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Review

Neonatal hypoglycemia

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SUMMARY

A consistent definition for neonatal hypoglycemia in the first 48 h of life continues to elude us. Enhanced understanding of metabolic disturbances and genetic disorders that underlie alterations in postnatal glucose homeostasis has added useful information to understanding transitional hypoglycemia. This growth in knowledge still has not led to what we need to know: "How low is too low and for how long?" This article reviews the current state of understanding of neonatal hypoglycemia and how different approaches reach different "expert" opinions.

1. Introduction

Management of low glucose concentrations in the first 48 h of life is one of the most frequently encountered issues in newborn care. The levels used to make decisions remain more a matter of expert opinion than based on evidence. The data needed to establish agreement on levels to treat have not been definitive enough to gain consensus. Recently a number of studies as well as position papers from two pediatric organizations have provided some new substance for debate and suggest that the design of studies may move toward a more evidence-based approach to neonatal hypoglycemia [1,2].

More than 50 years ago, Marvin Cornblath recognized that low blood glucose levels in small for gestational age (SGA) and preterm infants were associated with seizures [3]. It became clear that symptomatic hypoglycemia could lead to long-term neurologic deficits. However, the definition of clinically significant hypoglycemia still eludes us. Therefore, we still have limited evidence-based consensus regarding the screening and management of infants at risk for hypoglycemia. While there is agreement that recurrent severe hypoglycemia causes brain injury, there are now more recent studies fueling the debate about the relationship of neurodevelopmental outcomes and transient neonatal hypoglycemia [4,5].

The American Academy of Pediatrics (AAP) Committee on Fetus and Newborn (COFN) recently ratified for another five years their statement on postnatal glucose homeostasis including an algorithm for screening and management of low glucose levels (Fig. 1) [1]. Also, recommendations and a re-evaluation of transitional hypoglycemia has been published by the Pediatric Endocrine Society (PES) [2,6]. A recent editorial called "Imperfect Advice" contrasts the two organizations' approaches and offers suggestions to merge both [7]. The purpose of this review is to evaluate the approaches taken by the two organizations and combine advice for management of low glucose levels over the first 48 h and how to diagnose potential cases of persistent hypoglycemia prior to discharge. The review includes a discussion of postnatal glucose homeostasis including transitional hypoglycemia. This is followed by a discussion contrasting neuroendocrine and metabolic data versus individual risk assessment, examination of the infant and corroboration of these levels with neurodevelopmental outcome data to reach recommendations for action.

2. Postnatal glucose homeostasis

At birth, the infant's blood glucose concentration is about 70% of the maternal level. It falls rapidly to a nadir by 1 h to a value as low as 20–25 mg/dL [8]. This nadir and the lower levels are prevalent in healthy neonates and are seen in all mammalian newborns. These levels are transient and begin to rise over the first hours and days of life. This observation is considered to be part of the normal adaptation for postnatal life that helps establish postnatal glucose homeostasis [8–10]. Are there advantages to having a lower blood glucose concentration compared with adults for the first two days of life? A decrease in glucose concentration soon after birth might be essential to stimulate physiological processes that are required for postnatal survival, including promoting glucose production

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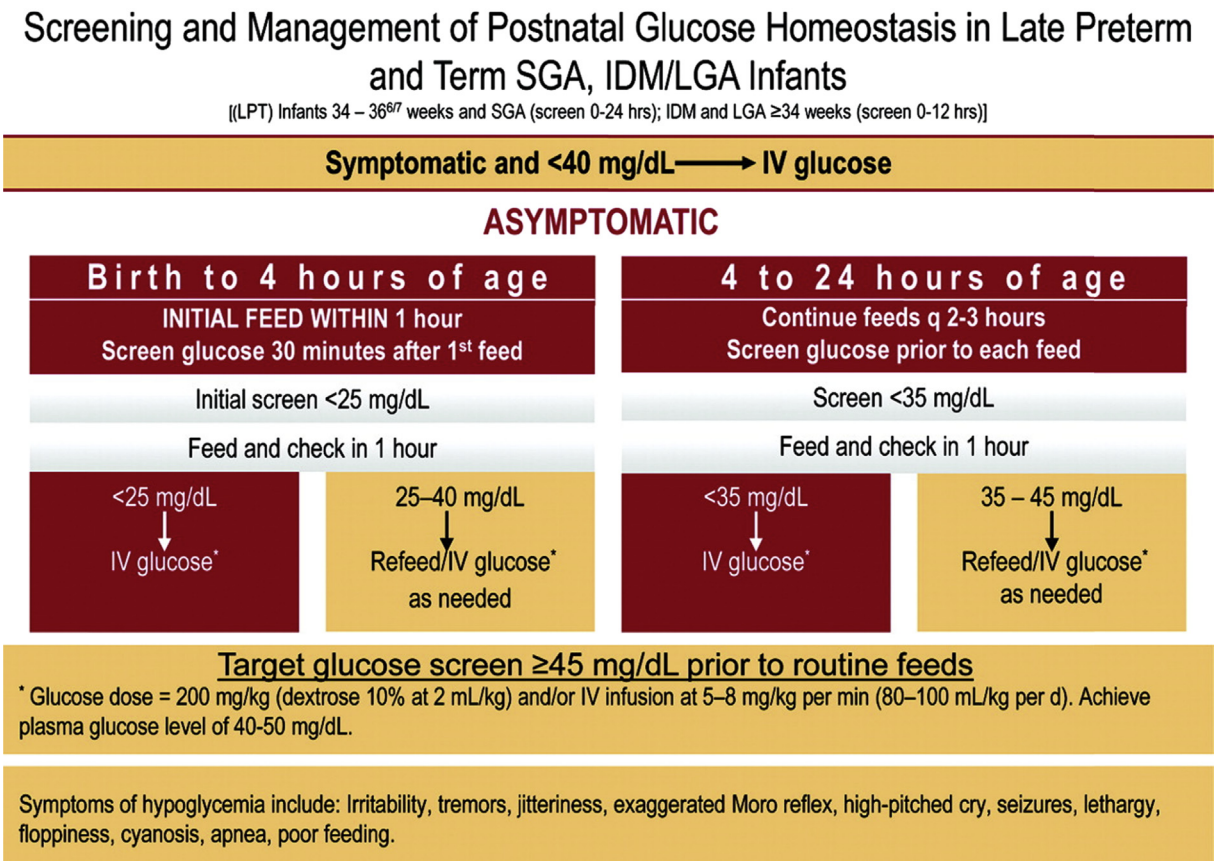

Fig. 1. Screening for and management of postnatal glucose homeostasis in late preterm (LPT 34–36$^{6/7}$ weeks) and term small for gestational age (SGA) infants and infants who were born to mothers with diabetes (IDM)/large for gestational age (LGA) infants. LPT and SGA (screen 0–24 h), IDM and LGA ≥34 weeks (screen 0–12 h). IV, intravenous. Reproduced with permission from Adamkin [1].

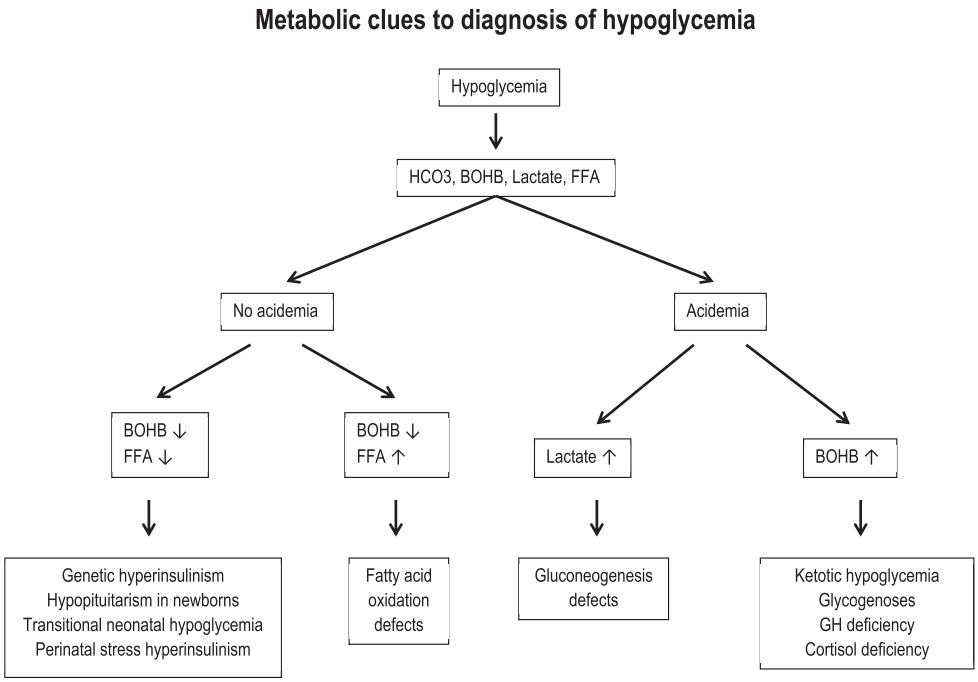

Fig. 2. Algorithm showing how the major categories of hypoglycemia may be determined with information from the critical sample. BOHB, beta-hydroxybutyrate; FFA, free fatty acids; GH, growth hormone. Reproduced with permission from Thornton et al. [2].

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