Diabetic Ketoacidosis (DKA)

History and Clinical signs

- Polyuria continuing despite dehydration
- Polydipsia
- Weight loss
- Nausea and frequent vomiting (which may be mistaken for gastroenteritis)
- Abdominal pain (mimicking acute abdomen)
- Weakness, lethargy
- Tachypnea (which may be mistaken for pneumonia)
- Rapid deep sighing respiration (Kussmaul respiration)
- Smell of acetone
- Disordered sensorium (Disoriented, drowsy, rarely comatose)
- Fever (only when infection is present)

Risk Factors for DKA

- Poor metabolic control in known diabetes mellitus (DM)
- History of previous DKA, non-compliance
- Peripubertal and adolescent
- Children with limited medical services
- Acute decompensating with DKA has been recognized at the time of diagnosis in 25% of T2DM, should suspect in overweight/ obese children with risk factor like history of T2DM in first or second degree relative, signs of insulin resistance

Biochemical Features

- Hyperglycaemia >11 mmol/L (~200 mg/dL)
- Venous pH <7.3 or bicarbonate <15 mmol/l
- Ketonemia and ketonuria

Initial Laboratory Tests

- Serum glucose, Hb A_1C
- Urea & electrolytes including bicarbonate, creatinine
- Full blood count, PCV
- Blood β hydroxyl butyrate (if available)
- Blood gas (if available)
- Infection screen (if indicated) blood culture, urine culture, CXR, CSF, throat swab
- Urine ketone
- ECG

Additional Calculation (From ISPAD Guideline, 2014)

- Anion gap = $Na-(CI+HCO_3)$
  - Normal 12 ± 2 mmol/L
  - In DKA typically anion gap is 20-30 mmol/L, if >30 mmol/L suggests concomitant lactic acidosis
- Corrected Na (mmol/L) = $\frac{\text{Measured Na} + 2(\text{Plasma glucose} - 5.6)}{5.6}$
- Effective osmolality(mmol/L) = 2(Na) + Glucose

Management

Emergency assessment

- Weigh the child
- Assess the severity of dehydration (See the table)
- Assess the level of conscious (GCS)

Emergency management

Airway

- Ensure the airway is patent and if the child is comatose, insert an oropharyngeal airway
- If consciousness reduced or child has recurrent vomiting insert N/G tube, aspirate and leave on open drainage

Breathing - Give 100% 0, to child with shock

Circulation - Insert IV cannula and take blood samples

- For patients who are severely volume depleted but not in shock, volume expansion (resuscitation) should begin immediately with 0.9% saline to restore the peripheral circulation. The volume administered typically is 10-20ml/kg over 1-2 hr
- Only if shocked (poor peripheral pulses, poor capillary filling with tachycardia, and/or hypotension), give 10 ml/kg 0.9% (normal saline) as bolus and repeat if necessary, to give maximum 30 ml/kg

Cardiac monitor should be used for continuous ECG monitoring to access T waves for evidence of hyper or hypokalaemia

Deficit replacement fluid calculation

$$\text{Deficit [ml)} = \%\ \text{Dehydration x Body weight (Kg) x 10}$$

$$\text{Requirement} = \text{Maintainence} + \text{Deficit fluid} - \text{fluid already given}$$

$$\text{Hourly rate} = \frac{(\text{48 Hour maintainene} + \text{defcit}) - \text{Resuscitation fluid already given}}{48}$$

Table 14.1 Degree of Dehydration

Mild	3%	Is only just clinically detectable
Moderate	5%	Dry mucous membranes, reduced skin turgor
Severe	8%	Above with sunken eyes, poor capillary return
+Shock		May be severely ill with poor perfusion, thready and rapid pulse (reduced blood pressure is not likely and it's a very late sign)
Overestimation of degree of dehydration is dangerous; therefore do not use more than 8% dehydration in calculation		

Maintenance Requirement

Weight

0-12.9 kg	80 ml/kg /24 Hr
13-19.9 kg	65 ml/kg/24 Hr
20-34.9 kg	55 ml/kg/24 Hr
35-59.9 kg	45 ml/kg/24 Hr
Adult >60 kg	35 ml/kg/24 Hr

Neonatal DKA will require special consideration and larger volumes of fluid than those quoted may be required, usually 100-150 ml/kg/24 Hr

Sample calculation

If BW 14 kg and 8% dehydration, resuscitation fluid 10 ml/kg

The maintenance	910 mlx2 (For 48 hours) = 1820 ml
Dehydration	8x14x10 = 1120mml
Total	2940-140+48 = 58 ml/hr for 48 Hr

Type of Fluid

- *Initially* use 0.9% saline with 20 mmol KCL in 500 ml and continue this Sodium concentration for 12 hours

Blood Glucose (BG) has fallen to 14 mmol/L

- Before 12 hour, add 5% glucose to 0.9% Saline (5 % Dextrose saline) + 20 mmol KCL
- After 12 hour, change to 0,45% saline + 5 % dextrose + 20 mmol KCL
- if plasma sodium is falling, continue with normal saline (with or without glucose depending on blood glucose levels)
- Corrected sodium levels should rise as blood glucose levels fall during treatment.

- If they do not, then continue with normal saline and do not change to 0.45%saline. *(Na should rise by 0.5 mmol/L for each 1 mmol/l decrease in glucose concentration)*

Electrolytes on blood gas machine (if available) can helpful for trends whilst awaiting laboratory results.

Insulin therapy

- Do not start insulin until intravenous fluids has been running for at least one hour
- Once rehydration fluids and K* are running, blood glucose levels will start to fall
- Continuous low-dose-insulin infusion is preferred method, there is no need for an initial bolus

Dose - 0.1 unit/kg/hr (Consider 0.05 units/kg/hr if <5 yr)

Preparation

- Add 50 units (0.5 ml) of soluble insulin to 50 ml of 0.9% normal saline to make 1 unit = 1 ml solution and run 0.1 unit/kg/hr = 0.1 ml/kg/hr
- Draw up 50 units soluble insulin and add to a 500 ml bag of 0.9% normal saline, the resulting concentration of insulin infusion is 1 unit of insulin per 10ml of 0.9 % normal saline, prime the drip set by flushing 50 ml of the solution containing the insulin, Insulin binds to the plastic tubing, then the rate is 0.1unit/kg/hr = 1 ml/kg/hr
- ***Do not add insulin directedly to rehydration fluid, it's important to label clearly to avoid confusion with the rehydration fluid***

Aim optimal rate of decrease of BG is 2-5 mmol/L/hr (Should not exceed more than 5 mmol/L/hr)

If BG level fall to 14 mmol/L

- Change the fluid to contain 5% glucose, do not reduce insulin
- Insulin dose needs to be maintained to switch off ketogenesis

If BG level fall to 4 mmol/L

- Give bolus of 2 ml/kg of 10% Glucose and increase glucose concentration (10% Glucose with 0.45% Saline with 20 mmol/L of Potassium)
- Insulin can temporarily be reduced for 1 hour

Subcutaneous insulin

- In circumstances where continuous IV administration is not possible, hourly or 2 hourly SC or IM administration of short or rapid acting insulin is safe and may be effective as IV regular insulin injection, ***but should not use in subjects whose peripheral circulation is impaired*.**
- Initial dose SC0.3 units/kg, followed 1 hour later by SC 0.1 unit/kg every hour or 0.15-0.2 units/kg every two hours
- If BG falls to <14 mmol/L (250 mg/dL) before DKA has resolved, add 5%Glucose and continue with insulin as above

When to review

- If biochemical parameters of DKA (pH, anion gap) do not improve, reassess the patient, review insulin therapy, and consider the delivery problem of insulin, dose of insulin, errors in preparations, adhesion insulin to the tubing with very dilute solution and other cause of impaired response (sepsis).
- For the child who are already on long acting insulin (especially Glargin) continue at usual dose and time throughout the DKA treatment, in addition to the IV insulin infusion, in order to shorten the length of stay after recover from DKA

Potassium

- Once the child has been resuscitated potassium should be commenced immediately with rehydration fluid unless anuria is suspected
- Levels in the blood will fall once insulin is commended
- Dose-Add 20 mmol of KCL to 500 ml fluid

Monitoring

- Hourly vital signs
- Hourly blood glucose
- Hourly fluid input and output
- Neurological status at least hourly–GCS, warning signs of cerebral edema
- Electrolyte two hour after starting of intravenous therapy, then should check 4 hourly for the first 12 hour of intravenous therapy
- Urine ketones until cleared, if available every two hourly
- Monitor ECG for T wave changes

- Body weight measure twice a day
- Check amount of administered insulin

Complication of Therapy

- Inadequate rehydration
- Hypoglycemia
- Hypokalemia
- Hyperchloemic acidosis
- Cerebral edema

Cerebral oedema

Warning signs and symptoms of cerebral edema

- Headache and slowing of HR
- Change in neurological status (restlessness, irritability, increased drowsiness, incontinence)
- Specific neurological signs (e.g. Cranical nerve palsies)
- Rising BP
- Decreased SpO_2

Risk factor for cerebral oedema

- Younger age
- New onset of diabetes mellitus
- Longer duration of symptoms
- Severe acidosis
- Increased blood urea nitrogen (BUN)
- Bicarbonate treatment
- Administration of insulin in first hour of fluid treatment
- Greater volume of fluid bolus >30 ml/kg
- Attenuated rise in measured serum sodium during therapy

Treatment of cerebral edema (exclude hypoglycaemia)

- Initiate treatment as soon as the condition is suspected
- Reduced the rate of fluid administration by one third
- Give IV Manitol 0.5-1 g/kg (7-10 ml/kg) over 20 minutes and repeat if there is no initial response in 30 minutes to 2 hours
- Hypertonic saline 3% (5-10 ml/kg over 30 min), may be alterative to mannitol or second line therapy if there is no initial response to mannitol
- Elevate the head of bed
- Intubation may be necessary for the patient with impending respiratory failure, but aggressive hyperventilation (PCO_2 <2.9 kPa (22 mmHg)) has been associated with poor outcome and is not recommended
- After treatment of cerebral edema has been started, a cranial CT scan should obtain to rule out other possible intra cerebral causes of neurologic deterioration, especially thrombosis or hemorrhage, which may benefit from specific therapy.
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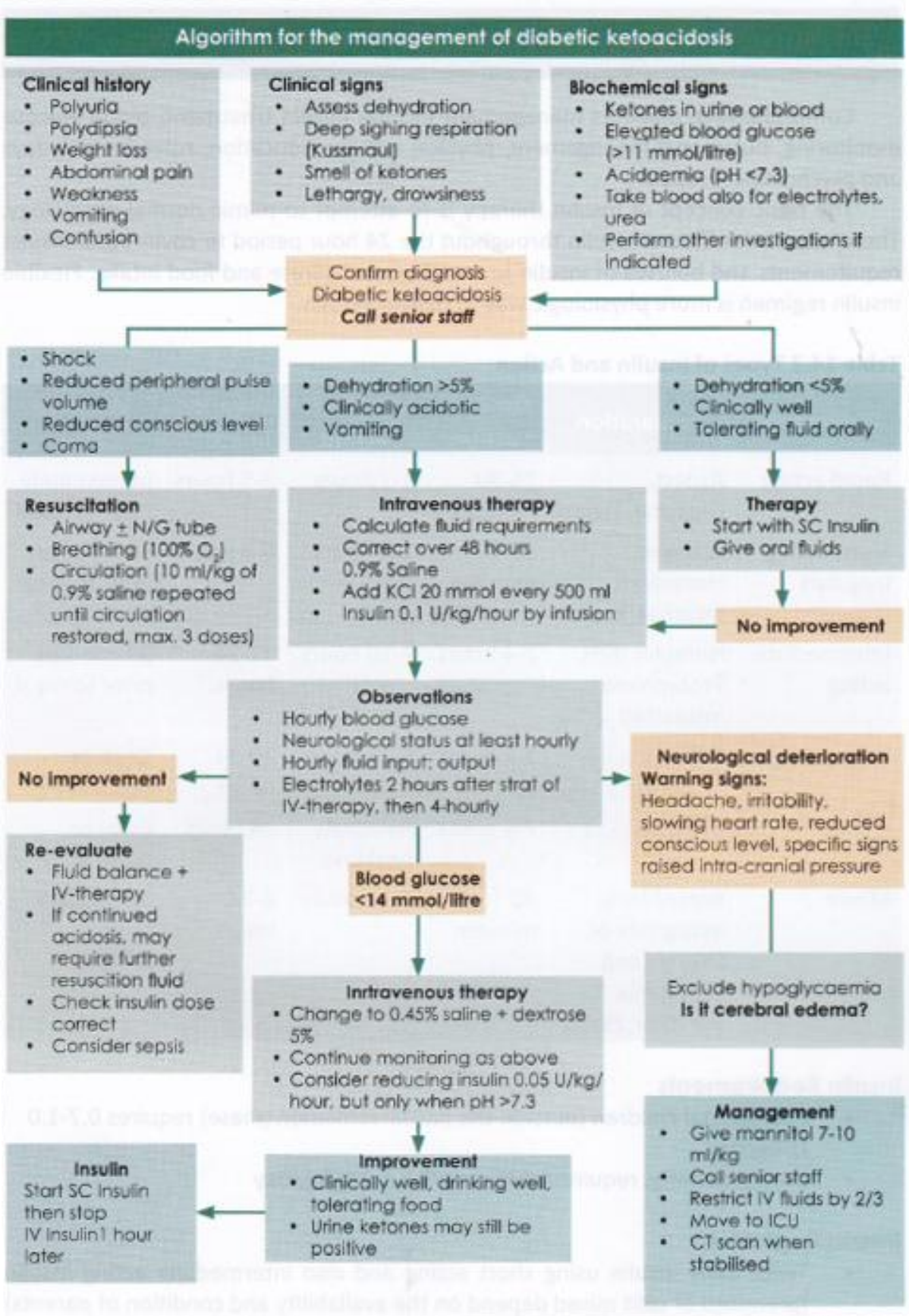
Introduction of Oral Fluid and Transition to SC insulin Injections

- Oral fluid should be introduced only when substantial clinical improvement has occurred (mild acidosis/ketosis may still be present)
- When oral fluid is tolerated, IV fluid should be reduced
- When ketoacidosis has resolved, oral intake is tolerated, and to change SC insulin as planned, the most convenient time to change to SC insulin is just before a mealtime
- To prevent rebound hyperglycemia, the first SC injection should be given 15-30 minutes (with rapid-acting insulin) or 1-2 hours (with regular insulin) before stopping the insulin infusion to allow sufficient time for the insulin to be absorbed


Algorithm for the management of diabetic ketoacidosis
Clinical history
Polyuria
Polydipsia
Weight loss
Abdominal pain
Weakness
Vomiting
Confusion
Clinical signs
Assess dehydration
Deep sighing respiration (Kussmaul)
Smell of ketones
Lethargy, drowsiness
Biochemical signs
Ketones in urine or blood
Elevated blood glucose (>11 mmol/litre)
Acidaemia (pH <7.3)
Take blood also for electrolytes, urea
Perform other investigations if indicated
Confirm diagnosis
Diabetic ketoacidosis
Call senior staff
Shock
Reduced peripheral pulse volume
Reduced conscious level
Coma
Dehydration >5%
Clinically acidotic
Vomiting
Dehydration <5%
Clinically well
Tolerating fluid orally
Resuscitation
Airway ± N/G tube
Breathing (100% O2)
Circulation (10 ml/kg of 0.9% saline repeated until circulation restored, max. 3 doses)
Intravenous therapy
Calculate fluid requirements
Correct over 48 hours
0.9% Saline
Add KCl 20 mmol every 500 ml
Insulin 0.1 U/kg/hour by infusion
Therapy
Start with SC Insulin
Give oral fluids
No improvement
Observations
Hourly blood glucose
Neurological status at least hourly
Hourly fluid input: output
Electrolytes 2 hours after strat of IV-therapy, then 4-hourly
No improvement
Re-evaluate
Fluid balance + IV-therapy
If continued acidosis, may require further resuscition fluid
Check insulin dose correct
Consider sepsis
Neurological deterioration
Warning signs:
Headache, irritability, slowing heart rate, reduced conscious level, specific signs raised intra-cranial pressure
Blood glucose <14 mmol/litre
Inrtravenous therapy
Change to 0.45% saline + dextrose 5%
Continue monitoring as above
Consider reducing insulin 0.05 U/kg/hour, but only when pH >7.3
Exclude hypoglycaemia
Is it cerebral edema?
Management
Give mannitol 7-10 ml/kg
Call senior staff
Restrict IV fluids by 2/3
Move to ICU
CT scan when stabilised
Improvement
Clinically well, drinking well, tolerating food
Urine ketones may still be positive
Insulin
Start SC insulin then stop IV insulin1 hour later