Study of Correlation between Non-invasive Measurement of Carboxyhemoglobin and Bilirubin Level Measurement in Near- Term and Term Neonates as a Predictor of Neonatal Hemolysis

Thesis

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By

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Abstract

Background: Neonatal hyperbilirubinemia is common in the neonatal period. Yet, serious pathological hyperbilirubinemia may cause kernicterus with detrimental neurologic sequalae. Carbon monoxide is the byproduct of the breakdown of heme, it is transported as carboxyhemoglobin to the lungs to be exhaled. Thus, carboxyhemoglobin levels increase as a result of hemolysis, and is therefore considered a sensitive index for the degree and severity of the subsequent hyperbilirubinemia.

Objectives: To correlate between non-invasive carboxyhemoglobin levels and bilirubin levels in near-term and term neonates starting hour 1 of life.

Subjects and methods: A total of 100 near-term and term neonates were studied, by measuring carboxyhemoglobin by a Pulse Co-oximetry and serum bilirubin level (hour1) as well as transcutaneous bilirubin (TcB) hourly since birth for the 1st 6 hours then every 6 hours till the time of discharge in a cross sectional case-control study.

Results: A cut off value of 4 for non-invasive carboxyhemoglobin with sensitivity of 81.25%, specificity of 95.24% was found to the earliest non-invasive predictor for subsequent jaundice. In patients with proven hemolysis, carboxyhemoglobin when compared to TcB was found to increase significantly in the first 3 hours of life more than TcB, starting hour 4 till time of discharge it was increased yet statistically insignificant

Conclusion: We found that non-invasive carboxyhemoglobin is an effective early predictor for subsequent jaundice starting first hour of life. It can be used as a screening tool for hemolytic jaundice especially in hospitals with early discharge policy.

Key words: Neonatal jaundice, Carboxyhemoglobin, Hemolysis, Pulse co-oximetry.

List of Abbreviations

Abb.	Full term
ABE	*Acute Bilirubin Encephalopathy*
ABR	*Auditory Brainstem Response*
ANOVA	*Analysis of Variance*
ATP	*Adenosine Triphosphate*
AUC	*Area under the Curve*
BIND	*Bilirubin Induced Neurological Dysfunction*
CB	*Conjugated Bilirubin*
CBC	*Complete Blood Count*
CFL	*Conventional Fluorescent Light*
CMV	*Cytomegalovirus*
CNS	*Central Nervous System*
CO	*Carbon Monoxide*
COHb	*Carboxyhemoglobin*
CRP	*C-reactive Protein*
DCT	*Direct Coomb's Test*
ET	*Exchange Transfusion*
ETCO	*End Tidal Carbon Monoxide*
FDA	*Food and Drug Administration*
FFA	*Free Fatty Acids*
G6PD	*Glucose 6 - Phosphate Dehydrogenase*
GGT	*Gamma Glutamyl Transpeptidase*
GI	*Gastro-Intestinal*
GST	*Glutathione S – Transferase*
H	*Hours*
HDFN	*Hemolytic Disease of Fetus and Neonate*
HO	*Heme Oxygenase*
IgG	*Immunoglobulin G*
IQR	*Interquartile Range*

List of Abbreviations cont...

Abb.	Full term
IVIG	*Intravenous Immunoglobulins*
LDH	*Lactate Dehydrogenase*
LED	*Light Emitting Diode*
MRCP	*Magnetic Resonance Cholangio-Pancreatography*
NADPH	*Nicotinamide Adenine Dinucleotide Phosphate Hydrogenase*
NEC	*Necrotizing Enterocolitis*
NICU	*Neonatal Intensive Care Unit*
OFC	*Occipito – Frontal Circumference*
PCV	*Packed Cell Volume*
RBCs	*Red Blood Cells*
Retics	*Reticulocytic count*
RHDN	*Rhesus Hemolytic Disease of the Newborn*
ROC	*Receiver Operating Characteristic*
SD	*Standard Deviation*
SPSS	*Statistical Program for Social Science*
TcB	*Transcutaneous Bilirubin*
TLC	*Total Leucocytic Count*
TORCH	*Toxoplasma, Rubella, Cytomegalovirus, Herpes Simplex*
TSB	*Total Serum Bilirubin*
UCB	*Unconjugated Bilirubin*
UDP	*Uridine Diphosphate*
UDPGA	*Uridine Diphosphate Glucuronic Acid*
UDPGT	*Uridine Diphosphate Glucuronyl Transferase*

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INTRODUCTION

One of the most prevalent clinical conditions in newborn is hyperbilirubinemia ***(Olusanya et al., 2015).*** Neonatal jaundice is a common clinical problem encountered during the neonatal period especially in the first week of life ***(Bhutani et al., 2013).***

The most common cause of jaundice is hemolytic jaundice. Hemolytic disease of the fetus and neonate (HDFN) is a group of hemolytic disorders occurring in the perinatal period. This term is generally used to designate immune-mediated hemolytic process such as; Rh or ABO hemolytic disease ***(Stockman, 2001).*** Hemolysis can be due to a number of acquired (usually transient) or inherited (often chronic) conditions ***(Perrone et al., 2012).***

Carbon monoxide is a natural byproduct of the breakdown of protoporphyrin to bilirubin. Carboxyhemoglobin (COHb) is formed by the binding of carbon monoxide to hemoglobin. Thus, carboxyhemoglobin levels increase as a result of hemolysis ***(Wu and Wang, 2005).***

Because heme breakdown yields equimolar amounts of carbon monoxide and biliverdin, bilirubin production can be indirectly assessed by measuring CO production ***(Stark and Bhutani, 2017)***.

Up to our knowledge there has been no previous studies correlating carboxyhemoglobin levels (measured non-invasively) with indirect bilirubin in term and near-term neonates measured since birth.

AIM OF THE WORK

The aim of this work is to correlate between carboxyhemoglobin levels (measured non-invasively) and indirect bilirubin levels in near term (35+ weeks) & term (37+ weeks) neonates so as to be able to use it as an earlier indicator of hemolysis and a predictor of subsequent hyperbilirubinemia.

Chapter 1

NEONATAL JAUNDICE

Definition & Background

Neonatal jaundice is yellowish discoloration of the skin, sclera, and mucous membranes due to accumulation of bilirubin pigment in the skin ***(Mitra and Rennie, 2017).*** The term jaundice is from the French word "jaune," which means yellow. Neonatal jaundice in most newborns is a mild and transient event, yet may lead to long-term neurological sequelae. Thus, it is imperative to identify newborns with jaundice as early as possible for proper treatment to avoid these complications ***(Ogunfowora and Daniel, 2006).***

Incidence

Neonatal hyperbilirubinemia is a common clinical problem encountered during the neonatal period, especially in the first week of life ***(Bhutani et al., 2013).*** Approximately 85% of all term newborns and most premature infants develop clinical jaundice. Also, 6.1 % of well term newborns have a maximal serum bilirubin level >12.9 mg/dL. A serum bilirubin level >15 mg/dL is found in 3% of normal term babies ***(Burke et al., 2009).***

Source of bilirubin

Bilirubin is not merely a nuisance molecule that has dire consequences, but it is an important antioxidant circulating in