Incidence and risk factors of Hyperglycemia in Very Low Birth Weight infants.

THESIS

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Abstract

- Premature infants often develop hyperglycemia. Stress, intravenous glucose, neonatal steroids, and inotropes may increase the incidence of hyperglycemia in premature infants . In very low birth weight (VLBW) infants(birthweight <1,500g) hyperglycaemia is associated with increased rates of morbidity (late onset sepsis , intraventricular hemorrhage , necrotizing enterocolitis) and mortality .
- Our study aim to study the incidence of hyperglycemia in very low birth weight infants and relation to antenatal risk factors (placental insufficiency , antenatal steroids in pregnant mothers , premature rupture of membranes) and post natal risk factors (receiving steroids , inotropes , intravenous glucose, total parenteral nutrition , milk intake & infection in 1st week of life) and relation of hyperglycemia to complications(late onset sepsis, intraventricular hemorrhage, necrotizing enterocolitis), prolonged hospitalization >28 days and outcome of these neonates.
- This cross-sectional comparative study carried out in the NICU of El-Kasr El-Aini hospital, Cairo University & Abu El Rish El Monira Hospital between February 2015 and July 2015 included 60 VLBW neonates who were admitted since birth to NICU . Random blood glucose was measured during 1st week of life (checked every 3 hours in the 1st 48 hours, then every 6 hours for the next 5 days) using glucometer BG strips through a heel pin prick .Thorough maternal history taking focusing on maternal diseases causing placental insufficiency, antenatal steroids intake , mode of delivery , PROM . Assessment of birth weight , gestational age, Apgar score at 1 ,5 and 10 minutes , medications , nutritional assessment and IV fluid intake

during 1st week of life . Assesment of development of complications was performed .

- In our study , 40 neonates (66.7%) developed hyperglycemia during 1st week of life . The mean gestational age of studied neonates was 30.1 ±1.8 weeks, mean birth weight was 1.285± 0.17 kg , mean Apgar score at 1 min , 5min , 10 min was 3.4 ± 1.7 , 6.7 ±1.6 and 8.2 ± 1.4 respectively. Among hyperglycemic cases 20 neonates (50%) developed severe hyperglycemia while 16 (40%) developed moderate hyperglycemia and only 4 (10%) had mild hyperglycemia. Among hyperglycemic cases, 34 (85%) developed hyperglycemia during 1st 48 hours of life, while 6 (15%) had hyperglycemia after 48 hrs of life. There was statistically significant relation between hyperglycemia and gestational age , birth weight , placental insufficiency during pregnancy , receiving inotropes and milk intake after birth (p=0.05 , 0.042 , 0.044 , 0.001 and 0.007 respectively). There was statistically significant relation between hyperglycemia and LOS, IVH, death (p= 0.001, 0.003 & 0.022 respectively). There was statistically significant relation between severity of hyperglycemia and infection in 1st week and IVH (p=0.025 & 0.05 respectively).There was no statistically significant relation between hyperglycemia and gender, APGAR score, mode of delivery, antenatal steroids, PROM , post natal steroid intake, sepsis in the first week, total mean dextrose, amino acid and lipid infusions ($p > 0.05$). There was no statistically significant relation between hyperglycemia and NEC, prolonged hospitalization >28 days (p= 0.825 & 0.271 respectively).

Conclusion of our study: There was high incidence of hyperglycemia in VLBW (66.7%). There was statistically significant relation between hyperglycemia and different neonatal parameters (gestational age, birth

weight), risk factors (placental insufficiency , receiving inotropes , milk intake after birth), complications (LOS , IVH, death)

- Key words: Hyperglycemia, Very Low Birth Weight infants.

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List of Abbreviations

The Abbreviation	Refers to
AAP	American Academy of Pediatrics
BG	Blood glucose
BPD	Bronchopulmonary dysplasia
BP	Blood pressure
BW	Birth weight
CBC	Complete blood count
CKD	Chronic kidney disease
CLD	Chronic lung disease
CNS	Central nervous system
CPAP	Continous positive airway pressure
CP	Cerepral palsy
CRP	C –reactive protein
CS	Cesarean section
DIC	Disseminated intravascular coagulation
DW	Dextrose water
ELBW	Extremely low birth weight
EONS	Early onset neonatal sepsis
GA	Gestational age
GIR	Glucose infusion rate
GLUT	Glucose transporter
GU	Genito-urinary
HIV	Human immune dificiensy virus
IGF	Insulin like growth factor
Iu	International unit
IVH	Intraventricular hemorrhage
IV	Intravenous
IWL	Insensible water loss
Kg	Kilogram
LONS	Late onset neonatal sepsis
LOS	Late onset sepsis

mmol/L	**Millimol per liter**
NEC	**Necrotizing enterocolitis**
NICU	**Neonatal intensive care unit**
NIRTURE	**Neonatal Insulin Therapy in Europe**
NRP	**Neonatal resussitation program**
NVD	**Normal vaginal delivery**
PDA	**Patent ductus arteriosus**
PEPCK	**phosphoenolpyruvate carboxykinase**
PMA	**Post menstrual age**
P	**P value**
PROM	**Premature rupture of membranes**
RDS	**Respiratory distress syndrome**
ROP	**Retinopathy of prematurity**
r	**Spearman correlation coefficient**
SD	**Standard deviation**
SGA	**Small for gestational age**
TPN	**Total parenteral nutrition**
U.S	**United states**
VLBW	**Very low birthweight**
WHO	**World health organization**

Introduction

Very low birth weight (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 **(Fanaroff et al., 2007).**

Studies have reported normal outcomes in approximately 73% of these preterm neonates, figures vary widely from country to country with reports of up to 90% survival from developed countries to 40% in the developing world **(Ruegger et al., 2012).**

Although hyperglycemia is common in very low birth weight (VLBW) infants, particularly in extremely low birth weight (ELBW) neonates, still no consensus has been reached on a specific blood sugar level that would define hyperglycemia in neonates **(Sabzehei et al., 2014).**

Hyperglycemia is defined as two consecutives values >8.3 mmol/L (150 mg/dL) during the first 14 days of life in premature neonates **(Dreyfus et al., 2015).**

The prevalence of hyperglycemia in neonates has been estimated as 20%–88%; wide variations in the reported prevalence result from different definitions, varying birth weights (BW), degree of stress, and volume and rate of intravenous infusions of dextrose water (DW) in studied newborns **(Kairamkonda & Khashu, 2008).**

Prematurity is an important risk factor in the complex pathogenesis of hyperglycemia. Insulin resistance develops due to a high circulating level of inflammatory markers, cytokines and catecholamines. Consequently, glucose production in the liver is not inhibited. The pancreas needs to produce insulin to compensate, but is probably unable to do so due to immature beta-cells, leading to relative insulin deficiency **(Beardsall & Dunger, 2008).**

Predisposing factors for neonatal hyperglycemia include low birth weight, low gestational age, severity of underlying disease, sepsis, hypoxia, low Apgar scores,

surgery and stress. In addition, administration of the following medications results in an increased risk of hyperglycemia: rapid infusions of intravenous dextrose, intralipid solution, inotropic drugs, theophylline and steroids for Chronic lung Disease (CLD) **(Beardsall et al., 2010).**

Hyperglycemia causes an osmotic diuresis resulting in dehydration; other associated findings include; late-onset sepsis (LOS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC) and prolonged hospitalization **(Alexandrou et al., 2010).**

REVIEW OF LITERATURE

Chapter 1

Introduction on Prematurity

Definition :

Preterm birth, defined as birth that occurs on or before the end of the 37th week (259th day) of pregnancy, counting from the first day of the last menstrual period **(WHO, 2010).**

Preterm birth can be further sub-divided based on gestational age:

- Extremely preterm (<28 weeks)
- Very preterm (28 - <32 weeks)
- Moderate preterm (32 - <37 completed weeks of gestation).

Moderate preterm birth may be further split to focus on late pre-term birth (34 - <37 completed weeks) **(Marlow, 2012).**

Babies born before the 34th week of pregnancy have the highest risk for early death and enduring health problems, but recent research has shown that even late preterm infants (at 34 to 36 weeks of pregnancy) have greater health risks than full-term babies **(Martin et al., 2009).**

Incidence:

Worldwide**,**15 million babies born in 2010 were born prematurely, of these preterm births, 84% occurred at 32 to 36 weeks gestational age (GA), 10% occurred at 28 to <32 weeks GA, and 5 percent occurred at <28 weeks GA, more than 1 million died as a result of their prematurity **(Blencowe et al., 2012).**