The Effect of Head Covering on Phototherapy-Induced Hypocalcemia in Jaundiced Full-Term Neonates

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Amira Said Mohamed

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List of Abbreviations

Abb.	Full term
μw / cm² / nm	*Microwatts / centimeter squre / nanometer*
1,25(OH)2D	*1,25 dihydroxy vitamin D*
ABE	*Acute bilirubin encephalopathy*
Aka	*Also known as*
CB	*Conjugated bilirubin*
CFL	*Compact fluorescent lamp*
cm	*Centimeter*
CNS	*Crigler-Najjar syndrome*
d	*Day*
DJS	*Dubin-Johnson syndrome*
G6PD	*Glucose-6-phosphate dehydrogenase*
gm	*Gram*
GMP	*Guanosine monophosphate pathway*
GS	*Gilbert syndrome*
Hct	*Hematocrit*
HDFN	*Haemolytic disease of the fetus and newborn*
HDN	*Haemolytic disease of the newborn*
hr	*Hour*
IDM	*Infant of diabetic mother*
IV	*Intravenous*
kg	*Kilogram*
LED	*Light emitting diode*
mg /dl	*Milligram / deciliter*

List of Abbreviations

Abb.	Full term
mg /dl/hr	*Milligram/ deciliter/hour*
NICUs	*Neonatal intensive care units*
nm	*Nanometer*
PET	*Partial exchange transfusion*
PKD	*Red cell pyruvate kinase deficiency*
PROM	*Premature rupture of membrane*
PTH	*Parathyroid hormone*
TcB	*Transcutanous bilirubin*
TORCH	*Toxoplasma, Rubella, Cytomegalo virus, Herpes virus*
TPN	*Total parentral nutrition*
TSB	*Total serum bilirubin*
UCB	*Unconjugated bilirubin*
UDPGT	*Uridine diphosphate glucoronyl transferase*
UGT1A1	*Uridine glucorinyl transeferase 1A1*
wk	*Weeks*

INTRODUCTION

Jaundice is a common cause of morbidity encountered in the first week of life. It is almost concern for the physician and a source of anxiety for the parents ***(De Luca, 2010; Khosravi et al., 2001)***. High bilirubin level may be toxic to the developing central nervous system and may elicit neurological impairment in newborns ***(Kaplan et al., 2011).*** About 60% of term newborns become visibly jaundiced in the first week of life. In most of the cases, it is benign and no intervention is required ***(Dijk et al., 2009).*** Approximately 5-10% of them have clinically significant jaundice that signifies the use of phototherapy ***(Hansen, 2010).***

Phototherapy is the most commonly used intervention to treat severe jaundice and reduces the risk of exchange transfusion ***(Ip et al., 2004).*** It blunts the rise of indirect bilirubin level regardless of the etiology of jaundice ***(Maisels and Kring, 2002).*** Phototherapy decreases the serum bilirubin level by transforming bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver ***(Stokowski, 2006).***

However, this treatment modality may itself result in the development of some complications ***(Ehsanipoor et al., 2008).*** Though it is considered safe, a few side effects encountered in phototherapy are loose stools, hyperthermia, dehydration due to fluid loss, skin burn, retinal damage, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency and DNA damage. A lesser known side effect, but a potential complication of phototherapy is hypocalcemia ***(Cloherty et al., 2008).***

The overall prevalence of hypocalcemia in neonates receiving phototherapy was suggested to be 8.7% in full-term newborn ***(Yadav et al., 2012).*** The mechanism of hypocalcemic effect of phototherapy was reported by inhibition of pineal gland via transcranial illumination, resulting in decline of melatonin secretion that further decreases the release of cortisol leading to increase bone uptake of calcium and induce hypocalcemia ***(Hunter, 2004; Alizadeh-Taheri et al., 2013).***

Clinical picture of hypocalcemia in neonates includes jitteriness, irritability, excitability, lethargy and convulsions, as well as other complication like rash, loose stool, fever and dehydration ***(Yadav et al., 2012).*** Hypocalcemia affects many biochemical processes including cell membrane integrity, blood coagulation, function of cell membrane, neuromuscular excitability and cellular enzymatic activity ***(Borkenhagen et al., 2013).***

AIM OF THE WORK

The aim of this study was to assess the effect of head covering on calcium levels in full term neonates with hyperbilirubinemia treated with different types of phototherapy.

Chapter 1

NEONATAL JAUNDICE

Neonatal Jaundice is a yellowish discoloration of skin and sclera by bilirubin which is clinically detectable in the newborn ***(Wong et al., 2018).***

Hyperbilirubinemia is either unconjugated (which is potentially neurologically toxic and may be physiological or pathological) or conjugated (not toxic and always pathological ***(Chen et al., 2011).***

Sources of bilirubin:

Bilirubin is the end product of heme breakdown. About 80% of bilirubin originates from degradation of erythrocyte hemoglobin in the reticuloendothelial system; the remaining 20% comes from inefficient erythropoiesis in the bone marrow and degradation of other heme proteins such as cytochromes, catalase, peroxidase and tryptophan pyrrolase ***(Wong et al., 2007).***

The heme ring from heme-containing proteins is oxidized in reticuloendothelial cells to biliverdin by the microsomal enzyme (Heme oxygenase) ***(Erlinger et al., 2014).***

This reaction releases carbon monoxide (CO); (excreted from the lung); and iron (reutilized). Biliverdin is then reduced to bilirubin by the enzyme Biliverdin reductase ***(Gregory et al., 2012).***

Bilirubin production:

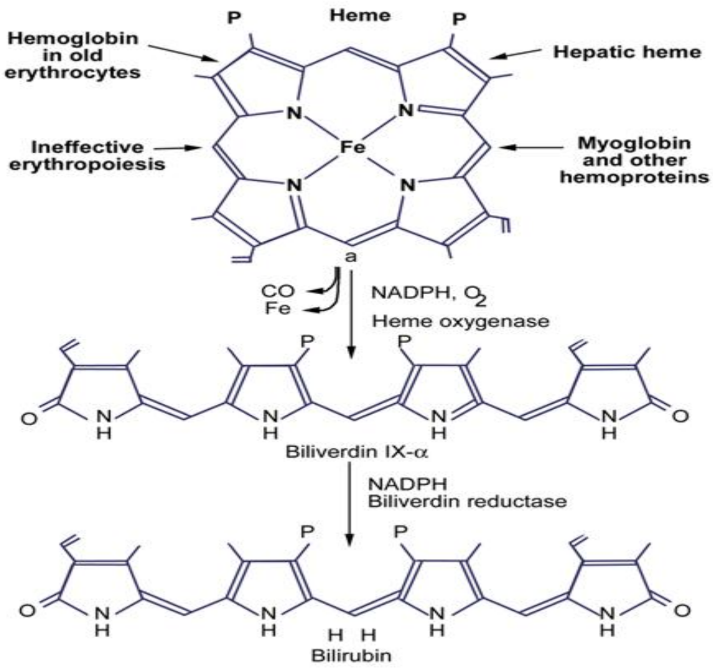

Figure (1): Production of Bilirubin ***(Hisham et al., 2014).***

The normal newborn produces 6 to 10 mg of bilirubin/Kg/day. One gram of haemoglobin results in the production of 34 mg of bilirubin ***(Gregory et al., 2012).***

Unconjugated bilirubin (UCB) exists in several forms in the blood but is predominantly bound to albumin. One gram of albumin binds 8.5 mg of bilirubin in a newborn. A minute fraction of unconjugated bilirubin in serum is not bound to albumin ***(Erlinger et al., 2014).*** UCB is taken by hepatocytes at their sinusoidal surface. The impairment of uptake will result in unconjugated hyperbilirubinemia ***(Moerschel et al., 2008).***

Inside the liver cells, about 60% of bilirubin is found in the cytosol and about 25% in microsomes. Ligandin; a glutathione S-transferase; is responsible for binding bilirubin inside the cells ***(Hansen, 2010).*** UCB is converted to water soluble conjugated bilirubin (CB) in the smooth endoplasmic reticulum by uridine diphosphate glucoronyl transferase (UDPGT) enzyme ***(Huang et al., 2004).***

Once bile reached the intestine, conjugated bilirubin is reduced to colorless tetrapyrroles by bacteria in the colon ***(Cashore, 2012).*** However, some deconjugation occurs in the proximal small intestine by β-glucuronidases located in the brush border ***(Ann et al., 2012).*** This unconjugated bilirubin can be reabsorbed into the circulation, increasing the total plasma bilirubin pool. This cycle known as **'Enterohepatic Circulation'** ***(Fujiwara et al., 2015).*** The process may be extensive in the neonate, partly because of limiting intake in the first days of life, prolonging the intestinal transit time by decreasing excretion of stool ***(Fujiwara et al., 2015).***

The bulk of bilirubin, urobilinogen, urobilin, stercobilinogen and stercobilin are excreted in the feces. Small amounts of bilirubin and urobilinogen are reabsorbed by the intestine and return to the liver. The bilirubin is reconjugated in the liver and re-excreted in the feces. Some of the reabsorbed urobilinogen is excreted in the urine ***(Moerschel et al., 2008).***