

Use of Diazoxide for Hyperinsulinism in Neonates

A case study

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Objective

To explore the use of diazoxide for hyper-insulinemic hypoglycaemia in neonates.

Clinical Features

- A 31-week-old neonate with a birth weight of 1404 grams was delivered via emergency caesarean section for abnormal dopplers in the setting of maternal type-II diabetes mellitus (treated with insulin).
- The patient had persistent hypoglycaemia over the first 14 days of life despite glucose boluses and infusions and higher total fluid intakes.
- A hypoglycaemia screen was done on day 4 which showed a normal cortisol (164 mmol/L) and growth hormone (58.7 mU/L) and a high insulin level (2.1 mU/L), suggestive of potential hyper-insulinemic hypoglycaemia.
- After a normal echocardiogram result, the patient was initiated on diazoxide 10 mg/kg/day which was gradually weaned and ceased after 10 days.
- Hydrochlorothiazide 1mg/kg/dose twice daily was also initiated for fluid retention prophylaxis and its hypoglycaemic effect during diazoxide therapy.

Timeline and Interventions

Day of Life	Diazoxide dose	Blood Glucose Levels
15	10 mg/kg/day	3.2, 2.7, 3.9
16	10 mg/kg/day	5.9, 4.5, 7.8, 8.7
17	7.5 mg/kg/day	9.4, 12.4, 11.1, 6.6
18	7.5 mg/kg/day	8.2, 6.0, 8.1
19	7.5 mg/kg/day	8.3, 8.0, 8.3
20	7.5 mg/kg/day	6.7, 9.0
21	5 mg/kg/day	11.0, 8.7
22	2.5 mg/kg/day	11.8, 6.9
23	2.5 mg/kg/day	8.2
24	Ceased	6.7, 7.0, 6.2

Literature review

Findings from five retrospective and two prospective studies suggested that diazoxide had a rapid onset of action and was effective for the management of hyper-insulinemic hypoglycaemia. However, its use has been associated with new onset pulmonary hypertension and feeding difficulties among other adverse effects.^{1,2,3}



Pharmacist Interventions, Case Progress and Outcomes

- The patient was monitored post cessation of diazoxide with no further hypoglycaemic episodes.
- The patient was as an inpatient for 9 days post cessation of diazoxide due to hyponatraemia and then transferred to their local hospital in the context of nasogastric feeds.
- The pharmacist was involved in formulating and compounding of the medicine, providing advice on administration, monitoring of the side effects and management of special access scheme (SAS).
- The neonatal intensive care unit (NICU) pharmacists are also responsible for updating and producing new medication protocols along with being an active part of the multi-disciplinary team.

Discussion

Whilst diazoxide works effectively, it can pose significant adverse effects such as fluid retention and feeding difficulties. The patient in this case study also experienced some feeding difficulties. Additionally, diazoxide is not registered in Australia and hence, further studies are required to find alternative medicines for treatment of hyperinsulinemia in neonates with better safety profile.

References:

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3. Theodorou CM, Hirose S. 2020; 52(101356):101356