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Can prophylactic oral dextrose solution prevent hypoglycemia in high risk newborns?

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Abstract

Prophylactic oral dextrose gel recommended to prevent hypoglycaemia in high risk babies is not readily available and affordable. This study was therefore conducted to find out if oral dextrose solution decreases the incidence of hypoglycaemia in high risk neonates. This study included 186 high risk newborns. Oral 10% dextrose 2ml/kg was given at 30 minutes, 2, 6 and 12 hours of life, along with direct breastfeeding. Capillary blood glucose measurement was monitored at 2, 6, 12, 24, 48 and 72 hours of life. Low blood sugar levels were confirmed by simultaneous venous blood sampling. Statistical tests used were chi square for proportions and ANOVA for means. Of the 186 high risk babies maximum babies were small for gestational age (n = 68, 36.5%). Among the high risk babies, 7 (3.7%) developed hypoglycaemia. All were asymptomatic. A higher proportion of hypoglycaemia was seen IUGR babies (n = 2/9, 22.2%) and in those delivered by caesarean section (n =3/71, 4.2%). Compared to the incidence of hypoglycaemia (7.2%) in the historical control group the incidence of hypoglycaemia (3.7%) in interventional group was lower though statistically not significant (p=NS). There is a decrease in the incidence of hypoglycemia in high-risk infants given prophylactic oral dextrose solution. However, this trend was not statistically significant.

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INTRODUCTION

Hypoglycemia is a commonly encountered problem among neonate [1]. Ten to fifteen percent of neonates are at high risk for hypoglycemia [2]. Hypoglycemic episodes in newborns can be symptomatic or asymptomatic. Whether symptomatic or asymptomatic, hypoglycemic episodes cause not only short term complications but also lead to long term neurodevelopmental problems [3]. Owing to the long-term consequences of hypoglycemia it is important to anticipate and prevent hypoglycemia especially asymptomatic hypoglycemia in high-risk newborns.

Widely practiced preventive measure for hypoglycemia in normal high-risk newborns in most newborn care centers is early breast feeding. Studies have shown that oral dextrose gel application on the buccal mucus membrane of newborns not only prevented but also corrected hypoglycemia [4][5][6]. However oral dextrose gel may not be readily available in resource limited settings and even if available is expensive. This study was therefore conducted to see the effectiveness of oral dextrose solution

administration to prevent hypoglycemia in high-risk newborns as it is feasible and cost effective.

METHODOLOGY

This study was conducted in a tertiary health care hospital, from January 2019 to May 2020 after getting the Institutional Medical Ethical Committee approval (PG dissertation/02/2019/57). Study was registered in Clinical Trials Registry of India (REF/2020/10/037649-CTRI). Newborns meeting the inclusion criteria were enrolled in the study after obtaining written informed consent from the parents. Inclusion criteria were high risk babies including late preterm, Infant of diabetic mothers (IDM), Large for gestational age (LGA), Small for gestational age (SGA) and Intrauterine growth restricted babies (IUGR). Babies with birth asphyxia, respiratory distress, major congenital anomalies and those requiring NICU admission were excluded. For this study purpose a blood glucose value of <47mg/dl (2.6 mmol) was considered as hypoglycemia [7].

Sample size: With an estimated prevalence of hypoglycemia in high risk babies of 11% and allowing an error of 5% sample size for the study was calculated to be 186.

All consecutive high-risk babies were included in the study till the sample size was attained. They were given oral dextrose solution (2ml/kg of 10% dextrose) in two divided doses at 30 minutes, 2 hours, 6 hours and 12 hours and started on direct breastfeeds as soon as possible. Feeds were continued every 2-3 hours on demand and the duration of each feed was not less than 20 minutes. Capillary blood glucose measurement using point of care glucose strips was taken at 2, 6, 12, 24, 48 and 72 hours of life. Blood glucose values of <47mg/dl were confirmed by simultaneous venous blood sample values. Babies with asymptomatic hypoglycaemia were treated only with oral feeds/ paladai feeds. Any baby having more than two episodes of hypoglycaemia and babies with symptomatic hypoglycemia were admitted in NICU and managed as per protocol.

The ethical committee did not permit the conduct of randomised control trial. Therefore the incidence of hypoglycemia documented in the case records of high risk newborns during the previous calendar year was taken as control.

Data including basic details of gestational age, mode of delivery, birth weight, date of birth, risk factors in mother, anthropometry, blood sugar values were recorded in a pretested standardized proforma and entered into Microsoft Excel spread sheet (2010) and analysed using SPSS version 16 statistical software. Chi square test was used for data analysis for qualitative variables. One way ANOVA was used for Quantitative data.

RESULTS

Our study included 186 high risk babies out of which maximum babies were SGA (n= 68, 36.5%). Distribution of high-risk babies and incidence of hypoglycemia are given in **Table 1**

In our study, among 186 babies 7 (3.7%) babies had hypoglycemia. They were all asymptomatic. Among the babies in high-risk group, highest proportion of hypoglycemia was seen in babies with IUGR (n= 2, 22.2%) followed by LGA (n=1; 6.2 %) (Table 1). Out of 71 babies delivered by LSCS, 3 (4.2%) developed hypoglycemia and out of

Table 1 Distribution of babies according to high risk category and incidence of hypoglycemia

Category	Number (n)	Number of babies who developed hypoglycemia	Relative risk	P value
Late preterm	58 (31.1%)	1 (1.7%)	Ref	0.06
Infant of diabetic mother (IDM)	35 (18.8%)	1 (2.8%)	1.72	0.32
Large for gestational age (LGA)	16 (8.6%)	1 (6.2%)	3.8	0.78
Small for gestational age (SGA)	68 (36.5%)	2 (2.9%)	1.7	0.58
Intra uterine growth restriction (IUGR)	9 (4.83%)	2 (22.2%)	16.2	0.63
Total	186	7 (3.7%)		

115 babies delivered by SVD, 4 (3.4%) developed hypoglycemia. Comparing among the high-risk groups, the relative risk of developing hypoglycemia was 16.2 times more for IUGR babies when compared to late preterm babies. Compared to high-risk babies delivered by SVD, the relative risk of developing hypoglycaemia in babies born to LSCS mothers was 1.2 times higher (p value=0.79, CI=0.17 to 3.7). It was observed that according to high-risk category, lowest mean blood sugar was at 2 hours with steady increase in sugar values except for a dip in IDM babies at 6 hours and LGA babies at 12 hours as shown in the **Figure 1**. The lowest sugar values were observed in IUGR babies who subsequently showed a steady rise in sugar values.

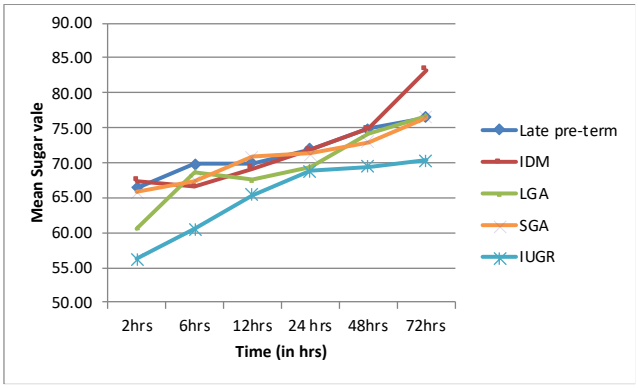

Figure 1 Showing the pattern of sugar values in high risk group (oral dextrose given)

There were 360 high risk newborns in the previous calendar year out of which 26 babies had documented hypoglycemia (7.2%). This group formed the control in our study. Comparing the incidence of hypoglycemia to this historical control groups it was observed that there was no statistically significant difference in incidence of hypoglycemia between the control and the intervention groups as shown in **Table 2**.

DISCUSSION

Undertaken within the precincts of a tertiary healthcare institution from January 2019 to May 2020, this research garnered the imprimatur of the Institutional Medical Ethical Committee and was duly registered in the esteemed Clinical Trials Registry of India. Neonates, meeting predefined criteria, were graciously enrolled with parental assent. Oral dextrose solution was tenderly administered, whilst vigilant surveillance of blood glucose levels ensued. In light of ethical imperatives, this inquiry juxtaposed hypoglycemia occurrences with antecedent archival data, thus eschewing the rigors of a randomized controlled trial.

In this study we observed that maximum high-risk babies were SGA (36.5%) followed by late preterm babies (31.1 %). Other investigators have found a lower incidence of SGA in their studies. While the incidence was 11% in a study done by Deborah et al, Bromiker et al in his study observed the percentage of SGA babies to be 6.2% [8][2]. This high proportion of SGA babies in our study might be due to higher number of SGA babies being delivered in India. Black found the estimated prevalence of SGA to be highest in South Asia and in Sahelian countries of Africa. India has the world's largest number and a high proportion of SGA births [9][10].

In this study babies born by LSCS had a higher incidence of hypoglycemia (4.2%) when compared to babies born by spontaneous vaginal delivery (3.4%) though not statistically significant. Similar

Table 2 Comparison of Incidence of Hypoglycemia Between Control and Interventional Group among High Risk Newborns

Category	Interventional group (n= 186)	p Value	RR (Control group as reference)	Confidence interval
Late preterm	1 (1.7%) (n= 58)	0.13	0.25	0.03 to 1.8
Infant of diabetic mother	1 (2.8 %) (n= 35)	0.16	0.25	0.03 to 2
Large for gestational age	1 (6.2%) (n= 16)	0.86	0.83	0.09 to 7.4
Small for gestational age	2 (3%) (n=68)	0.67	0.72	0.14 to 3.6
Intra uterine growth restriction	2 (22 %) (n= 9)	0.63	1.44	0.31 to 6.5

observation was made by Kumar TJ et al [11] where the incidence of hypoglycemia in babies born by LSCS and vaginal delivery was 41% and 16% respectively [9]. The higher proportion of hypoglycemia in babies born by LSCS could be because of delay in initiating feeds, difficulty in feeding or nursing staff paying more attention to mothers.

We observed that among the high-risk group, the risk of developing hypoglycemia was 16.2 times more for the intrauterine growth restriction babies compared the other risk categories. The reason for hypoglycaemia in this high risk category group can be due to poor glycogen stores and inadequate gluconeogenesis. Bromiker et al [2] observed that among the high risk babies, incidence of hypoglycemia was 10.6% in low birth weight, 9.1% in IDM and 5.8% in SGA while we observed the same to be 22.2% in IUGR babies, 2.9% in SGA and 2.8% in IDM mothers which is different from his observations [2]. The differences could be due to difference in sample size.

In our study the trend of mean blood sugars among high-risk newborns who received oral dextrose showed low blood sugars at initial 2 hours of life thereafter steadily increasing except for 2 groups of babies. Sugar values in IDM and LGA babies showed a dip at 6 and 12 hours of life respectively probably because of reactive fall in blood sugar values. In a study done by Kumar TJ et al [11] low blood sugar values were observed at 2 hours in 51%. at 6 hours in 31%, 16% at 12 hours and 2% in 24 hours. Absence of low sugar values beyond 2 hours in our study could be because of better breast feeding by our mothers.

Compared to historical control group, the proportion of children with hypoglycaemia in high risk babies was lower although not significantly different statistically. Other investigators [8][4] have found oral application of dextrose gel to be effective in in treating hypoglycemia and increased the likelihood of exclusive breastfeeding. However, in study from Thailand, the investigators found no significant difference between control and interventional group in the blood sugar values except in babies born to IDM with birth weight lower than 2.5 kg where the blood sugar values were higher in the intervention group. They used 24% oral sucrose solution and not dextrose gel [12]. This is similar to our findings. Perhaps oral dextrose or sucrose solution is not as effective as oral dextrose gel because of the difference in the rates of absorption. Oral dextrose solution might be absorbed faster, reach peak level earlier and perhaps causes a reactive fall in blood sugar values. More studies comparing the efficacies of oral dextrose / sucrose solutions and oral dextrose gel have to be conducted to understand the phenomenon better. The purpose of the study described earlier was to determine how neonatal hypoglycemia affects cognitive development over the long run. The study examined cognitive functioning, motor abilities, and other developmental domains through thorough assessment, which included standardized tests and developmental evaluations. The study's conclusions provide important new information about the possible effects of newborn hypoglycemia on the early stages of neurodevelopment. [13]

Conclusion

Out of 186 high risk babies for hypoglycemia, IUGR babies had the highest incidence of hypoglycemia (22.2%) Overall incidence of hypoglycemia (3.7%) showed a trend to be lower in the intervention group when compared to a historical control group (7.2 %) though it did not reach significance. However, in view of the findings of this study, a larger study is required to find out if this trend reaches clinical significance. If so, it will be a cost-effective intervention to prevent hypoglycemia in high risk newborns

What is already Known?

High risk infants are prone to develop hypoglycemia

What this study adds?

Oral 10% dextrose solution administered to high risk infants prophylactically did not significantly reduce the incidence of hypoglycemia in the study sample although there is a trend in that direction.

Limitations

The study did not have a concurrent control group since the ethical committee did not give approval for the same. Study on a larger sample size with concurrent controls might have yielded a more convincing outcome.

Ethical Approval

This research was conducted in accordance with guidelines established by the Institutional Animal Ethic Committee (IAEC). Approval number: PG DISSERTATION/02/2019/57 dated 27.02.2019 was obtained from the IAEC prior to the commencement of the study. All procedures involving animals were carried out with care and consideration for their welfare, in compliance with ethical standards and regulations.

Author Contribution

All authors made substantial contributions to the conception, design, acquisition, analysis, or interpretation of data for the work. They were involved in drafting the manuscript or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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Author Contribution

All authors have contributed significantly in the research and write up.

REFERENCES

[1] A. Sharma, A. Davis, and P. S. Shekhawat, "Hypoglycemia in the preterm neonate: etiopathogenesis, diagnosis, management and long-term outcomes," *Transl Pediatr*, vol. 6, no. 4, pp. 335–348, Oct. 2017. [Online]. Available: http://tp.amegroups.com/article/view/16974/17488. Accessed: 7th June 2020.

[2] R. Bromiker et al., "Early neonatal hypoglycemia: incidence of and risk factors. A cohort study using universal point of care screening," *J Matern Fetal Neonatal Med*, vol. 32, pp. 786–792, 2019.

[3] C. J. D. McKinlay et al., "Association of Neonatal Glycemia With Neurodevelopmental Outcomes at 4.5 Years," *JAMA Pediatrics*, vol. 171, no. 10, Oct. 2017. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5710616/. Accessed: 7th June 2020.

[4] P. J. Weston et al., "Oral dextrose gel for the treatment of hypoglycaemia in newborn infants," *Cochrane Database of Systematic Reviews*, May 4, 2016. [Online]. Available: http://doi.wiley.com/10.1002/14651858.CD011027.pub2. Accessed: 20th June 2020.

[5] T. Edwards et al., "Oral dextrose gel for the treatment of hypoglycaemia in newborn infants," *Cochrane Database of Systematic Reviews*, Mar. 18, 2022. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/35302645/. Accessed: 24th June 2023.

[6] T. Edwards et al., "Oral dextrose gel to prevent hypoglycemia in at-risk newborns," *Cochrane Library*, May 17, 2021. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8127543/. Accessed: 23rd June 2023.

[7] P. J. Rozance and W. W. Jr. Hay, "Describing hypoglycemia - definition or operational threshold?," *Early Human Development*, vol. 86, no. 5, pp. 275, May 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900507/. Accessed: 8th June 2020.

[8] D. L. Harris et al., "Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial," *Lancet*, vol. 382, no. 9910, pp. 2077–2083, Dec. 21, 2013.

[9] R. E. Black, "Global Prevalence of Small for Gestational Age Births," *Low-Birthweight Baby: Born Too Soon or Too Small*, pp. 1–7, 2015.

[10] S. Yadav and D. Rustogi, "Small for Gestational Age: Growth and Puberty Issues," *Indian Pediatr*, vol. 52, pp. 135–140, 2015.

[11] T. J. Kumar, M. Vaideeswaran, and A. T. Seeralar, "Incidence of hypoglycemia in newborns with risk factors," *Int J Contemp Pediatr*, vol. 5, pp. 1952–1955, 2018.

[12] S. Surachaidungtavil, P. Chanvorachote, and N. Suksumek, "A Randomized Control Trial of Oral Sucrose Solution for Prevention of Hypoglycemia in High Risk Infants," *In Vivo*, vol. 34, no. 3, pp. 1493–1497, Jun. 2020.

[13] M.-Q. Wang, Y.-N. Zheng, and Y. Zhuang, "Oral glucose gel in the prevention of neonatal

hypoglycemia: A systematic review and meta-analysis," *Medicine*, vol. 102, no. 48, p. e36137, Dec. 01, 2023.