h hours, ideally 12 hours.
- Subsequent replacement fluid should be 0.45% saline with added 20mmol KCL/500ml
- Once the blood glucose has fallen to $<17 \text{ mmol/l}^2$, add glucose to the fluid (See fluid calculator).

Formula for 5% glucose solution with electrolytes:

Withdraw 50ml 0.9% or 0.45% sodium chloride/KCl from 500ml bag and discard. Add 50ml of 50% glucose to the bag. This makes a solution which is approximately 5% glucose with 0.9% or 0.45% saline (+KCl).

- If the plasma sodium is falling, continue with 0.9% saline (with or without glucose depending on blood glucose levels) and consider reducing the fluid rate.
- Check urea and electrolytes two hours after resuscitation began and then <u>at least</u> 4 hourly (electrolytes on blood gas machine can be helpful for trends)

3. Oral Fluids

- Nil by mouth unless mild DKA being managed with oral fluids and subcutaneous insulin. An N/G tube may be necessary in the case of gastric paresis.
- When good clinical improvement occurs before the 48hr rehydration period is completed, oral intake may proceed and IV infusion rate reduced accordingly. Most patients are able to be switched to subcutaneous insulin injections at this time (see Section F)

4. Potassium

- Once the child has been resuscitated, potassium should be added immediately to rehydration fluid unless anuria is suspected. Discuss with Consultant if K⁺>6mmol/L or in acute renal failure.
- Potassium is mainly an intracellular ion, and there is <u>always</u> massive depletion of total body potassium although initial plasma levels may be low, normal or even high. Levels in the blood will fall once insulin is commenced.
- Ensure that every 500 ml bag of fluid contains 20 mmol KCl (40 mmol per litre). More is occasionally required.
- **Hypokalaemia**. Use a cardiac monitor and observe frequently for T wave changes. If serum K+ falls below 3.0mmol/L, the first warning sign could be flattening of T waves on ECG monitor. Give KCl 0.5mmols/kg/hr for 4 hours and reassess.

5. Insulin Management

DO NOT start insulin until intravenous fluid has been running for at least an hour.

Once rehydration fluids and potassium are running, blood glucose levels will start to fall. There is some evidence that cerebral oedema is more likely if insulin is started early.

Add 50 units of regular (Actrapid or Humulin R) or analog (Novorapid, Humalog) insulin to 49.5ml of 0.9% saline. This will make a 1 unit/ml solution. Label carefully. It can last for 24 hours.

Start infusion at 0.1 unit/kg/hr unless otherwise directed (consider starting insulin at 0.05U/kg/hr in the very young).

- Once the blood glucose level falls to <17mmol/l change the fluid to contain 5% glucose (generally 0.9% saline with 5% glucose and potassium 20mmol/500ml). **DO NOT** reduce the insulin infusion rate. The insulin dose needs to be maintained at 0.1 units/kg/hour to switch off ketogenesis.
- Consider adding glucose earlier if the initial rate of fall of blood glucose is greater than 5-8 mmol/l per hour, or if the patient is very hyperosmolar, to help protect against cerebral oedema. Discuss with the on call Paediatrician/Paediatric Endocrinologist.
- Target Blood Glucose: aiming for blood glucose range of 8-10mmol/L is safest when managing DKA, rather than trying to normalise.
- Hypoglycaemia (BGL<4mmol). DO NOT stop the insulin infusion while glucose is being infused, as insulin is required to switch off ketone production. Give a bolus of 2 ml/kg of 10% glucose and increase the glucose concentration of the infusion (to a maximum of 10%). See Fluid Calculator for making glucose solutions of various concentrations. Insulin can temporarily be reduced for 1 hour.
- If the blood glucose rises out of control, or the pH level is not improving after 4-6 hours consult senior medical staff and re-evaluate (possible sepsis, insulin errors or other conditions), and consider starting the whole protocol again.
- For children on continuous subcutaneous insulin infusion (CSII) pump therapy, stop the pump when starting DKA treatment.

5a. Insulin Management in Mild DKA

- For mild DKA with good oral intake, insulin may be initiated sub-cutaneously. Refer to local policy for initiating insulin or see <u>appendix</u>
- These patients are insulin resistant and may need increased insulin doses
- Patient may eat and drink, but consider IV fluids if significantly hyperglycaemic (>30mmol/L)
- Consider a sliding scale for additional rapid acting Analog insulin to be given every 4 hours PRN overnight for BGLs >15mmol/L (0.1-0.15u/kg/dose)
- Check BGL and blood gas after 2 hours then 4 hourly
- Check TPR and neurological observations hourly (see <u>D.5</u>)
- If there is any clinical deterioration or acidosis is not correcting see <u>section F</u> and consider IV fluids and Insulin Infusion as per the algorithm

6. Sodium Bicarbonate.

Rarely, if ever, necessary. Continuing acidosis usually means insufficient resuscitation or insufficient insulin. Bicarbonate should only be considered in children who are profoundly acidotic (pH < 6.9) and shocked with circulatory failure. Its only purpose is to improve cardiac contractility in severe shock. It should only be considered in discussion with a Paediatric Endocrinologist/PICU Specialist.

7. Phosphate

There is always depletion of phosphate, another predominantly intracellular ion. Plasma levels may be very low. There is no evidence in adults or children that replacement has any clinical benefit and phosphate administration may lead to hypocalcaemia.

8. Anti-coagulant prophylaxis

There is a significant risk of femoral vein thrombosis in young and very sick children with DKA who have femoral lines inserted. Discuss with Paediatrician or Paediatric Endocrinologist on call. See PICU guidelines for dosage.

F. Continuing Management

- Urinary catheterisation should be avoided but may be useful in the child with impaired consciousness.
- Documentation of fluid balance is vital. All urine needs to be measured accurately (and tested for ketones <u>if blood ketones</u> are not being monitored). All fluid input must be recorded (even oral fluids).
- If a massive diuresis continues, fluid input may need to be increased. If large volumes of gastric aspirate continue, these will need to be replaced with 0.45% saline with KCl.
- Check biochemistry, blood pH, and laboratory blood glucose 2 hours after the start of resuscitation, and then at least 4 hourly. Review the fluid composition and rate according to each set of electrolyte results.

1. If acidosis is not correcting, check blood ketones

- Ketones not falling
 - Insufficient insulin to switch off ketones
 - Check infusion lines, calculation and dose of insulin
 - Consider giving more insulin.
- Ketones falling
 - O Inadequate resuscitation (fluid input)
 - 0 Sepsis
 - Hyperchloraemic acidosis
 - Salicylate or other prescription or recreational drugs

2. Insulin Management once Ketoacidosis has resolved

- Continue with IV therapy until the child is drinking well and able to tolerate food.
- Only change to subcutaneous insulin once pH >7.25 and bicarbonate >16mmol/L and glucose is <15mmol/l.
- This may occur before 48 hours of treatment; there is no need to wait for complete metabolic normalisation.
- At the next breakfast or dinner mealtime stop the IV fluids
- Stop the insulin infusion after the first subcutaneous injection
- The child can eat and drink normally.
- Subcutaneous insulin should be started according to local protocols for the child with newly diagnosed diabetes (see appendix), or the child should be started back onto their usual insulin regimen at an appropriate time (discuss with Paediatrician/Paediatric Endocrinologist).

G. Cerebral Oedema

- This is unpredictable, occurs more frequently in younger children and newly diagnosed diabetes and has a mortality of around 25%.
- The causes are not known, but this protocol aims to minimise the risk by producing a slow correction of the metabolic abnormalities.

The signs and symptoms of cerebral oedema include:

- Headache & slowing of heart rate (>20 bpm not related to sleep or initial resuscitation)
- Change in neurological status (restlessness, irritability, increased drowsiness, incontinence)
- Specific neurological signs (e.g. cranial nerve palsies)
- Rising BP (diastolic BP >90mmHg), decreased O2 saturation
- Abnormal posturing

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

Management:

If cerebral oedema is suspected inform Paediatrician/Paediatric Endocrinologist immediately.

The following measures should be taken immediately while arranging transfer to PICU:

- Exclude hypoglycaemia as a possible cause of any behaviour change
- Give hypertonic (3%) saline (5mls/kg over 5-10 mins) OR Mannitol 0.5 1.0 g/kg (2.5 5 ml/kg Mannitol 20% over 20 minutes). This needs to be given as soon as possible if warning signs occur (e.g. headache or pulse slowing).
- Restrict IV fluids to 1/2 maintenance and recalculate to replace deficit over 72 rather than 48 hours
- The child will need to be moved to PICU (or ICU if outside Auckland and discuss with Paediatric Endocrinologist and/or Starship PICU Specialist)
- Discuss with PICU consultant. Do not intubate and ventilate until an experienced doctor is available
- Once the child is stable, exclude other diagnoses by CT scan other intracerebral events may occur (thrombosis, haemorrhage or infarction) and present similarly
- A repeated dose of Mannitol OR Hypertonic Saline may be required after 2 hours if no response
- Document all events (with dates and times) very carefully in medical records

Other associations with DKA require specific management:

Continuing abdominal pain is common and may be due to liver swelling, gastritis, bladder retention, and ileus. However, beware of appendicitis and ask for a surgical opinion once DKA is stable. A raised amylase is common in DKA.

Other problems are pneumothorax \pm pneumo-mediastinum, interstitial pulmonary oedema, Unusual infections (e.g. TB, fungal infections), hyperosmolar hyperglycaemic non-ketotic coma, Ketosis in type 2 diabetes.

Discuss these with the consultant on-call.

Appendix

- 1. Emergency contact details for Starship Paediatric Endocrinologist: ADHB operator
- 2. Na+ (corrected) = Na+ (measured) + [0.3x (glucose-5.5)]
- 3. Osmolality = (2x Na) +glucose
- 4. Formulae for making dextrose solutions: (or see Fluid Calculator)
 - a) 0.45% saline with 2.5% dextrose:
 - Add 25mls 50% dextrose to 500ml bag of 0.45% saline
 - b) 0.45% saline with 5% dextrose:
 - Add 50ml 50% dextrose to 500ml bag of 0.45% saline
 - c) 0.45% saline with 10% dextrose:
 - Add 100ml 50% dextrose to 500ml bag of 0.45% saline
- 5. Bedside blood ketone interpretation:
 - a) <1.0 negative to trace ketonaemia
 - b) 1.0-1.4 mild ketonaemia
 - c) 1.5-2.9 moderate ketonaemia
 - d) ≥ 3.0 high ketonamia
- 6. Starting subcutaneous insulin in newly diagnosed child with diabetes (or see local protocols):
 - a) Using twice daily intermediate /short acting regime

| Age | Dose Range (use higher dose for mild DKA) |
|--------------------|---|
| Pre-pubertal child | 0.5 - 1.2 units/kg/day |
| Pubertal child | 0.7 - 1.5 units/kg/day |

2/3 total daily dose pre-breakfast 1/3 total daily dose pre-dinner

2/3 intermediate acting (Protophane); 1/3 short acting (Actrapid or Novorapid) at each dose

e.g. 18kg 5yo (TDD 0.5units/kg/day =9u) Pre-breakfast = 2/3 x 9units = 6units (2u Actrapid, 4u Protophane) Pre-dinner = 1/3 x 9u = 3u (1u Novorapid, 2u Protophane)

b) Using MDI (Multiple daily injections):

| Age | Dose Range (use higher dose for mild DKA) | | | | | |
|--------------------|---|--|--|--|--|--|
| Pre-pubertal child | 0.5-1.2 units/kg/day | | | | | |
| Pubertal child | 0.7-1.5 units/kg day | | | | | |

50% Basal insulin (Glargine)50% Novorapid or Humalog in three divided doses (breakfast, lunch and dinner)

E.g. 40kg 13yo (TDD 1.2 units/kg/day= 48 units) Pre- breakfast = 0.5 x 48 units = Lantus 24u Pre meals = (0.5 x 48)/3 = Novorapid 8u, 7u, 9u (If not easily split equally give dinner most, and then breakfast, then lunch)

| Weight | Mild | Mod | Sev | Weight | Mild | Mod | Sev | Weight | Mild | Mod | Sev |
|--------|------|-----|-----|--------|------|-----|-----|--------|------|-----|-----|
| (kg) | 3% | 5% | 8% | (kg) | 3% | 5% | 8% | (kg) | 3% | 5% | 8% |
| 5 | 23 | 25 | 28 | 20 | 73 | 81 | 93 | 38 | 102 | 118 | 141 |
| 7 | 32 | 35 | 40 | 22 | 76 | 85 | 99 | 40 | 105 | 122 | 147 |
| 8 | 37 | 40 | 45 | 24 | 79 | 89 | 104 | 42 | 108 | 126 | 152 |
| 10 | 46 | 50 | 57 | 26 | 82 | 93 | 109 | 44 | 112 | 130 | 157 |
| 12 | 52 | 57 | 64 | 28 | 86 | 97 | 115 | 46 | 115 | 134 | 163 |
| 14 | 57 | 63 | 71 | 30 | 89 | 101 | 120 | 48 | 118 | 138 | 168 |
| 16 | 62 | 69 | 79 | 32 | 92 | 105 | 125 | 50 | 121 | 142 | 173 |
| 18 | 67 | 75 | 86 | 34 | 95 | 109 | 131 | 52 | 125 | 146 | 179 |

7. <u>Guide / check of fluid administration</u> (including deficit and maintenance) Hourly rate to be given over 48hr according to degree of dehydration. This does not account for fluid boluses given.

Table adapted from the Royal Children's Hospital (Melbourne) Clinical Practice Guidelines for Diabetes Mellitus

8. Glasgow Coma Scale

Best Motor Response

- 1 = none
- 2 = extensor response to pain
- 3 = abnormal flexion to pain
- 4 = withdraws from pain
- 5 = localises pain
- 6 =responds to commands

Eye Opening

- 1 = none
- 2 = to pain
- 3 =to speech
- 4 =spontaneous

Best Verbal Response

- 1 = none
- 2 = incomprehensible sounds
- 3 = inappropriate words
- 4 = appropriate words but confused
- 5 = fully orientated

Modification of verbal response score for younger children:

- 2-5 years < 2 years
- 1 = none1 = none
- 2 = grunts2 = grunts
- 3 = cries or screams
- 4 = monosyllables
- 5 = words of any sort
- 3 = inappropriate crying or unstimulated screaming 4 = cries only
- 5 = appropriate non-verbal responses (coos, smiles, cries)

Maximum score 15, minimum score 3

References:

- 1. BSPED recommended DKA Guidelines 2013, Julie A Edge
- 2. Global IDF/ISPAD Guideline for Diabetes in Childhood and Adolescence 2011
- 3. Diabetic ketoacidosis in children and adolescents with diabetes. Pediatric Diabetes 2009: 10(Suppl. 12): 118–133
- 4. Paediatric Society of New Zealand Working Group, National guidelines for the management of moderate to severe diabetic ketoacidosis (DKA) in children and young people, 2005.
- 5. Australasian Paediatric Endocrine Group, Clinical Practice Guidelines: Type I diabetes in children and adolescents, March 2005
- 6. Fagan, M et al. Initial fluid resuscitation for patients with diabetic ketoacidosis: how dry are they? Clin Pediatr (Phila). 2008 Nov; 47(9):851-5. Epub 2008 Jul 14
- 7. Ugale, J et al. Measured degree of dehydration in children and adolescents with type 1 diabetic ketoacidosis. Pediatr Crit Care Med. 2012 Mar; 13(2):e103-7.

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Revision Date: April 2016