Introduction:
Pyruvate dehydrogenase deficiency (PDH) results in the impaired production of ATP from glucose metabolism. Consequently, the ketogenic diet (KD) is suggested as a treatment therapy for individuals with PDH, as ketones generated provide an alternative fuel.

Aim:
We aimed to initiate the KD in a 2-week-old infant with newly diagnosed PDH requiring intubation and ventilation due to intractable seizures and poor prognosis.

Method:
• KD was initiated with combined parenteral lipid (IV) and continuous enteral nutrition (EN) using expressed breast milk, before transition to full EN using ketogenic formula: Ketocal 3:1®.
• Monitoring of blood glucose (BGL) and blood ketones (BKL) continued until adequate ketosis (2.4-5.5 µmol/L) without hypoglycaemia (BGL>2.5 µmol/L) was achieved.
• Subsequent loss of adequate ketosis required ongoing feed manipulation with an increased ketogenic ratio to 4:1 from Ketocal 3:1® with MCT supplementation.
• Carbohydrate content of medication was minimised and infant was treated with thiamine supplements.
• A recurrence of seizures required ongoing use of anticonvulsant therapy.
Results:

- KD commenced with ratio 1:1 and reached target ratio 3:1 on D3. IV lipid was weaned on D2 and estimated energy (100kcal/kg) and fluid requirement (TFI:150ml/kg/d) was met by D4.
- BGL of 2.5 µmol/L required treatment on D2 then stabilised.
- BKL reached target by D3.
- Cessation of seizure activity and improved neurological state allowed decreased ventilation support on D4 and extubation on D6.
- Post extubation metabolic acidosis causing an over-compensatory respiratory alkalosis with a likely transient tubulopathy was managed with IV and oral bicarbonate supplementation, which was gradually weaned.
- BKL decreased from D9, and ketogenic ratio was increased to 3.5:1 then 4:1 with MCT supplements.
- Seizure activity from D17 required resumption of anti-convulsant therapy with no further seizures observed.
- Increased energy provision above estimated requirement was required due to poor growth.
- Free carnitine levels were supplemented for 3 days but remained in the normal range.
- Discharge home occurred on D34 with NGT in situ, no seizure activity, on 4:1 ketogenic diet and anticonvulsant therapy.
- Home monitoring showed improved BKL but not ‘ideal’ with no seizure activity.

**Table 1**: Nutritional regimen, ketogenic ratio and ketone level during and post diet initiation

**Figure 2**: Morning and evening blood ketone levels µmol/L over period on ketogenic diet
Initiation of the classical ketogenic diet in a critically unwell neonate with PDH

Results:

Energy intake over time on ketogenic diet

![Energy intake kcal/kg/d over duration of diet](image1)

Figure 3: Energy intake kcal/kg/d over duration of diet

Weight-for-age Percentiles (Boys, birth to 2 years)

![Weight-for-age Percentiles](image2)

Figure 4: weight-for-age over duration of diet

Length-for-age Percentiles (Boys, birth to 2 years)

![Length-for-age Percentiles](image3)

Acknowledgement to ASIEM for conference funding
Discussion:

• Seizures were controlled initially on 3:1 ketogenic diet when delivered by continuous feeds with IV lipid supplements.
• Once extubated, BKL was difficult to maintain in ‘ideal range’ despite use of 4:1 ratio with additional MCT supplementation and bolus feeding.
• Time to reach higher BKL appeared excessively long and at this point, has not consistently reached ‘ideal’.
• Energy intake to stimulate growth was higher than anticipated and may contribute to lower BKL.
• Fat deposition in NGT tubing due to 90% fat feeds may have affected ketosis and required strategies to minimise impact.
• Cessation of seizures was achieved and is likely to enable weaning of anticonvulsant therapy.
• Experience of initiating successful ketogenic diet in an infant with PDH was different and anecdotally more difficult to other infants with intractable seizures using the same ketogenic protocol.
• Reasons for lower BKL in this patient remain unclear.

Conclusion:
The classical ketogenic diet can be initiated in an unwell infant with PDH and uncontrolled seizures. However, frequent dietary manipulations, including higher energy intake and higher ketogenic ratio than expected, were required to promote adequate growth and therapeutic BKL. Documentation of clinical challenges and shared experiences will help to determine if these clinical findings are consistent for PDH, so that mechanisms for determining cause for these difficulties can be explored.

References: