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Comparative Study of Glycemic Status of Very Low Birth Weight Neonate Treated with 10% Dextrose Versus 05% Dextrose

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Key words:
Very low birth weight, hypoglycemia, hyperglycemia, morbidity, mortality

Abstract:

Background: *Low birth weight and preterm birth account for major public health problems in developing countries (including Bangladesh) and are major determinants of public health status. Metabolic complication of low birth weight neonate is common including hypoglycemia as well as hyperglycemia. Both of which is associated with short term mortality and long-term morbidity.*

Objectives: *The objective of this study was to compare the glycemic status of very low birth weight neonate when treated with 10% dextrose and 5% dextrose.*

Methods: *The study was conducted in Department of Pediatrics in Shahid Ziaur Rahman Medical College Hospital, Bogra. Study period was from march 2016 to august 2016. Neonates were divided into two groups, group 1 received 10% dextrose and group 2 received 5% dextrose. Baseline blood glucose and six hourly blood glucose monitored. Total five blood glucose value including one baseline value were taken from each neonate to compare the effect of blood glucose on dextrose infusion in between two group. Total 60 patients were included in the study.*

Result: *Baseline blood sugar were within normal ranges between 2.5 to 7.0 mmol/ l. At 6, 12, 18- and 24-hour hyperglycemia develop in 21(58.3%), 19(52.8%),15(41.7%) and 12(33.3%) of patient in 10% dextrose group respectively. In 5% dextrose group corresponding number is 6(25%),5(20,8%),2(8.3%) and 2(8.3%) at 6, 12,18 and 24 hours respectively. The difference between two group is statistically significant ($p < 0.05$). On the other hand, hypoglycemia developed in 2(8.3%) patient at 12 hours in 5% Dextrose group and only 1(2.8%) at 6 hours in 10% Dextrose group.*

Conclusion: *In this study we found that VLBW neonate developed hyperglycemia if they are treated with 10% Dextrose. On the other hand, VLBW neonate treated with 5% Dextrose maintain normal blood glucose without development of hypoglycemia or hyperglycemia.*

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Introduction:

Low birth weight (LBW) and preterm birth (PTB) represent major public health problems in developing countries and are major determinants of perinatal survival as well as infant morbidity and mortality.[1,2] The Preterm babies weighing less than 1500 grams – very low birth weight (VLBW), are of major concern because of maximum perinatal morbidity and mortality found in this group.[3] Every year it is estimated that 18 million LBW babies are born globally, making up nearly 16% of all live births.[4] More than 95% of the LBW babies are born in developing countries.[5] VLBW infants comprise between 4-8% of live-births but about one-third of deaths during the neonatal period occur in this group of newborns.[6,7]

VLBW baby are prone to develop various complication including apnea, (60.1%), hypothermia (56.5%), respiratory distress syndrome (RDS 44.6%), anemias, hyperbilirubinemia (45.2%) glucose abnormalities (63.1%).[8]

Preterm VLBW neonates have the potential problem of hypoglycemia due to diminished hepatic glycogen stores, which can be potentiated by conditions frequently present in this birth weight group: asphyxia, cold stress, hypoxia, polycythemia, intrauterine growth restriction, maternal diabetes.[9]

Neonatal hypoglycemia causes neurologic impairment.[10] The neonatal hypoglycemic brain injury (NHBI) depends on the duration of hypoglycemia rather than its severity .[11]Recurrent or protracted hypoglycemia seems to be a more sinister risk factor rather than a single low value of blood sugar .[12,13]

Hyperglycemia will lead to osmotic diuresis, cause changes in turn lead to effects such as electrolyte disturbances, dehydration and intraventricular bleed.

Percentage of glucose infusion appears to be a crucial factor in the development of hyperglycemia in these neonates. [14] The risk of hyperglycemia also increased with increasing dextrose dose. [15] There was a highly significant trend toward an increasing risk of hyperglycemia with decreasing body weight.

So VLBW babies may develop hypoglycemia during 5% dextrose infusion at the same time may develop hyperglycemia on 10% dextrose infusion.

So, the aim of our study is is to determine the effect of 5% dextrose and 10% dextrose administration on VLBW and to evaluate which one can maintain normal blood glucose level without causing significant hypoglycemia or hyperglycemia.

Methods and Materials:

This is experimental comparative study.The study conducted in Department of Pediatrics in collaboration with the Department of Obstetrics and Gynecology in Shahid Ziaur Rahman Medical College Hospital, Bogra. Study Period march March 2016 to August 2016. VLBW neonates admitted in neonatal word of Shahid Ziaur Rahman Medical college Hospital who were delivered in this hospital or home were the study participants. Preterm very low birth weight (weight 1000 gram to 1499 gram) neonate, whose parents gave informed consent to allow their babies to participate in the study, were included in the study. Neonate having the following are excluded from the study:

Neonate with sepsis, infant of diabetic mother, neonate receiving corticosteroid, dopamine and neonate with any congenital anomaly. Following operational definition was used, preterm: Neonate born before 37 completed weeks of gestation, VLBW:1000 gm to 1499 gm, extreme low birth weight: weight less than 1000gm, hypoglycemia: Blood glucose less than 45mg/dl(2.5mmol/L), yyperglycemia: Blood glucose more than 125mg/dl (6.9 mmol/L). Sugar estimation done with "EMP 168 Biochemical Analyzer" (made in German) and "Humalyser 3000" (made in German). A structured questionnaire containing all the variables of interest were used as research instrument.

Procedure:

A baby of suspected VLBW was seen by attending doctor of admission unit and the attending doctor thoroughly informed the investigating doctor. The investigating doctor examined the patient thoroughly and took obstetrical, medical and antenatal history and if patient fulfilled the inclusion criteria were enrolled in the study. Blood sample was taken from baby and sent to laboratory for blood sugar, CBC, CRP and Blood grouping. Baseline blood glucose was done. Patient were selected randomly into two treatment group. Treatment started and blood sugar level were monitored six hourly. Four blood glucose reading

after starting treatment was considered for calculation of result. All clinical and laboratory information were recorded in case record sheet.

Regarding fluid therapy 10% dextrose group got 10% dextrose in aqua and 5% dextrose group got 5% dextrose in aqua at the same rate of 80 ml/ kg during first 24 hours of age. Age above 24 hours 10% dextrose group got 10% dextrose in 0.225% normal saline and 5% dextrose group got 5% dextrose in 0.225% normal saline. The amount of fluid calculated was 100 ml/ kg, 120 ml/kg, 140 mg/ kg, 150 ml/ kg in 2nd, 3rd, 4th, 5th day &above in both group of patients respectively.

Result:

This is an experimental comparative study, total 60 patient were included in the study, 36 in 10% dextrose group (group 1) and 24 in 5% dextrose group (group 2). Table I shows neonatal information of the study patients. The difference of length was statistically significant ($p<0.05$) between two groups. There is no difference in two group in respect to age, sex and weight of the patient. P value reached by unpaired t test.

Table I: Distribution of the study patients by demographic information (n=60)

Neonatal information	Group I(n=36)		Group II(n=24)		P value
	n	%	n	%	
Age (in hrs)					
≤12	25	69.4	20	83.3	
13-24	4	11.1	3	12.5	
25-48	5	13.9	0	0.0	
>48	2	5.6	1	4.2	
Range (min, max)		0.5,360		0.5, 2	
Sex					
Male	22	61.1	14	58.3	0.726
Female	14	36.1	10	41.7	
	Mean ±SD		Mean ±SD		
Weight (kg)	1.23±0.16		1.16±0.16		0.102
Range (min, max)	1.0, 1.5		1.0, 1.4		

Table II: *Distribution of the study patients by gestational age (n=60)*

Gestational age (wks)	Group I (n=36)	Group II (n=24)	P value
	Mean±SD	Mean±SD	
According to LMP	32.2±2.8	31.5±3.2	0.374
Range (min, max)	27, 36	26,36	
According to USG	32.3±2.7	31.3±3.6	0.224
Range (min, max)	28, 36	26, 34	
According to New	32.4±2.9	30.0±6.4	
Ballard score			0.053
Range (min, max)	27, 37	26, 36	

p value reached from unpaired t-test

Table II shows gestational age of the study patients. The difference was statistically not significant ($P>0.05$) between two groups.

Table III: *Medication status of study patients (n=60)*

Name of drug	Group I (n=36		Group II (n=24)	
	n	%	n	%
Dopamine				
Yes	0	0.0	0	0.0
NoAminophiline	36	100.0	24	100.0
Yes	4	11.1	2	8.3
No	32	88.9	22	91.7
Antibiotic				
Yes	36	100	24	100
No	0	0	0	0
Oradexon				
Yes	0	00	0	00
No	36	100	24	100

Table III shows medication of the study patients. The difference was statistically not significant ($P>0.05$) between two group.

Table IV: *Distribution of the study patients by maternal factor (n=60)*

Maternal factor	Group I(n=36)		Group II(n=24)	
	n	%	n	%
ANC	14	38.9	6	25.0
PROM	24	66.67	16	66.67
HTN	4	11.1	2	8.3
Journey during pregnancy	1	2.8	0	0.0
APH	2	5.6	2	8.3
Obesity	1	2.8	0	0.0
Oedema	2	5.6	0	0.0
Trauma during pregnancy	2	5.6	0	0.0
Chicken pox	1	2.8	0	0.0
GOH	1	2.8	0	0.0
High fever	1	2.8	5	20.8
Bipedal oedema	0	0.0	1	4.2
Ascities	0	0.0	1	4.2
None	19	52.8	8	33.3

ANC -antenatal care, APH -Antepartum hemorrhage, GOH -Gross Oligohydramnios, HTN -Hypertension, PROM -Premature rupture of membrane.

Table IV shows comorbidity (maternal factor) of the study patients. It was observed that majority (38.9%) patients had ANC in group I and 6(25.0%) in group II. 24 (66.67%) patients had PROM in group I and 16(66.67%) in group II. Four (11.1%) patients had maternal HTN in group I and 2(8.3%) in group II. Other findings are depicted in the above table.

Table V: *Blood glucose level of study population (n=60)*

Blood sugar level	Group I (n=36)		Group II (n=24)		P value
	n	%	n	%	
Baseline					
Hypoglycemic (<2.5mmol/L)	0	0.0	0	0.0	
Normal	36	100.0	24	100.0	
Hyperglycemic (>7mmol/L)	0	0	0	0	
Mean±SD		5.4 ±1.9		4.4±2.7	[a]0.073
Range (min, max)		2.5, 7.0		2.5, 7.0	
At 6 hrs					
Hypoglycemic (<2.5mmol/L)	1	2.8	0	0.0	
Normal	14	38.9	18	75.0	
Hyperglycemic (>7mmol/L)	21	58.3	6	25.0	
P value baseline vs at 6 hrs		[b]0.002		[b]0.001	
Mean±SD		9.4±6.8		6.1±3.3	[a]0.031
Range (min, max)		1.9, 33.4		2.5, 18.2	

Table V: *Blood glucose level of study population (n=60)*

Blood sugar level	Group I (n=36)		Group II (n=24)		P value
	n	%	n	%	
At 12 hrs					
Hypoglycemic (<2.5mmol/L)	0	0.0	2	8.3	
Normal	17	47.2	17	70.9	
Hyperglycemic (>7mmol/L)	19	52.8	5	20.8	
Mean±SD		8.5±5.6		6.0±2.5	[a]0.044
Range (min, max)		3.2, 30.6		2.3, 14.5	
P value baseline vs at 12rs		[b]0.004		[b]0.001	
At 18 hrsHypoglycemic (<2.5mmol/L)	0	0.0	0	0.0	
Normal	21	58.3	22	91.7	
Hyperglycemic (>7)	15	41.7	2	8.3	
Mean±SDRange (min, max)		7.7±4.43.326.7		5.7±2.03.2, 13.9	[a]0.041
P value baseline vs at 18rs		[b]0.016		[b]0.001	
At 24 hrsHypoglycemic (<2.5mmol/L)	0	0.0	0	0.0	
Normal	24	66.7	22	91.7	
Hyperglycemic (>7mmol/L)	12	33.3	2	8.3	
Mean±SDRange (min, max)		7.5±3.93.2, 26.7		5.7±2.13.0, 14.2	[a]0.041
P value baseline vs at 24rs		[b]0.028		[b]0.001	

a -p value reached from unpaired t-test b -p value reached from paired t-test

Table V shows blood glucose level of the study patients. P value baseline vs at 6 hrs in both group is statistically significant. At six-hour 2.8% patient developed hypoglycemia and 58.3 % patient developed hyperglycemia in 10% dextrose group while none of the patient developed hypoglycemia but 25% of patient developed hyperglycemia in 5% dextrose group. P value is statistically significant.

Mean blood glucose at 12 hours was 8.5±5.6 mmol/L in group I and 6.0±2.5 mmol/L in group II. P value baseline vs at 12 hours was significant in both group. P value compared to two group is also significant. At 12 hour no patient developed hypoglycemia in 10% dextrose group but 8.3% of patient of 5% dextrose group developed hypoglycemia. At the same time hyperglycemia developed 52 % of patient in 10% dextrose group and 20.8% of patient in 5% dextrose group.

Mean blood glucose at 18 hours was 7.7±4.4 mmol/L in group I and 5.7±2.0 in group II. P value baseline vs at 18rs was significant in both groups. P value compared to two group is also statistically significant. At 18 hour no patient developed hypoglycemia in both groups but hyperglycemia developed 41.7 % in 10% dextrose group and 8.3 % in % dextrose group. P value is statistically significant.

Mean blood glucose at 24 hours was 7.5±3.9 mmol/L in group I and 5.7±2.1 mmol/L in group II. P value baseline vs at 24rs was statistically significant in both groups. P value compared to two group is statistically significant. At 24 hour no patient developed hypoglycemia in both groups but hyperglycemia developed in 33.3% of patient in 10% dextrose group and 8.3% patient in 5% dextrose group. P value is statistically significant.

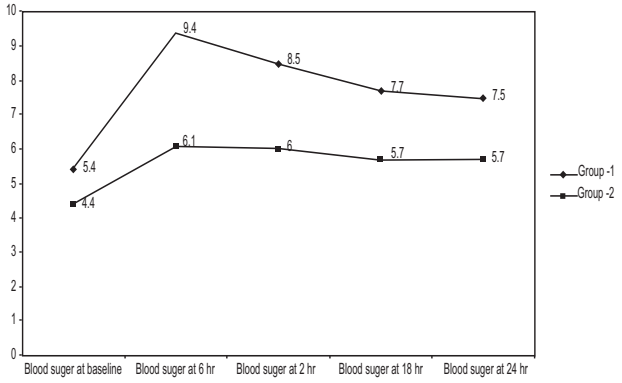

Fig.-1: *Line diagram shows trends of blood glucose in two groups of patients.*

Figure 1 shows trends of blood glucose in two groups of patients. This line diagram is based on mean blood glucose value of two groups at different observation time, that is at baseline, at six hour, at twelve hour, at eighteen hour and at twenty four hour. Mean blood glucose of group I remain above the normal range and of group II remain within normal ranges.

Figure 2 shows frequency of normal blood sugar, hypoglycemia and hyperglycemia in group I patient. At baseline all patient has normal blood sugar level. Ay 6-hour 58.3% patient develop hyperglycemia and 2.8% patient develop hypoglycemia, rest of the patient have normal blood sugar. At 12hour, 18 hour and 24 hour none of the patient develop hypoglycemia and hyperglycemia develop 52.8%, 41.7% and 33.3% of patient respectively.

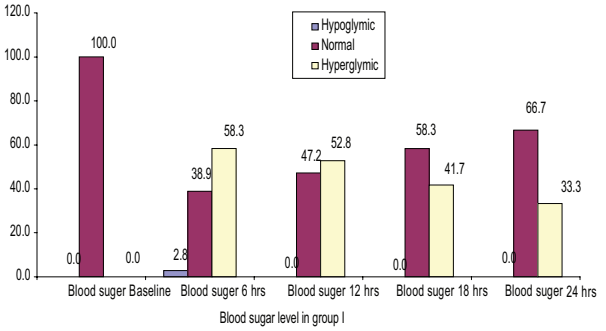

Fig.-2: *Bar diagram shows blood sugar level in group I patients*

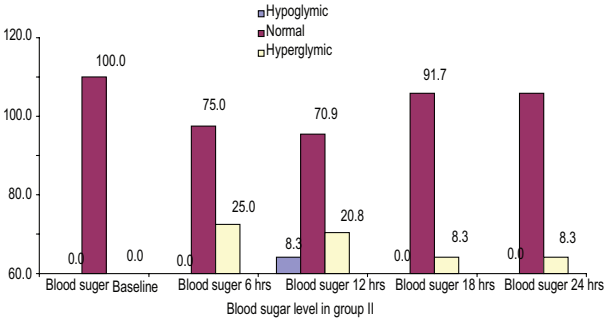

Fig.-3: *Bar diagram shows blood sugar level in group II patients*

Figure 3 shows frequency of normal blood sugar , hypoglycemia and hyperglycemia in group II patient. At baseline all patient have normal blood sugar. Hyperglycemia develop 25% at 6 hour and 20.8% at 12 hour, and 8.3% at 18 hour and 24 hour . Hypoglycemia develop only at 12 hour in 8.3% of patient.

Discussion:

Glucose is the major source of energy for organ function. The human brain uses it almost exclusively as a substrate for energy metabolism, especially in newborn, because their immature counter regulatory response limits the availability of other molecules such as lactate & ketone bodies, which may alternately be used as a substrate for energy production. VLBW newborn are prone to development of both hypoglycemia as well as hyperglycemia.

Various factor is responsible for this unstable glycaemia of newborn. Glucose infusion are also responsible for hyperglycemia of newborn. This study reveals glycemic status of VLBW newborn treated with 10%Dextrose and 5%Dextrose.

In this study 36 (60%) newborn are male and 41 (40%) newborn are female and male female ratio was 0.82. This result is not consistent with Nadeem et al, where male was 65.4% and female was 34.6%.

The age of the patient ranges from 0.5 to 360 hours in group I and 0.5 to 2 hours in group II. Age of neonate is important determinant of blood glucose in this age group. Blood glucose value are unstable in this period especially first 24 hours of age. After that blood glucose remain stable. In this study patient's age range is wide, but baseline blood glucose is normal in all participant. So, age variation may not affect the subsequent blood glucose value. The cause of advanced age of neonate is delayed arrival in the hospital, who were delivered outside of hospital.

Gestational age is calculated by considering last menstrual period (LMP), USG and New Ballard score. There is no significant difference in respect to gestational age in between the two-study group. At birth, the continuous flow of energy substrates from mother to the fetus is curtailed with severance of the umbilical cord. A normal term infant accomplishes this transition via a series of metabolic and hormonal adaptation, leading to glycogenolysis, lipolysis and beta - oxidation of fatty acid, thus maintaining adequate glucose for newborn.

This glycogen storage in the liver and body fat deposition mostly occur in third trimester of pregnancy. So, the gestational age is another determinant of blood glucose in both preterm and small for gestational age infant. As there is no difference in gestational age between two group subsequent blood glucose value are not due to difference in gestational age.

Drug is an important contributory factor for abnormal glucose value. Some drug used to treat VLBW baby causes hyperglycemia. None of the patient received treatment with dopamine, on the other hand all patient got treatment with antibiotic.

Use of dexamethasone and aminophylline are associated with hyperglycemia, but there is no significant difference between two group. Patient treated with dexamethasone are excluded in the study.

Regarding the perinatal information, both groups of patients received antenatal care, maternal hypertension and obesity was present in both groups, although the number in two group is not same. Premature rupture of membrane was present in both group of babies in high number.

Baseline blood glucose level are normal in both group of patients, that is between 2.5 mmol/L to less than 7.0 mmol/ L. There was no significant difference in two group of patients in respect to baseline blood glucose value, this indicate that both group (10% Dextrose group and 5%Dextrose group) are similar at the time of enrollment into the study.

Blood glucose were measured before starting treatment and at six hourly intervals after starting treatment.10% Dextrose group developed more hyperglycemia in comparison with 5% Dextrose group at all measured time. When compared with baseline value it revealed that it is significantly different at all measured time. It is observed in both group of patients. This result indicate that dextrose infusion is effective way of maintaining blood glucose in VLBW baby. It also indicates that 10% dextrose infusion were associated with higher incidence of hyperglycemia. On the other hand, 5% Dextrose group also develop hyperglycemia, but in low incidence. There is significant difference of hyperglycemic episode in between two groups. The striking finding is that 5% Dextrose group developed only two episode of hypoglycemia and only one patient in 10% Dextrose group also developed hypoglycemia.

Similar result found in study conducted by Cowett RM et al. In their study they divided the study population into three group depending on the rate of infusion of dextrose. All patient was VLBW and age was between 3 to 38 days. The clinical condition was stable during the period. Group 1 get 8 mg/ kg/min, group 2 get 11mg/ kg/ min and group 3 get 14mg/kg /min.

In group1 there was no significant increase in plasma glucose concentration during glucose infusion. In groups 2 and 3, the plasma glucose concentration increased significantly over baseline values($P<.05$). Using 150mg/dl as the arbitrarily defined level for hyperglycemia, none of the infants receiving 8mg/kg/mime of glucose developed this complication. Of the infants receiving 11mg/kg/mim of exogenous glucose, 8 of 16 became hyperglycemic and 7 evidenced glucosuria. All infants receiving 14.0mg/kg/mim developed hyperglycemia and glucosuria. The mean maximum plasma glucose concentrations in groups 1, 2, and 3 during the glucose infusion were 95±13, 168±16, and 210±10mg/dl, respectively. This finding strongly corelate with our present study but one difference is that their study period is only 3 hours but our study includes 24 hours of glucose infusion.[16]

Another study conducted by Falcao MC et al revealed that higher rate of glucose infusion associated with glycosuria and hyperglycemia in very low birth weight infants. In this study higher rate of hyperglycemia observed in patient who get more than 5% glucose infusion. This finding also corelate with our recent finding. They also devided the patient into clinically stable and unstable group, but both groups developed more frequent hyperglycemia who gets more than 6% glucose infusion.[17]

Study to determine the occurrence of hypoglycemic episodes in very low birth weight preterm infants under total enteral nutrition and identify potential risk factors was done by researcher. [18]

In this single center cohort study, they analyzed the patients' charts of preterm infants with a gestational age <32 weeks (n = 98). Infants were

analyzed in two groups (group 1: birth weight <1000 g, n = 54; group 2: birth weight 1000-1499 g, n = 44). A total of 3640 pre-feeding blood glucose measurements were screened. Risk factors for the development of hypoglycemia were identified by linear and multiple logistic regression analyses. In group 1, 44% (24 of 54) of infants experienced at least one asymptomatic episode of blood glucose <45 mg/dl (<2.5 mmol/l) as compared with 23% (10 of 44) in group 2. Regression analysis identified low gestational age and high carbohydrate intake as potential risk factors for the development of hypoglycemia. Finally, they conclude that numerous preterm infants experience hypoglycemic episodes once on total enteral nutrition, especially those who are <1000 g at birth and those with a higher carbohydrate intake. This finding is similar with our recent study.

Study done by Popow C et al also concluded that sick very low birth weight infants tend to develop hyperglycemia, glucosuria, impaired glucose disposal, and renal caloric wasting when exogenous glucose is supplied at a rate of 8 mg/kg/min, which is usually well tolerated by healthy premature. [19] So, our study result is very much consistent with most of the study done elsewhere.

Conclusion:

This is an experimental comparative study conducted in a tertiary level hospital of Bangladesh, where home delivery is common. In this study we found that maintaining parenteral nutrition with 10% dextrose in VLBW baby was associated with development of hyperglycemia. On the other hand, while given 5% dextrose baby remain free from hyperglycemia as well as avoid the risk of hypoglycemia.

Limitation:

Blood glucose monitoring done six hourlies. Continuous blood glucose monitoring is best at least for this type of experimental study. Sample size is small. For accurate result large size sample should be taken. Age of some neonate who participated in the study was more than twenty hours, this may mislead us.

Recommendation:

VLBW baby should be treated with 5% Dextrose instead of 10% Dextrose but very large study should be conducted before implementation of this result.

Conflict of interest:

No conflict of interest.

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