PREVENTION OF HYPOGLYCEMIA: A CONTROLLED EVALUATION OF SUGAR FORTIFIED MILK FEEDING IN SMALL-FOR-GESTATIONAL AGE INFANTS

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ABSTRACT

The study population included 110 term healthy small-for-gestational age (SGA) infants having a blood sugar of >30 mg/dl at the age of <30 minutes. They were randomized into two groups; (a) Group I (study group) received sugar-fortified milk formula and (b) Group II (control group) received standard milk formula. A minimum of 80 ml/kg/24 hour of milk was given. The first feeding was given within 45 minutes of birth and subsequently at 2 hours of age and then every 2 hourly till the age of 24 hours. The blood sugar (initial within 30 minutes of birth) was monitored at the age of 2, 4, 12 and 24 hours by dextrostix. The babies on fortified feeds received significantly ($p<0.001$) higher amount of carbohydrate (8.1 mg/kg/min) as compared to those on standard milk (5.1 mg/kg/min). The incidence of hypoglycemia was reduced significantly ($p<0.01$) by the sugar-fortified feeds. The mean blood sugar level in babies receiving fortified feeds was significantly higher at all the ages as compared to those receiving standard feeds. Nearly all the babies who subsequently developed hypoglycemia had a preceding blood sugar value of less than 60 mg/dl. The study highlights that sugar-fortified milk feeds are useful in preventing hypoglycemia in SGA infants and should be routinely recommended along with breast feeding in developing countries especially when facilities for monitoring of blood sugar are unsatisfactory or not available.

Key words: *SGA infants, Sugar-fortified milk feeds, Hypoglycemia.*

Hypoglycemia which is one of the common metabolic problems of the neonates, is associated with neuromotor developmental retardation. The overall incidence varies from 0.2 to 11.4%(1). However, an incidence as high as 15 to 30% has been reported in small-for-gestational age (SGA) infants(2-7). The utility of oral or gavage feedings, with 5 or 10% dextrose water, for reducing this high incidence, has been suggested but there is hardly any objective evaluation of this recommendation. Moreover, only a limited amount of 10% dextrose water can be given orally (due to high osmolality of around 600 m Osm/L), which may not meet the high carbohydrate requirements of these babies. Sugar-fortified milk formula has been found to be useful in reducing hypoglycemia, to a significant proportion, in large-for-gestational age infants(8). This controlled trial was undertaken to establish whether the sugar-fortified milk formula would be helpful in the prevention of hypoglycemia in SGA infants as well.

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Material and Methods

The study population included 110 term (>37 weeks of gestation) uncomplicated SGA infants (<10th percentile)(9) born at the All India Institute of Medical Sciences Hospital, New Delhi over a period of one year. The neonates with birth asphyxia, respiratory distress, septicemia, metabolic disorders, *i.e.,* hypocalcemia, polycythemia and hypoglycemia (blood sugar <30 mg/dl) at or before 30 minutes of age and those requiring intravenous infusion were excluded from the study. The babies thus selected were transferred to the Neonatal Intensive Care Unit and were randomized into two groups: (*a*) *Group I* (study group)–received fortified feeds which were prepared by adding one sachet (containing 1.5 g) of powdered sugar to 30 ml of standard milk formula and (*b*) *Group II* (control group)–received standard milk formula. The standard milk formula contained 60 g of carbohydrate (lactose 18 g, sucrose 18 g, maltodextrin 24 g) per 100 g of milk powder. The administration of minimum amount of at least 80 ml/kg/24 hours was ensured. The standard milk formula provided carbohydrates at a rate of 5 mg/kg/minute while fortified feeds were calculated to deliver 7.8 mg/kg/minute. Some neonates accepted larger volumes of feeds which were given *ad lib* and the records maintained. The first feeding was offered within 45 minutes of birth and subsequently at 2 hours of age and then every 2 hourly till the age of 24 hours.

The blood sugar(the first one at the age of <30 minutes) was monitored at the age of 2, 4, 12 and 24 hours by dextrostix (Ames Dextrometer). Dextrostix procedure was diligently followed as recommended by the manufacturer in order to ensure accuracy of results. During the course of study, any baby showing hypoglycemia (blood sugar <30 mg/dl) was taken off the study protocol and treated by intravenous dextrose. After 24 hours all infants whether on standard or fortified feeds, were transferred to the mother and breast fed. Blood sugar was monitored 12 hourly for the next 48 hours.

Various relevant antenatal, intranatal and immediate post-natal events were observed and recorded. Rectal temperature of the baby was taken immediately on transfer to the nursery. Capillary blood hematocrit (PCV) was assessed at the age of 3h and 24h. Any evidence of intolerance to either of the feed, *i.e.,* refusal to such on bottle, vomiting, diarrhea, distension of abdomen, *etc.* were looked for and recorded.

The results were analyzed using the Chi-square and Student's 't' tests.

Results

The demographic characteristics of the newborns randomized into fortified and standard feeds are shown in *Table I.* The neonates on sugar-fortified feeds received significantly (p0001) higher amount of glucose as compared to those on standard feeds. The other core characteristics of the two groups, *i.e.,* birth weight, gestation, rectal temperature, time of first feed, amount of feed and hematocrit (*Table I*) were comparable. SGA infants in both the groups were of malnourished (asymmetric IUGR) type. The results of blood glucose values, in the study group and control group obtained with dextrostrip method are shown in *Table II.* The incidence of hypoglycemia in the study group was significantly lower ($p<0.01$), compared to the incidence in the control group (*Table III*). The initial blood sugar (within 30 minutes of age) was comparable in the two groups

but subsequently there was a significant rise in blood sugar level of babies receiving fortified feeds (*Table II*). In standard feeding regimen, the number of babies developing hypoglycemia at the age of 2h, 4h, 12h and 24h were 1, 4, 3, and 3, respectively while in the fortified group, hypoglycemia was observed only in two babies (*Table III*). In babies receiving standard milk feeds the peak blood glucose level (mean 52.2 mg/dl) was achieved at the age of 24h while babies receiving fortified feeds attained a mean blood sugar level of 60.8 mg/dl at the age of 4 hours (*Table II*). After shifting the babies to their mothers, four neonates belonging to the standard feed group developed hypoglycemia at the ages of 34h, 40h, 44h and 48h, respectively while all the infants in the fortified feed group maintained normal blood sugar levels. The various feeding problems observed in Group I and Group II ($p>0.05$) were refusal to suck on the bottle (6 cases and 3 cases, respectively), vomiting (3 cases and 2 cases, respectively) and diarrhea (4 cases and 2 cases, respectively). No baby in either group developed distension of abdomen. In cases of unacceptability (refusal of bottle feeding), which lasted for 7-12h, gavage feeding was given. Both vomiting and diarrhea were of transient nature.

TABLE I—*Basic Characteristics of Population (Mean ± SD)*

Characteristics	Study group (n = 55)	Control group (n = 55)
Birth weight (g)	1910 ±260	1940 ± 230
Gestation (wks)	38.6 ±1.2	38.4 ± 1.1
Rectal temp (°C)	36.6 ±0.4	36.5 ± 0.3
Time of first feed (min)	25.8 ±4.6	24.6 ± 5.1
Amount of glucose* (mg/kg/minute)	8.1 ±0.9	5.1 ± 0.7
Hematocrit		
3 h	63.6 ±3.4	64.2 ± 3.6
24 h	56.8 ±3.2	56.4 ± 2.8

* $p<0.001$

Discussion

The requirements of glucose in SGA infants are high in order to maintain normal blood sugar levels(6,7). In the present study, the incidence of hypoglycemia in

TABLE II—*Blood Sugar Levels in Two Groups (Mean ± SD)*

Feeding group	Blood sugar at different ages (mg/dl)				
	Within 30 min	2h	4h	12h	24h
Study	42.6 ± 6.6 (n = 55)*	53.4 ± 6.8 (n = 53)	60.8 ± 6.3 (n = 53)	64.4 ± 7.4 (n = 53)	68.2 ± 6.1 (n = 53)
Control	43.4 ± 6.2 (n = 55)	45.6 ± 7.0 (n = 54)	46.8 ± 7.8 (n = 50)	49.9 ± 6.6 (n = 47)	52.2 ± 6.1 (n = 44)
	p>0.05	<0.001	<0.001	<0.001	<0.001

* n indicates number of babies left after excluding those who developed hypoglycemia.

TABLE III—*Feeding Group and Hypoglycemia*

Group	Total No. of babies	Babies developing hypoglycemia (%)
Study	55	2 (3.6)
Control	55	11 (20.0)

$p<0.01$; Odds ratio 0.15
95% confidence interval: 0.03, 0.71

infants, receiving sugar-fortified milk formula, was nearly one-fifth compared to those feed with standard milk formula ($p<.01$). It could be because of maintenance of higher blood glucose levels in babies receiving fortified feeds in whom hypoglycemia was detected only upto the age of 2 hours when the mean blood sugar rose to 53.4 mg/dl while in babies receiving standard milk formula, hypoglycemia occurred even up to the age of 24 h when the mean blood glucose was only 52.2 mg/dl. It would appear that when blood sugar level exceeds 60 mg/dl, the risk of hypoglycemia is minimal. Further when the babies were shifted to breast feeding, some of the babies (7.3%) on standard feed developed hypoglycemia while all the neonates on fortified feeds were able to maintain normal blood sugar which again could be because of maintenance of higher blood glucose, as well as building up of some glucose reserves. These observations are in accordance with those obtained with the use of fortified milk feeds in large-for-gestational age infants(8).

The fortification of the milk feeds was found to be safe; various problems, *i.e.,* refusal to suck on bottle, vomiting, *etc.,* encountered with fortified feeds, were comparable to the standard milk feed. Similar observations were also made in our previous study. There was no significant alteration in the osmolality after fortification (osmolality of fortified feed and standard feed being 363 mOsm/l and 290 mOsm/l, respectively). However, in accordance with the previous study, more babies on fortified feeds (10.9%), compared to that on standard feeds (5.5%), did not relish the taste. It may be explained on the basis of rather too sweet taste or developing satiety earlier with fortified feeds.

In the light of these observations, it is recommended that SGA infants should not only be fed early but preferably with sugar-fortified milk feeds to reduce the incidence of hypoglycemia. In view of the fact that many neonatal units in the developing countries do not have adequate facilities to monitor blood glucose levels, it is recommended that in addition to breast feeding which should be initiated as early as possible, routine supplementation with fortified milk feeds preferably with a cup and spoon should be considered in all term SGA neonates especially in the first 12-48 hours of life. The optimum amount of fortified milk feeds to minimize the risk of hypoglycemia in breast fed babies need to be further examined.

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NOTES AND NEWS

THIRD SUMMER COURSE IN BIOSTATISTICS–1993

The Department of Biostatistics, CMC, Vellore, jointly with the Epidemiology and Health Management Network of India (EPIDMAN), will be organizing 5 intensive, application-oriented 3-week courses from June 14 to July 2, 1993; (*a*) Introduction to Biostatistics and Hospital Statistics: to develop skills in proper collection, use and interpretation of vital, health and hospital statistics; (*b*) Epidemiological methods and Analysis: to describe disease frequencies, design and analysis of cohort, cross-sectional, and case-control studies as well as clinical trials; (*c*) PC-based Statistical software in health care: both Advanced level and Introductory; (*d*) Applied Multivariate Techniques, to better use of statistical procedures, in different multivariate contexts; (*e*) Demographic analysis and their Biostatistical application, dealing with formal and practical demography. All courses include laboratory and computer time.

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