Neonatal Hypoglycemia – Neurodevelopmental follow up

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Hypoglycemia in neonates is a common problem. Around 5-15% neonates require treatment for hypoglycemia (1). In developing countries like India it is probably under reported due to lack of screening. The relation of hypoglycemia & neurological abnormalities is known for almost 8 decades. Neonatal Hypoglycemia is a red flag for follow up, as it is associated with neurological morbidities (2,3). Both term & preterm babies (4) are at high risk of neurological impairment. Hence it will be right to say that management of hypoglycemia does not end at NICU discharge, but it actually starts at discharge. These babies need a structured follow up program.

Symptomatic or Asymptomatic Hypoglycemia:

Prolonged & symptomatic hypoglycemia has long been related with long term neurological issues (2,3,5). Outcome of transient & moderate hypoglycemia has been subject of debate (6,7). It is considered part of postnatal developmental physiology & hence harmless by some. Tin et al (8) assessed cognitive function at 2 & 15 years in babies with recurrent moderate hypoglycemia. This study could not confirm association of neurological impairment & moderate hypoglycemia.

CHYLD study (9) also failed to show any long term impact of moderate & transient hypoglycemia. However, recent observations of a Swedish group differed with the notion of moderate hypoglycemia being harmless (10). They observed 50% higher rates of any

neurological or neurodevelopmental outcome at follow-up when babies had transient or moderate hypoglycemia. Moderate hypoglycemia almost doubled the rates of any developmental delay, motor and cognitive, as compared to normoglycemic infants. Incidence of autism spectrum disorders, tics, epileptic disorders & febrile seizures were 30-50% higher in hypoglycemic. So we need to be vigilant about hypoglycemia screening in neonates.

Discharging a neonate with hypoglycemia:

These are high risk babies & need to remain in High Risk follow up & Early Intervention Protocol. Neonatologist remains key person in loop with everyone. It's a multidisciplinary follow up. All the concerned specialties should be involved depending on the case. A few complicated patients may need highly specialized faculties like Geneticist. Hence the Neonatologist should conduct this opera delicately to avoid unnecessary strain on parents; at the same time not to miss vital links. I have discussed the follow up plan that is useful for most of the patients of neonatal hypoglycemia.

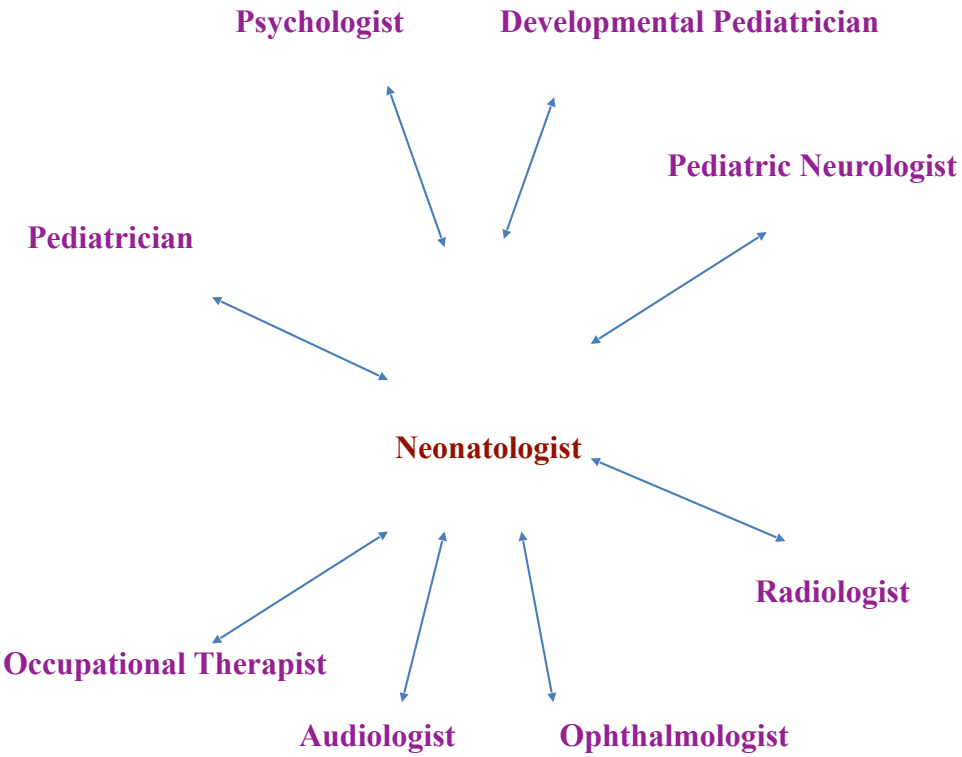

Fig. 1. Multidisciplinary approach for management of neonatal hypoglycemia

1) **Pediatrician-**

   a. Pediatrician looking after the baby should be aware of high risk flags.

   b. Anthropometric measurements should be documented with special attention to Head circumference plotting.

   c. These babies may be on medicines like oral anticonvulsant & insulin lowering drugs. Monitoring the drug doses with weight changes & decision to taper the dose should be discussed on time to time.

2) **Occupational Therapist-**

a. A trained occupational therapist is important in early intervention program.

b. Tone abnormalities can be soft marker in early follow up. Tone assessment & therapy are integral in early intervention. Mother or any relative looking after baby should be closely involved in therapy. Mother or relative should be taught steps of therapy. Making a video of ongoing therapy can be a good guide for mother for continuing therapy at home.

c. Regularity of therapy is key to success in early intervention.

3) **Audiologist-**

a. Hearing deficit is one of the major handicaps of hypoglycemia.

b. All babies should be screened for hearing before discharge (Fig.2).

c. If the results are suspicious ENT surgeon should be involved to decide about role of hearing aid. Speech therapist is integral in such cases. These babies should be assessed for cochlear implant at right time for better results.

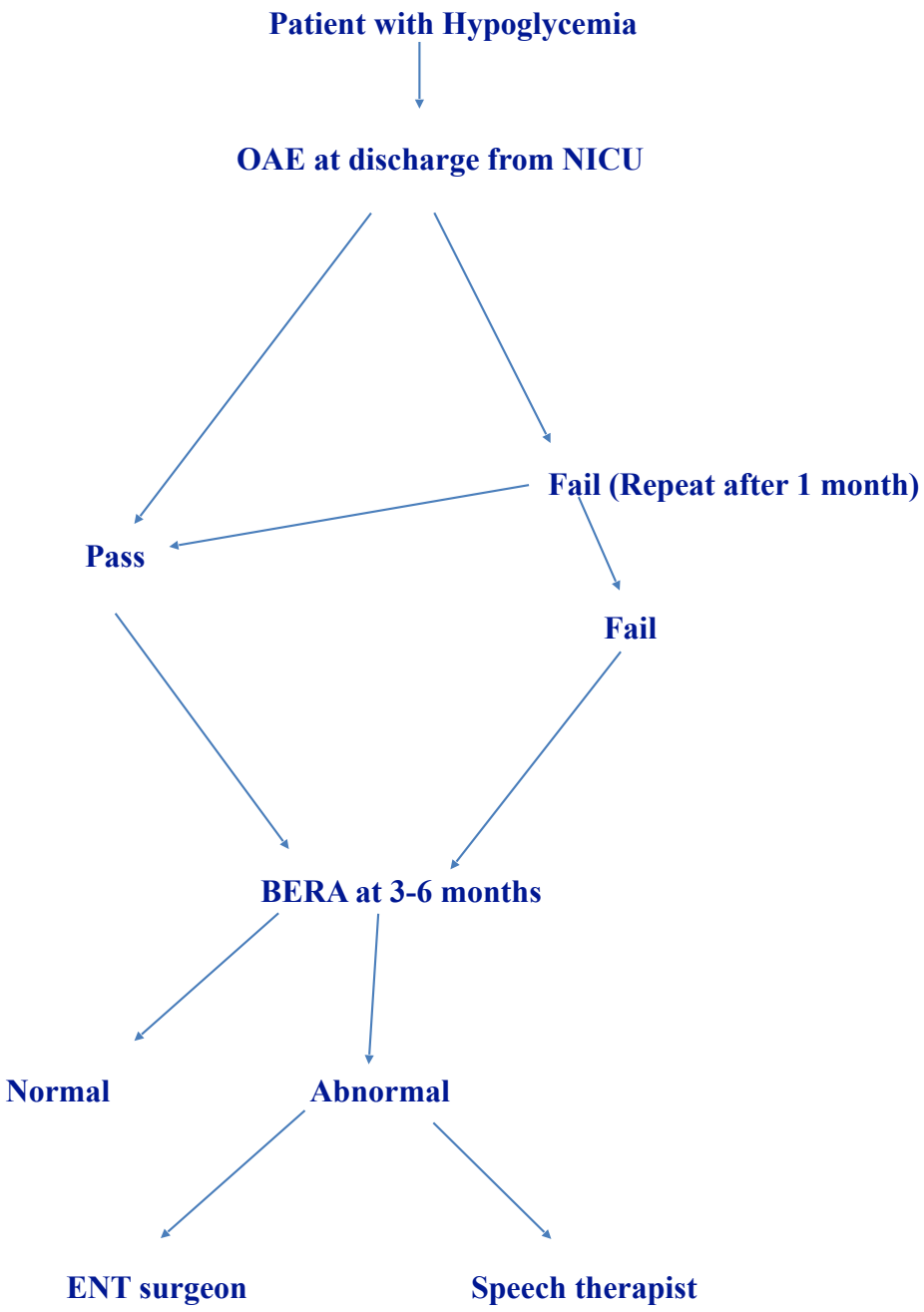

Fig. 2. Universal Newborn Hearing Screening

4) **Ophthalmologist-**

a. Visual manifestations of neonatal hypoglycemia are varied. Optic assessment should be done by ophthalmologist.

b. Hypoglycemia due to metabolic diseases like Galactosemia have ophthalmic manifestations like congenital cataract. Few old studies related neonatal hypoglycemia with cataract development (11,12), though it's not proved in recent studies (13). Optic nerve hypoplasia is associated to hypoglycemia by a case series (14). However, this is also doubtful.

c. Babies with hypoglycemia are at risk of cortical blindness. Hypoglycemia affects visual radiation (15) & posterior occipital neurons & underlying white matter (16).

d. VEP can aid in diagnosis (17) & should be discussed with Ophthalmologist.

5) **Radiologist-**

a. Hypoglycemia has specific parieto- occipital distribution (15,17,18). MRI Brain will show the involvement of cerebral areas precisely. Posterior brain involvement is known for long time (19). More recent studies have showed involvement of underlying white matter, corpus callosum & thalamus (5,20). Tam et al has found cortico-spinal tract involvement in neonatal hypoglycemia (21).

b. MRI findings (Table 1) help in anticipating neurodevelopmental issues in patient. Hypoglycemia is associated with other neonatal conditions causing

encephalopathy like hypoxia or infection (22,23). The associated condition can cause neurological injuries that can be seen on MRI. This helps in planning intervention in these patients.

Table. 1 Brain Imaging abnormalities and neurological outcome in severe neonatal hypoglycemia:

Neonatal blood glucose levels :
• ≤20 mg/dL: 74%
• ≤25 mg/dL: 90%
• ≤30 mg/dL: 95%
Major imaging findings :
• Occipital with or without parietal lesions (75%)
• Corticospinal tract involvement (15%)
• Watershed pattern (10%)
Neurological sequelae:
• Total 84%
• Developmental delay/mental retardation: 84%
• Seizures: 66%
• Visual impairment: 37% b
• Microcephaly: 32%

6) **Pediatric neurologist-**

a. Hypoglycemia is common cause of remote onset infantile seizures (24-26). Convulsion may be the first indication of hypoglycemia in neonatal period & such neonates may be on anticonvulsants at time of discharge. Some neonates with hypoglycemia are challenging cases for seizure control & may evolve in WEST syndrome.

b. Role of pediatric neurologist is vital in these cases to determine anticonvulsant choice, dose & duration.

c. Prognosis of WEST syndrome is rapidly improving with proper anticonvulsant therapy & early intervention.

7) **Developmental Pediatrician-**

a. Cognitive problems are reported after neonatal hypoglycemia for long time (2,27,28). Hypoglycemic neonates are known candidates for behavioral & scholastic issues. Parents may realise these problems in late childhood. Autism spectrum disorders need to be kept in mind, especially in patients with hearing deficits.

b. Holistic management of behavior issues can be done with the help of Developmental Pediatrician. Scholastic issues, dyslexia and other learning disorders may be missed initially because of the subtle manifestations. A trained Developmental Pediatrician is a great help.

8) **Psychologist-**

a. Role of Psychologist is better appreciated in recent times. Developmental assessment is integral to high risk follow up. Development Quotient (DQ) & Intellectual Quotient (IQ) can be used as guide for therapy. A trained psychologist will apply appropriate tests for proper results.

b. Autism spectrum disorders & other behavioral issues like Attention Deficit Hyperactivity Disorders (ADHD) need to be picked up early & intervened.

Key Message:

The neurodevelopmental follow up is an extension of treatment of hypoglycemia. It needs to be well planned & multidisciplinary. Every tertiary NICU should try to develop a Development Center to cater to such babies in a better fashion. This will definitely improve outcome of neonates with hypoglycemia.

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