The Turkish Journal of Pediatrics 1997; 39: 159-164

HYPOGLYCEMIA IN SMALL – FOR – GESTATIONAL – AGE NEONATES*

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SUMMARY: Karahasanoğlu Ö, Karatekin G, Köse R, Nuhoğlu A. (Pediatric Clinics, Şişli Etfal Hospital, İstanbul, Turkey). Hypoglycemia in small-for-gestational-age neonates. Turk J Pediatr 1997; 39: 159-164.

In this prospective study, we investigated the frequency of hypoglycemia and the proper intervals for screening in small-for-gestational-age (SGA) neonates. We determined test-strip blood glucose values at two, three, six, 12, 24 and 48 hours of age in 25 SGA and 16 appropriate-for-gestational-age (AGA) infants who were born after 37 completed gestational weeks at the Obstetrics Clinics of Şişli Etfal Hospital. Serum glucose determination was immediately done if a test-strip value was less than 40 mg/dl. The frequency of hypoglycemia in SGA neonates was significantly higher (p: 0097) than in AGA neonates. The first three hours, the sixth hour and the 48th hour postnatally were the most common hours for encountering hypoglycemia. Clinical signs were not true indicators of hypoglycemia. These data suggest that screening for hypoglycemia in SGA neonates should continue for 48 hours. *Key words: hypoglycemia, small-for-gestational-age infants.*

Regardless of the presence or absence of abnormal clinical signs, neonatal hypoglycemia can cause damage to both neuronal and glial cells, resulting in severe handicap or death[1,2]. Small-for-gestational-age (SGA) neonates are at risk of developing hypoglycemia for reasons such as increased utilization of glucose, decreased gluconeogenesis, decreased stores of fat and glycogen, and inefficiency in converting fatty acids to ketone bodies[3-11].

Though screening for hypoglycemia in SGA infants is recommended using a recent definition of hypoglycemia, the frequency of hypoglycemia and the proper duration of screening have only been documented in one work[12]. The purpose of this study was to determine the frequency of hypoglycemia and the age at which it occurred in SGA infants, using Srinivasan et al's[13] definition of hypoglycemia.

Material and Methods

The study group consisted of 25 proportional SGA neonates, and the control group consisted of 16 appropriate-for-gestational age (AGA) neonates who were born at term between March 1, 1993 and July 15, 1994, at Şişli Etfal Hospital.

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Reasons not to include other term SGA neonates who were born during this time period are listed in Table I. Infants were followed in the neonatal unit or in mothers' rooms in the Gynecology Department at Şişli Etfal Hospital.

Table I: Criteria for Not Enrolling in the Study

Maternal Reasons	Reasons Concerning Infant
– Toxemia	– Meconium staining of amniotic fluid
– Diabetes	– Apgar scores < 7 at 5 minutes
– Anemia	– Polycythemia
– Hypertension	– Respiratory distress syndrome
– Prenatal infection	– Congenital anomalies
– Fetal distress	– Neonate treated with intravenous dextrose solution for reasons other than hypoglycemia
– Medication ingestion during the last four weeks of pregnancy	

Only infants who were 38 to 42 weeks gestational age were included. Assessment of gestational age was done using the Ballard Score[14]. Neonates below the 10th percentile for birth weight according to Denver Intrauterine Growth Charts[15] were accepted as SGA, and between the 10th and 90th percentiles were accepted as AGA.

Birth weight, birth length, head circumference, sex, gestational age, ponderal index, presence of a twin pregnancy and type of delivery were documented in each case.

Serial blood samples were drawn from each infant in the study and control groups at two, three, six, 12, 24 and 48 hours of age using a capillary-glucose-test-apparatus, Glucocard (GT-1610, Kyoto Daiichi Kagaku Co.). Serum glucose determination was immediately done if a test strip reading was less than 40 mg/dl[12]. Hypoglycemia was defined as a serum glucose less than 35 mg/dl at less than three hours of age, less than 40 mg/dl at three to 24 hours of age, and less than 45 mg/dl at greater than 24 hours of age[13].

Only infants who were followed in the neonatal unit for some minor problems were fed 66 kcal/100 ml infant formula; all other infants were breastfed. All infants were nursed or fed immediately after the first blood glucose measurement was performed in the second hour.

All infants were fed or nursed every three hours. Neonates were observed for the symptoms of hypoglycemia prior to the collection of samples. Lethargy, apnea, cyanosis, poor feeding, irritability, tremors, weak or high-pitched cry and seizures were accepted as symptoms of hypoglycemia. Neonates with low test-strip values were fed 10-15 milliliters of formula after venous blood samples were drawn. If there were symptoms or if hypoglycemia persisted after feeding,

treatment was started immediately with an intravenous infusion of 200 mg/kg dextrose (2 ml/kg dextrose water, 10% concentrated) given over one minute and followed by a continuous infusion of 8 mg/kg/min.

Statistical analyses were done using Fisher's test, chi-square analysis, Student's-t test and Mann-Whitney U test, and p values greater than 0.05 were accepted as insignificant.

Results

While 11 infants in the study group were found to be hypoglycemic (44%), only one infant in the control group was hypoglycemic (6.2%) ($p < 0.05$). No statistical difference could be found between the study and control groups in terms of sex, multiple gestations and type of delivery (Table II).

Table II: Comparison of Study and Control Groups*

	SGA Neonates (n: 25)	AGA Neonates (n: 16)	P Value
Hypoglycemia	11	1	0.0097
Twins	6	2	0.31
Sex	14 males 11 females	8 males 8 females	0.84
Type of delivery			
Cesarean section	5	1	
Vaginal delivery	19	15	0.32
Other	1		

*: Fisher test and chi-square analysis were used.

There was no significant difference between hypoglycemic SGA infants and euglycemic SGA infants in terms of sex and with seven females and four males in the former group, and five females and nine males in the latter group ($p > 0.05$). Seven of the hypoglycemic SGA infants and 13 of the euglycemic SGA infants were delivered vaginally ($p > 0.05$).

As shown in Table III, there was no significant difference between hypoglycemic and euglycemic SGA infants in terms of birth weight, birth length, head circumference, ponderal index or presence of twin pregnancy.

Blood glucose values of hypoglycemic SGA neonates at two, three, six, 12, 24 and 48 hours of age are shown in Table IV. The first six postnatal hours and the 48th hour were the most commonly encountered ages for hypoglycemia in SGA neonates. Five infants in the study group had symptoms of hypoglycemia. These symptoms included irritability (n: 4), tachypnea (n: 2), poor feeding (n: 2), cyanosis (n: 2), high-pitched cry (n: 2) and tremors (n: 1).

Table III: Comparison of Hypoglycemic and Euglycemic SGA Infants in Terms of Birthweight, Birth Length, Head Circumference, Ponderal Index*

	Euglycemic Infants (n: 14)	Hypoglycemic Infants (n: 11)	P Value
Birthweight (g)	2085,71 ± 358.1	2027,27 ± 216.06	> 0.05
Birth length (cm)	46.57 ± 2.24	45.54 ± 2.21	> 0.05
Head circumference (cm)	32.10 ± 1.53	31.68 ± 1.66	> 0.05
Ponderal index	2.13 ± 0.18	2.12 ± 0.46	> 0.05

* Mean ± SD, Student's-t test was used.

Table IV: Blood Glucose Values of Hypoglycemic SGA Neonates in the First 48 Hours of Life

Postnatal Age (hours)	n	Blood Glucose (mg/dl)
2	5	25, 30, 33, 34, 35
2	3	25, 34, 36
6	4	30, 35, 35, 38
12	2	35, 39
24	1	44
48	3	35, 38, 40

Discussion

In the present study, we found the incidence of SGA neonates born after 37 completed weeks to be 6.4 percent. Similar results have been reported by others[8, 17, 20].

The definition of hypoglycemia is controversial. There is a wide variation in the definitions given, ranging from a glucose concentration of < 18 mg/dl to < 72 mg/dl[1, 5, 13, 20-22]. The definition of Srinivasan and colleagues[13] was accepted in our study. The reported incidence of hypoglycemia in SGA infants, a high-risk group for hypoglycemia, ranges between 12.7 and 29 percent[12, 16, 23]. In our study the incidence of hypoglycemia in SGA infants was found to be 44 percent. This difference may be related to the fact that the other studies, except for one[12], did not screen or test for glucose as often as we did. In the above-mentioned exceptional study, the incidence of hypoglycemia in SGA neonates was found to be 14.7 percent using Srinivasan et al's[13] definition. This difference between the two works may be related to the difference between birthweights of SGA neonates. In Holtrop's[12] study, the mean birthweight was 2,498 ± 363 grams in hypoglycemic SGA neonates, and 2,512 ± 336 in euglycemic SGA neonates. In our study, the mean birthweight was 2,027 ± 216 grams in nypoglycemic SGA

neonates and 2,085 ± 358 grams in euglycemic SGA neonates. Lower birth weights of SGA babies lead to more decreased stores of fat and glycogen, resulting in more severe and frequent episodes of hypoglycemia.

In the present study, 54 percent of hypoglycemic SGA infants had no clinical symptoms. This confirms the results of previous reports[1, 2, 12, 24]. In the present study, hypoglycemia was reported in 65 percent of hypoglycemic SGA infants at six hours after birth. Holtrop[12] reported that the mean age at which hypoglycemia occurred was 6.1 hours in SGA neonates. Sexson[25] reported that hypoglycemia occurs more frequently between 0.5 to 12 hours after birth. In the present study, three infants were found to be hypoglycemic at 48 hours of age, and in two of these, blood glucose values were normal for the first 48 hours. Similar results were reported by Holtrop[12].

On the basis of our findings, we recommend that SGA neonates be carefully screened for hypoglycemia for at least 48 hours, and the first six hours of life should be accepted as the most critical hours. Clinical signs alone should not be accepted as indicators of hypoglycemia.

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