The following articles on neonatal hypoglycemia will impact treatment recommendations in the next edition of The S.T.A.B.L.E. Program

Neonatal Hypoglycemia


First paragraph of article: A Committee of the Pediatric Endocrine Society was recently formed to develop guidelines for evaluation and management of hypoglycemia in neonates, infants, and children. To aid in formulating recommendations for neonates, in this review, we analyzed available data on the brief period of hypoglycemia, which commonly is observed in normal newborns during the transition from fetal to extrauterine life, hereafter referred to as transitional neonatal hypoglycemia in normal newborns. The goal was to better understand the mechanism underlying this phenomenon in order to formulate recommendations for recognizing neonates requiring diagnosis and treatment during the first days of life for disorders causing severe and persistent hypoglycemia.


First paragraph of article: During the first 24-48 hours of life, as normal neonates transition from intrauterine to extrauterine life, their plasma glucose (PG) concentrations are typically lower than later in life.1-3 Published guidelines for screening at-risk newborns and managing low PG concentrations in neonates focus on the immediate neonatal period, but do not address the diagnosis and management of disorders causing recurrent and prolonged hypoglycemia.4-6 Distinguishing between transitional neonatal glucose regulation in normal newborns and hypoglycemia that persists or occurs for the first time beyond the first 3 days of life is important for prompt diagnosis and effective treatment to avoid serious consequences, including seizures and permanent brain injury.


OBJECTIVES: Routine blood glucose screening is recommended for babies at risk of neonatal hypoglycemia. However, the incidence of hypoglycemia in those screened is not well described. We sought to determine the incidence of hypoglycemia in babies identified as being at risk, and also to determine differences in incidence between at risk groups. STUDY DESIGN: Infants (n = 514) were recruited who were born in a tertiary hospital, >/=35 weeks gestation and identified as at risk of hypoglycemia (small, large, infant of a diabetic, late-preterm, and other). Blood glucose screening used a standard protocol and a glucose oxidase method of glucose measurement in the first 48 hours after birth. RESULTS: One-half of the babies (260/514, 51%) became hypoglycemic (<2.6 mM), 97 (19%) had severe hypoglycemia (<2.0 mM), and 98 (19%) had more than 1 episode. The mean duration of an episode was 1.4 hours. Most episodes (315/390, 81%) occurred in the first 24 hours. The median number of blood glucose measurements for each baby was 9 (range 1-22). The incidence and timing of hypoglycemia was similar in all at risk groups, but babies with a total of 3 risk factors were more likely to have severe hypoglycemia. CONCLUSIONS: Hypoglycemia is common amongst babies recommended for routine blood glucose screening. We found no evidence that screening protocols should differ in different at risk groups, but multiple risk factors may increase severity. The significance of these hypoglycemic episodes for long-term outcome remains undetermined.
Dextrose gel is used to reverse hypoglycaemia in individuals with diabetes; however, little evidence exists for its use in babies. We aimed to assess whether treatment with dextrose gel was more effective than feeding alone for reversal of neonatal hypoglycaemia in at-risk babies.

METHODS: We undertook a randomised, double-blind, placebo-controlled trial at a tertiary centre in New Zealand between Dec 1, 2008, and Nov 31, 2010. Babies aged 35-42 weeks' gestation, younger than 48-h-old, and at risk of hypoglycaemia were randomly assigned (1:1), via computer-generated blocked randomisation, to 40% dextrose gel 200 mg/kg or placebo gel. Randomisation was stratified by maternal diabetes and birthweight. Group allocation was concealed from clinicians, families, and all study investigators. The primary outcome was treatment failure, defined as a blood glucose concentration of less than 2.6 mmol/L after two treatment attempts. Analysis was by intention to treat. The trial is registered with Australian New Zealand Clinical Trials Registry, number ACTRN1260800623392. FINDINGS: Of 514 enrolled babies, 242 (47%) became hypoglycaemic and were randomised. Five babies were randomised in error, leaving 237 for analysis: 118 (50%) in the dextrose group and 119 (50%) in the placebo group. Dextrose gel reduced the frequency of treatment failure compared with placebo (16 [14%] vs 29 [24%]; relative risk 0.57, 95% CI 0.33-0.98; p=0.04). We noted no serious adverse events. Three (3%) babies in the placebo group each had one blood glucose concentration of 0.9 mmol/L. No other adverse events took place. INTERPRETATION: Treatment with dextrose gel is inexpensive and simple to administer. Dextrose gel should be considered for first-line treatment to manage severe neonatal hypoglycaemia.
hypoglycaemia in late preterm and term babies in the first 48 h after birth. FUNDING: Waikato Medical Research Foundation, the Auckland Medical Research Foundation, the Maurice and Phyllis Paykel Trust, the Health Research Council of New Zealand, and the Rebecca Roberts Scholarship.

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**Issues Related to Maternal Obesity**


**IMPORTANCE:** Evidence suggests that maternal obesity increases the risk of fetal death, stillbirth, and infant death; however, the optimal body mass index (BMI) for prevention is not known. **OBJECTIVE:** To conduct a systematic review and meta-analysis of cohort studies of maternal BMI and risk of fetal death, stillbirth, and infant death. **DATA SOURCES:** The PubMed and Embase databases were searched from inception to January 23, 2014. **STUDY SELECTION:** Cohort studies reporting adjusted relative risk (RR) estimates for fetal death, stillbirth, or infant death by at least 3 categories of maternal BMI were included. **DATA EXTRACTION:** Data were extracted by 1 reviewer and checked by the remaining reviewers for accuracy. Summary RRs were estimated using a random-effects model. **MAIN OUTCOMES AND MEASURES:** Fetal death, stillbirth, and neonatal, perinatal, and infant death. **RESULTS:** Thirty eight studies (44 publications) with more than 10,147 fetal deaths, more than 16,274 stillbirths, more than 4311 perinatal deaths, 11,294 neonatal deaths, and 4983 infant deaths were included. The summary RR per 5-unit increase in maternal BMI for fetal death was 1.21 (95% CI, 1.09-1.35; I² = 77.6%; n = 7 studies); for stillbirth, 1.24 (95% CI, 1.18-1.30; I² = 80%; n = 18 studies); for perinatal death, 1.16 (95% CI, 1.00-1.35; I² = 93.7%; n = 11 studies); for neonatal death, 1.15 (95% CI, 1.07-1.23; I² = 78.5%; n = 12 studies); and for infant death, 1.18 (95% CI, 1.09-1.28; I² = 79%; n = 4 studies). The test for nonlinearity was significant in all analyses but was most pronounced for fetal death. For women with a BMI of 20 (reference standard for all outcomes), 25, and 30, absolute risks per 10,000 pregnancies for fetal death were 76, 82 (95% CI, 76-88), and 102 (95% CI, 93-112); for stillbirth, 40, 48 (95% CI, 46-51), and 59 (95% CI, 55-63); for perinatal death, 66, 73 (95% CI, 67-81), and 86 (95% CI, 76-98); for neonatal death, 20, 21 (95% CI, 19-23), and 24 (95% CI, 22-27); and for infant death, 33, 37 (95% CI, 34-39), and 43 (95% CI, 40-47), respectively. **CONCLUSIONS AND RELEVANCE:** Even modest increases in maternal BMI were associated with increased risk of fetal death, stillbirth, and neonatal, perinatal, and infant death. Weight management guidelines for women who plan pregnancies should take these findings into consideration to reduce the burden of fetal death, stillbirth, and infant death.


The definition of optimal glycemic control in pregnancies affected by diabetes remains enigmatic. Diabetes phenotypes are heterogeneous. Moreover, fetal macrosomia insidiously occurs even with excellent glycemic control. Current blood glucose (BG) targets (FBG </=95, 1-h post-prandial <140, 2 h <120 mg/dL) have improved perinatal outcomes, but arguably they have not normalized. The conventional management approach has been to replicate a pattern of glycemia in normal pregnancy. Although these patterns are lower than previously appreciated, a randomized controlled trial (RCT) has never compared current vs. lower glucose targets powered on maternal/fetal outcomes. This paper provides historical context to the current targets by reviewing evidence supporting their evolution. Using lower targets (FBG <90, 1 h <122, 2 h <110, mean BG </=95 mg/dL) may help normalize outcomes, but phenotypic differences (type 1 vs. type 2 vs. gestational diabetes) might require different glycemic goals. There remains a critical need for well-designed RCTs to confirm optimal glycemic control that minimizes both small for and large for gestational age across pregnancies affected by diabetes.

OBJECTIVE: To assess the relationship between second and third trimester glycemic control and adverse outcomes in pregnant women with type 1 diabetes, as uncertainty exists about optimum glycemic targets.

RESEARCH DESIGN AND METHODS: Pregnancy outcomes were assessed prospectively in 725 women with type 1 diabetes from the Diabetes and Pre-eclampsia Intervention Trial. HbA1c (A1C) values at 26 and 34 weeks' gestation were categorized into five groups, the lowest, <6.0% (42 mmol/mol), being the reference. Average pre- and postprandial results from an eight-point capillary glucose profile the previous day were categorized into five groups, the lowest (preprandial <5.0 mmol/L and postprandial <6.0 mmol/L) being the reference. RESULTS: An A1C of 6.0-6.4% (42-47 mmol/mol) at 26 weeks' gestation was associated with a significantly increased risk of large for gestational age (LGA) (odds ratio 1.7 [95% CI 1.0-3.0]) and an A1C of 6.5-6.9% (48-52 mmol/mol) with a significantly increased risk of preterm delivery (odds ratio 2.5 [95% CI 1.3-4.8]), pre-eclampsia (4.3 [1.7-10.8]), need for a neonatal glucose infusion (2.9 [1.5-5.6]), and a composite adverse outcome (3.2 [1.3-8.0]). These risks increased progressively with increasing A1C. Results were similar at 34 weeks' gestation. Glucose data showed less consistent trends, although the risk of a composite adverse outcome increased with preprandial glucose levels between 6.0 and 6.9 mmol/L at 34 weeks (3.3 [1.3-8.0]). CONCLUSIONS: LGA increased significantly with an A1C >/=6.0 (42 mmol/mol) at 26 and 34 weeks' gestation and with other adverse outcomes with an A1C >/=6.5% (48 mmol/mol). The data suggest that there is clinical utility in regular measurement of A1C during pregna