Management of Neonatal Hypoglycaemia

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Prevention of hypoglycaemia is mandatory in all neonates. Lower blood glucose values are normal in healthy neonates immediately after birth, which improve to reach normal ranges within hours after birth. This sort of transitional hypoglycemia usually resolves within 48 hours after birth. However, with presence of specific risk factors or a congenital hypoglycemia syndrome, some neonates may experience more prolonged and severe hypoglycemia. Neonates who continue to maintain low sugar levels beyond 48 hours are at a greater risk of suffering from persistent hypoglycemia Persistent hypoglycemia is defined as hypoglycemia persisting for 5-7 days at GIR of >12 mg/kg/min.

It is crucial to treat hypoglycaemia in neonates and identify underlying disorders. The ultimate objective is prevention of neurologic sequelae of neonatal hypoglycaemia

Prevention of hypoglycaemia:

Healthy infants should be breastfed as soon as possible after birth, preferably within the first hour of life, and fed every 2-3 hourly thereafter. Blood glucose concentrations should be measured frequently in infants at risk of hypoglycemia (Kindly read the article on monitoring for neonatal hypoglycemia)

Point of care reagent strips (glucose oxidase method) are commonly used for monitoring, however they are unreliable at low glucose levels. Therefore any low reading should be confirmed with lab analysis for plasma glucose. Treatment should be initiated without waiting for lab results. Plasma Glucose values (PG: those measured in the lab) are approximately 10-15% higher than whole blood glucose (those measured by the reagent strips) values.

Treatment of Infants with Asymptomatic Hypoglycemia:

Any infant with PG < 20 mg/dl should be started on IV therapy irrespective of symptoms

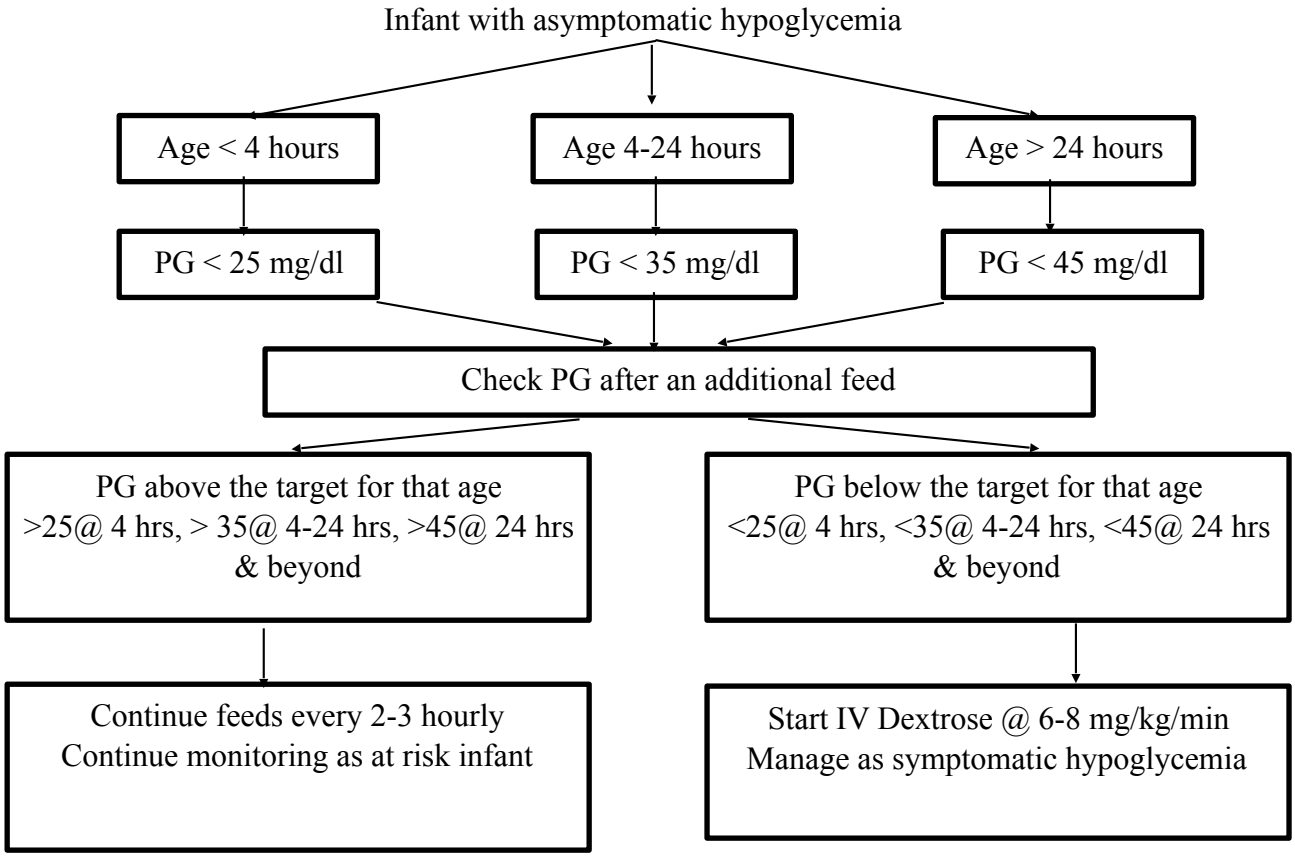

Fig.1. Management of infants with asymptomatic hypoglycemia [1]

The best intervention for asymptomatic hypoglycaemia is to increase feeding frequency and volume. Breastmilk feeding is the preferred milk. Buccal 40% dextrose gel if available, is an effective and safe therapy when used in conjunction with milk feeding for asymptomatic infants with hypoglycemia [8,9]. If the BG is persistently below the expected target despite these interventions, consider intravenous infusion of 10% Dextrose. Breastfeeding can be continued if the infant's condition allows in addition to IV dextrose. If not, plan to commence enteral feedings as quickly as possible and the sugars are stable.

Treatment of Infants with Symptomatic Hypoglycemia:

Symptomatic infants with hypoglycaemia (PG < 45 mg/dL) may have non-specific neurogenic/adrenergic symptoms like sweating, pallor, jitteriness, poor feeding, irritability, tachycardia, tachypnea, vomitting or they may have serious neuroglucopenic symptoms like apnoea, hypotonia, seizures or coma. All symptomatic hypoglycaemic babies should be reviewed immediately and admitted to the neonatal unit.

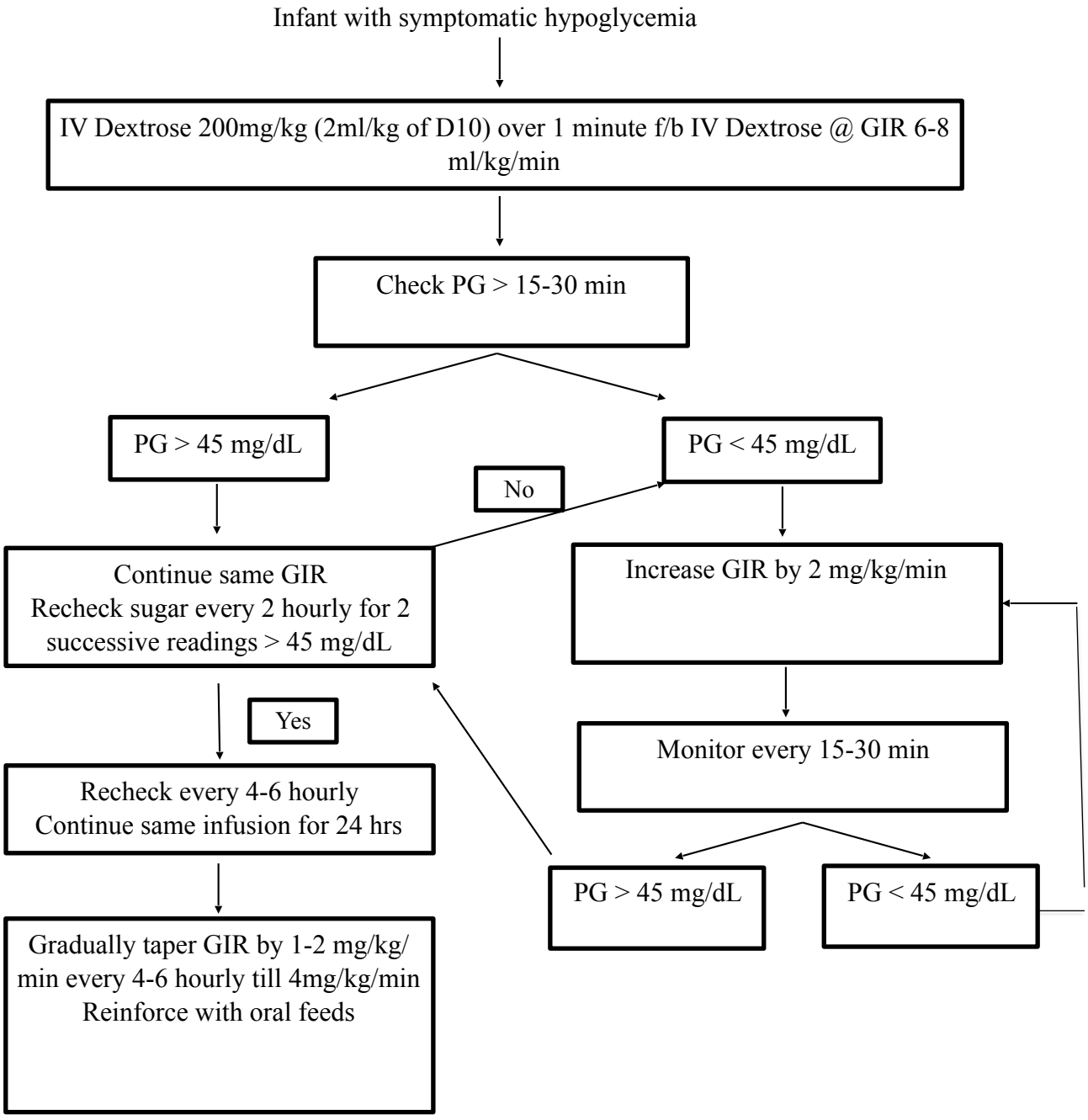

Fig.2. Management of Neonates with symptomatic hypoglycemia

If the BG is persistently low or for babies who are fluid restricted, these cases may require higher concentrations of glucose infusion. If the glucose concentration of the infusion is >12.5 mg%, then use of central line is essential.

Calculation of Glucose infusion rate (GIR)

$$\text{GIR (mg/kg/min)} = \frac{\%\text{ of dextrose infused X rate of infusion (ml/hr)}}{\text{Body weight (in kg) X 6}}$$

$$\text{GIR (mg/kg/min)} = \frac{\text{IV rate (ml/kg/day) X \% of dextrose}}{144}$$

Transitioning to oral feeding :

Small volumes of oral feeds may be introduced once sugars are maintained above target levels for 6 hours. Enteral feeds might be continued as tolerated (unless contraindicated) and normoglycaemia maintained with intravenous dextrose. IV Dextrose is gradually weaned after 24 hours of stable glucose levels with decrement of GIR of 2mg/kg/min every 6 hourly. Simultaneous increase in oral intake is advised. In our unit, we maintain the total fluid intake of the neonate as a sum of oral and IV intake with gradual increase in oral feeds 6 hourly and a simultaneous decrease in IV Dextrose 6 hourly.

Management of Persistent Hypoglycemia

Infants with persistent hypoglycemia need further evaluation with a 5 ml critical sample collected in plain bulb at the time of hypoglycemia and evaluated for plasma glucose, plasma insulin, beta-hydroxybutyrate, blood pH, bicarbonate, lactate, and free fatty acids. These initial tests are used to distinguish diagnostic categories for neonatal hypoglycemia and help determine if other blood tests should be obtained, including plasma C-peptide, growth hormone, cortisol, acylcarnitine profile, plasma free and total carnitine levels, serum amino acids, urine organic acids, or specific genetic tests.

Administration of glucocorticoid therapy (hydrocortisone 2 to 6 mg/kg per day divided in 2 to 3 doses orally or intravenously) in infants requiring a glucose infusion rate of 12 mg/kg per minute or greater can be tried. However, its use should be restricted to a short course (1 to 2 days), unless a patient has documented adrenal insufficiency. Glucocorticoids stimulate gluconeogenesis and reduction in peripheral glucose utilization. Serum cortisol and insulin concentrations during an episode of hypoglycemia should be measured before beginning glucocorticoid treatment, if possible.

Hyperinsulinemic hyperglycemia hypoglycemia is defined as inappropriately elevated plasma insulin concentration in presence of hypoglycemia in infants receiving GIR of more than 8 mg/kg/min with suppressed ketone body and free fatty acids and a positive glycemic response to glucagon - Inj. Glucagon 100 micrograms/kg intramuscularly/intravenously during hypoglycemia can cause a rise in plasma glucose of approximately 30 to 50 mg/dL within 15 to 30 minutes of administration, especially in hyperinsulinemic states, which can last for approximately one-two hours. If the plasma glucose does not rise within 20 minutes of glucagon administration, then a repeat dose of glucagon is given. A failure to respond to glucagon raises the possibility of a glycogen storage disorder, defect in glycogen synthesis or fatty acid oxidation disorder. In these patients, further evaluation is warranted.

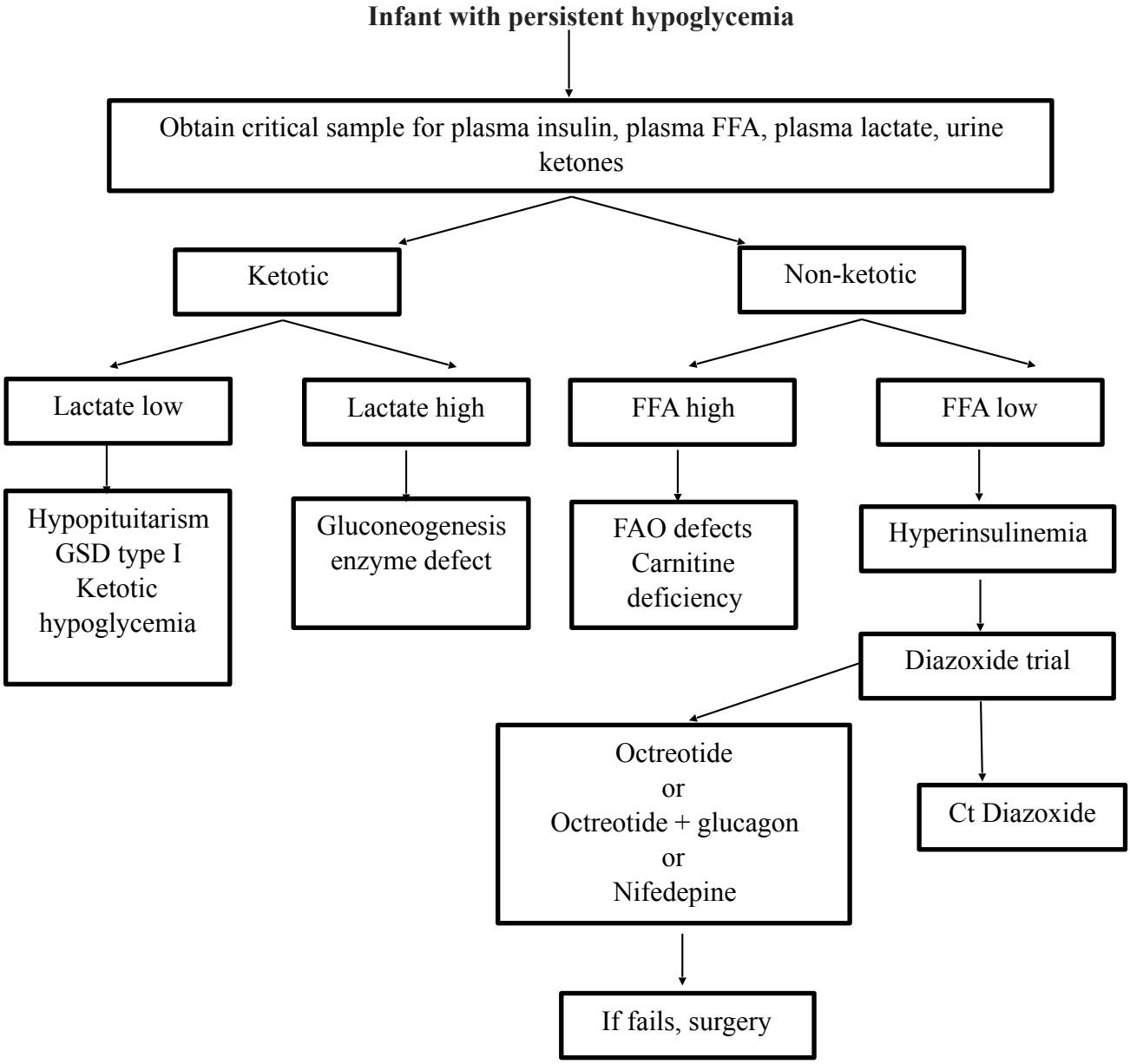

Fig.3. Approach to a neonate with persistent hypoglycemia [5]

Table. 1. Pharmacologic agents for treatment of Persistent hypoglycemia

Drug	Dosing	Administration	Side-effects
Diazoxide	10-15 mg/kg/day	Oral, 8 hourly	Hirsuitism, fluid retention, heart failure, nausea, vomiting
Glucagon	Bolus 100mcg/kg 1 mg/day	Intermittent infusion Continuous infusion	Hyponatremia, thrombocytopenia
Hydrocortisone	50 mg/m^2/day	Intravenous, 6 hourly	Hypertension, growth suppression
Nifedepine	0.5-0.8 mg/kg/day	Oral, 8 hourly	Hypotension
Octreotide	7-12 mcg/kg/day max 40 mcg/kg/day	Subcutaneous every 6 hourly, may be given continuously IV	Cholelithiasis

Discharge of a neonate with hypoglycemia

1. **Discharge criteria —**

    a. It is important to ensure that neonates are able to maintain plasma glucose concentrations in a normal range through cycles of feeding and fasting prior to discharge.

    b. However, data are lacking to determine the optimal discharge criteria, particularly the minimal required threshold glucose level.

    c. It is essential that preprandial glucose concentrations through three feed-fast cycles should be >60 mg/dL.

    d. For infants with a known or suspected genetic hypoglycaemia disorder, discharge criteria should be made on a patient-specific basis in consultation with an endocrinologist.

2. **Long term outcomes** are determined by multiple factors like severity, duration, recurrence of hypoglycaemia and cerebral utilisation of glucose. Assessment of vision is very crucial as these children have a high risk of developing cortical blindness. They need a structured follow up at corrected age 1,3, 6, 9, 12 and 18 months for developmental assessment, hearing and vision. MRI can estimate the extent of injury if done at 4-6 weeks.

Key messages:

- Transient low blood glucose concentrations are common in healthy term infants after birth. It is important to differentiate the normal physiologic transitional response from disorders that result in persistent or recurrent hypoglycemia, which if left untreated may lead to significant neurologic and developmental sequelae.
- The goals of managing neonatal hypoglycemia are to correct blood glucose levels in symptomatic patients, prevent symptomatic hypoglycemia in at-risk patients, and identify newborns with a serious underlying hypoglycemic disorder, while avoiding unnecessary treatment of infants with normal transitional low blood glucose, which will resolve without intervention. The long-term goal is to prevent long-term neurologic complications.
- Treatment of neonatal hypoglycemia is a stepwise process depending on the presence or absence of symptoms and signs, and the response of the infant at each step.
- Further diagnostic testing is usually reserved for the following infants with persistent hypoglycemia.
- It is important that neonates are able to maintain plasma glucose in a normal range through cycles of feeding and fasting prior to discharge.
- Symptomatic neonatal hypoglycemia has been associated with brain damage, demonstrated on magnetic resonance imaging, and poorer developmental outcome. However, there are no available data that clearly define the glucose concentration or the duration of hypoglycemia that correlate with long-term neurologic sequelae.

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