BIMDG
British Inherited Metabolic Disease Group

LIPIN 1 DEFICIENCY – ACUTE ILLNESS

IMMEDIATE ACTION

- **Triage to high priority**
- **Do not delay: the potassium concentration can rise rapidly & cause fatal arrhythmias**
- **Check electrolytes & monitor ECG**
- **Give IV methylprednisolone 1-2mg/kg immediately**
- **Give IV 10% Glucose/0.9% Sodium Chloride, initially at 5ml/kg/hr**
- **Monitor urine output & increase rate of fluids if >0.5ml/kg/hr after 2-4 hours**
- **Seek advice early from the child's specialist metabolic team ± intensivist & nephrologist**

1. Background

- Lipin 1 deficiency causes episodes of severe rhabdomyolysis (acute skeletal muscle necrosis) in young children, usually triggered by infections.
- Symptoms may include vomiting and muscle aches or stiffness.
- **Potassium is released from muscle and its plasma concentration can rise rapidly to very high levels, leading to cardiac arrest with VT or VF**. This precedes myoglobinuria.
- Steroids reduce mortality and parents are instructed to give prednisolone before coming to hospital; IV methylprednisolone should be started on arrival.

2. Assessment in hospital

Put on a cardiac monitor.
Check weight & vital signs.
Review the history & examine the child briefly.
Obtain IV access and **check electrolytes immediately (e.g. on a blood gas sample).**
If the potassium is above 5 mmol/L, call for help & start urgent management (section 4).

The following urgent tests should also be done:

BLOOD	Urea & electrolytes, Bone chemistry, Mg Liver function tests CK pH and blood gases Glucose Full blood count
ECG	Features of hyperkalaemia include peaked T waves, prolonged PR interval, widened QRS, loss of P wave and ultimately a sine wave appearance.

3. Management
Admit to PICU or HDU if possible.

a) Methylprednisolone
Give IV Methylprednisolone 1-2mg/kg daily for the first 3 days.

b) Intravenous fluids
If hypoglycaemic, give glucose 200 mg/kg at once (2 ml/kg of 10% glucose or 1ml/kg of 20% glucose) over a few minutes.

If shocked or obviously dehydrated (>7% weight loss), give 10-20 ml/kg 0.9% saline, with a further 10ml/kg subsequently if necessary.

Then start 10% glucose with 0.9% saline, initially at 5ml/kg/hr.

- If this is not immediately available, use 10% glucose with 0.45% saline, 5% glucose with 0.9% saline or 5% glucose with 0.45% saline.
- Potassium must not be given.
- Change the rate after calculating the deficit + maintenance & dividing by 24 hrs.
- Fluid depletion is common as it is sequestered in damaged muscle.
- 24 hr maintenance fluid = 100ml/kg for 1st 10kg, 50 ml/kg for next 10kg, then 20ml/kg

Subsequent adjustments:
If urine output is >0.5ml/kg/hr after 2-4 hours, increase fluids to $3L/m^2$ of 10% glucose with 0.9% saline.
If plasma potassium <3mmol/L & it is >24 hours since the onset of symptoms & urine is being passed, use fluids containing KCl 10mmol/L.
See section (d) Oliguria if urine output is less than 0.5 ml/kg/hr (<1 ml/kg/hr in infants).

Sodium bicarbonate administration is not recommended routinely unless there is hyperkalaemia or acidosis (see section 4).

c) Monitoring:

- Patients should be on a cardiac monitor.
- Consider catheterisation. Monitor urine output, fluid balance, twice daily weight.
- Initially measure potassium hourly (e.g. on a blood gas machine).
- After 1-2 hours, repeat U&E, Calcium, pH and blood gases, CK
- Clinical assessment should include PEWS.
- Continue to monitor 1-4 hourly depending on the results; frequent monitoring is essential if there is hyperkalaemia. The frequency can be reduced once it is clear potassium is not rising & >8 hours since onset of symptoms.
- Later, it may be appropriate to dipstick the urine, as myoglobin gives a false positive for haemoglobin, but hyperkalaemia usually precedes myoglobinuria.

4. Complications:

a) Hyperkalaemia

If the patient is on PICU, consider haemofiltration. If the child is not on PICU, discuss transfer.

- Is there hypocalcaemia (which increases the risk of arrhythmias)?

- If hyperkalaemia is associated with heart block or ventricular arrhythmias, give 0.5ml/kg of 10% calcium gluconate (maximum 20ml) as a slow IV bolus (e.g. over 5 minutes) via a large peripheral vein or central venous line. This stabilises the myocardium but does not lower the potassium. The line should be flushed afterwards (e.g. with saline), particularly before sodium bicarbonate is given as otherwise calcium carbonate will precipitate!

- If the potassium is over 5.5 mmol/L, some or all of the following should be undertaken:

  i) Salbutamol 2.5mg nebulised (5mg if over 5 yrs) or
  Salbutamol 4 micrograms/kg IV diluted to a concentration of 50 micrograms/ml in 5% glucose or 0.9% saline and given as a slow bolus over 5 minutes.

  ii) 8.4% Sodium bicarbonate 1 ml/kg IV (diluted 1:5 or 1:10 with 10% glucose) over 30-60 minutes if the plasma bicarbonate concentration is less than 21 mmol/L. This lowers the ionised calcium fraction and may cause tetany, convulsions, hypotension or arrhythmias, particularly at higher pH, if there is hypocalcaemia (which is common in rhabdomyolysis).

  iii) Increase fluids to 5ml/kg/hr 10% glucose 0.9% saline = 0.5g/kg/hr glucose.
  If BM >10 mmol/L, add insulin, initially at 0.05 unit/kg/hr and adjusted according to blood glucose (use local sliding scale for diabetes).

  iv) Furosemide 1-2mg/kg IV if patient is not anuric.

  v) Calcium resonium 1g/kg oral/NG or PR.

  vi) Haemofiltration should be considered if there is refractory hyperkalaemia, acidosis or oliguria and fluid overload.

b) Oliguria

Ideally, one wants the urine output to be approximately 3 ml/kg/hr. Seek advice from paediatric nephrologists if the urine output is less than 0.5 ml/kg/hr (<1 ml/kg/hr in infants). Transfer to PICU may be needed for haemofiltration or dialysis but first they may suggest

i) a fluid challenge with 20ml/kg of 0.9% saline as a bolus.
ii) diuretics (1-2mg/kg furosemide or mannitol), particularly there is fluid overload.

c) Acidosis

If the base excess is more negative than -10 mmol/L, consider giving 8.4% Sodium bicarbonate 1-2 ml/kg IV (diluted 1:10 with 10% glucose unless there is central access) over 2-3 hours. Note that this lowers the ionised calcium fraction and may cause tetany, convulsions, hypotension or arrhythmias if there is hypocalcaemia (which is common in rhabdomyolysis).

d) Other treatment

- Treat any infection.
- Analgesia (paracetamol or opiates) may be needed for muscle pain.
- Seek orthopaedic advice if there is concern about compartment syndrome.
- Though hypocalcaemia is common, intravenous calcium is only given if there are symptoms (e.g. tetany, seizures) or severe hyperkalaemia (e.g. with arrhythmias).

5. Progress:

Once it is clear the potassium is not rising & there is no myoglobinuria or it is improving, allow patient to drink & consider substituting this for some of the intravenous fluids.

6. Going Home: Only allow the child home if you and the family are entirely happy and you have discussed the problems with the consultant on call. The family must have a clear management plan and be prepared to return if the child deteriorates.

7. HELP: If there are any questions or concerns, contact the regional metabolic centre and/or paediatric nephrologist.

For further information please refer to:

Systemic corticosteroids for the treatment of acute episodes of rhabdomyolysis in **lipin-1**-deficient patients. Tuchmann-Durand et al. J Inherit Metab Dis. 2023;46(4):649-661.

Last Reviewed: March 2024 ***this guideline has been uploaded prior to full committee approval in view of the significant change in practice it recommends***