THE INFLUENCE OF PHOTOTHERAPY ON SERUM CYTOKINE CONCENTRATIONS IN NEWBORN INFANTS

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بسم الله الرحمن الرحيم

وَأَنْزَلَ اللهُ عَلَيْكَ الْكِتَابَ
والْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللهِ
عَلَيْكَ عَظِيمًا

صدق الله العظيم

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Abstract

Introduction: Neonatal jaundice in the first week of life is a common problem in newborns.The most important intervention for infants with severe hyperbilirubinemia is to initiate phototherapy without delay. Although phototherapy is the standard treatment for neonatal hyperbilirubinemia, it may lead to potential side effects such as retinal degeneration, diarrhea, dehydration, and skin rash. Phototherapy treatment can affect the function of the immune system in newborns via alterations in cytokine production. **Objectives:**In our study we hypothized that phototherapy can affect the level of pro-inflammatory and anti-inflammatory cytokines. We choosed interleukin 6 (pro-inflammatory) and interleukin 10 (anti-inflammatory) to study this effect because they are produced by keratinocytes. **Subjects and methods:** Forty term and near term jaundiced neonates were chosen to conduct the study; they presented with neonatal jaundice (NNJ) in the 1st week of life with body weight ranging from (2kg- 4kg). All of them were subjected to phototherapy for the management of NNJ. Interleukin [IL]-6 and Interleukin IL-10: (Before and after 72 hours of phototherapy **Results:** our study revealed an increase in serum level of IL6 after treatment with phototherapy. However no change was observed for IL 10 between basal values and treatment with statistically significant P value for IL-6 statistically insignificant for IL-10. **Conclusions**: Phototherapy used in the treatment of neonatal hyperbilirubinemia can affect the level of cytokines but as the previous studies were not homogenous so more studies are needed to be done to study the effect of phototherapy on serum cytokines concentration in the newborn.

Key words: phototherapy- Interleukin -NNJ

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AAP: American Academy of Pediatrics

AP-1: activator protein 1

APCs: antigen presenting cells

BBS: Bronze baby syndrome

BSF-2: cell–stimulating factor 2

CD4: cluster of differentiation 4

COX-2: Cyclo-oxygenase, Cyclo- oxygenase-2

CRP: C- reactive protein

CS: caesarian section

CSF: Colony-stimulating factors

DAMP: damage-associated molecular patterns

DNA: deoxyribonucleic acid

DSB: direct serum bilirubin

EHC: enter hepatic circulation

EPO: erythropoietin

G6PD: glucose-6-phosphate dehydrogenase

G-CSF: granulocyte colony-stimulating factor

GM-CSF: granulocyte- macrophage colony-stimulating factor

HBV: hepatitis B virus

HCV: hepatitis C virus

HIV: human immunodeficiency virus

HPV: Human papilloma virus

IFN: interferon

Ig: Immunoglobulin

IL: interleukins

IVIG: intravenous immunoglobulin

LED: Light-emitting diode

M-CSF: macrophage colony- stimulating factor

MHC: major histocompatibility

NF-IL-6: nuclear factor IL-6

NICUs: neonatal intensive care units

NK: natural killer

NNPT: neonatal phototherapy

PDA: patent ductus arteriosus

PT: Phototherapy

RCT: randomized control study

ROP: retinopathy of prematurity

ROS: reactive oxygen species

SAA: serum amyloid A

SLE: systemic lupus erythematosus

SP-1: specificity protein 1

SVD: spontaneous vaginal delivery

TAMs: Tumor associated macrophages

Th-2: T helper cells

TLR : transcriptional level receptor

TNF: tumor necrosis factor

TOS: total oxidant status

TPO: thrombopoietin

TSB: total serum bilirubin

UDPGT: uridinediphosphoglucuronosyl-transferase

UV: ultraviolet

WBC: white blood cell

X-SCID: x- linked form of Severe Combined Immunodeficiency

INTRODUCTION

Phototherapy (PT) has been widely used for the treatment of neonatal jaundice for more than 50 years. The side effects of this efficacious therapeutic method, which significantly decreases the exchange-transfusion rates, are still a matter of debate. It has been reported that PT may cause retinal and testicular damage, ileus, patent ductus arteriosus, and hypocalcemia as well as well-known temporary side effects, such as skin rash, abdominal distention, frequent defecation, and weight loss. Further, it was thought that oxidative stress that resulted from PT might contribute to premature infant diseases, such as retinopathy of prematurity, bronchopulmonary dysplasia, and necrotizing enterocolitis. Another concern related to PT is genotoxicity leading to DNA damage that may be related to cancer development. The light spectrum used for PT includes visible light that has a main therapeutic efficacy and, to a lesser extent, ultraviolet (UV) light. Along with well-known mutagenic and carcinogenic effects of UV light, it has been shown in many in vitro studies that visible light also leads to DNA damage. In the literature, there are few studies with incompatible and conflicting results investigating The effects of phototherapy on neonatal inflammatory response ***(Hasan et al., 2013)***.

We hypothize that as the phototherapy produces its effect through converts bilirubin in skin and subcutaneous tissues into water-solubleless lipophilic, presumably non-toxic, photo-products that are water soluble excreted through the intestine and in the urine and as the cytokines which are low-molecular-weight proteins produced and secreted by keratinocytes fibroblasts, monocytes, macrophages, and endothelial cells could be affected by phototherapy as well and consequently could affect the inflammatory response in the neonates undergoes phototherapy.

AIM OF THE STUDY

To evaluate the effects of phototherapy on pro- and anti-inflammatory cytokine concentrations in term and late preterm newborns under phototherapy treatment for jaundice. We chose to study the pro-inflammatory cytokines (interleukin [IL]-6) and anti-inflammatory cytokine IL-10 because they are produced by keratinocytes.

HYPERBILIRUBINEMIA

Neonatal jaundice is one of the most common diagnoses among infants. It is the most common morbidity in the first week of life, occurring in 60% of term and 80% of preterm newborn.it accounts the most common cause of readmission after discharge from birth hospitalization. While usually benign, serious neurodevelopmental issues can arise if jaundice is left unmonitored ***(Rennie et al., 2010).***

Definition of jaundice:

Jaundice is a yellowish discoloration of skin, sclerae, and mucous membranes that results from an increase in the serum concentration of bilirubin. Hyperbilirubinemia is defined as total serum bilirubin concentration > 1.5 mg/dL. ***(Schwartz et al.,2011).***

Typically characterized by the fraction of bilirubin that is increased, unconjugated (indirect), or conjugated (direct). Normal conjugated fraction accounts for < 5% of total serum bilirubin. Conjugated hyperbilirubinemia refers to direct bilirubin concentration > 2 mg/dL or > 20% of the total bilirubin concentration. Conjugated hyperbilirubinemia should always be considered important because it suggests liver or biliary tract dysfunction. ***(Bhutani et al., 2011).***

Jaundice in neonates is visible in skin and eyes when total serum bilirubin (TSB) concentration exceeds 5 to 7 mg/dL. In contrast, adults have jaundice visible in eyes (but not in skin) when TSB concentration exceeds 2 mg/dL. Increased TSB concentration in neonate results from varying contributions of three mechanisms namely increased production from degradation of red cells, decreased clearance by the immature hepatic mechanisms and reabsoption by enterohepatic circulation (EHC) ***(Kaur et al., 2011).***

Epidemiology:

Jaundice is the most common morbidity in the first week of life, occurring in 60% of term and 80% of preterm newborn. It is the most common cause of readmission after discharge from birth hospitalization ***(Lancet., 2008)***.

Nearly all newborn infants have a total serum bilirubin (TSB) value greater than 1 mg/dL (17.1 μmol/L), which is at the upper limit of normal for an adult. Most newborns appear clinically jaundiced. Pathologic hyperbilirubinaemia occurs when the TSB exceeds the hour-specific 95th percentile using the published nomogram in Figure (1) The nomogram was developed for a racially diverse population in Philadelphia in which nearly 60% were breastfed. Infants were excluded if they had hemolytic conditions or required phototherapy before 60 hours to control rapidly rising TSB levels ***(Sultan Qaboos Univ ., 2012).***

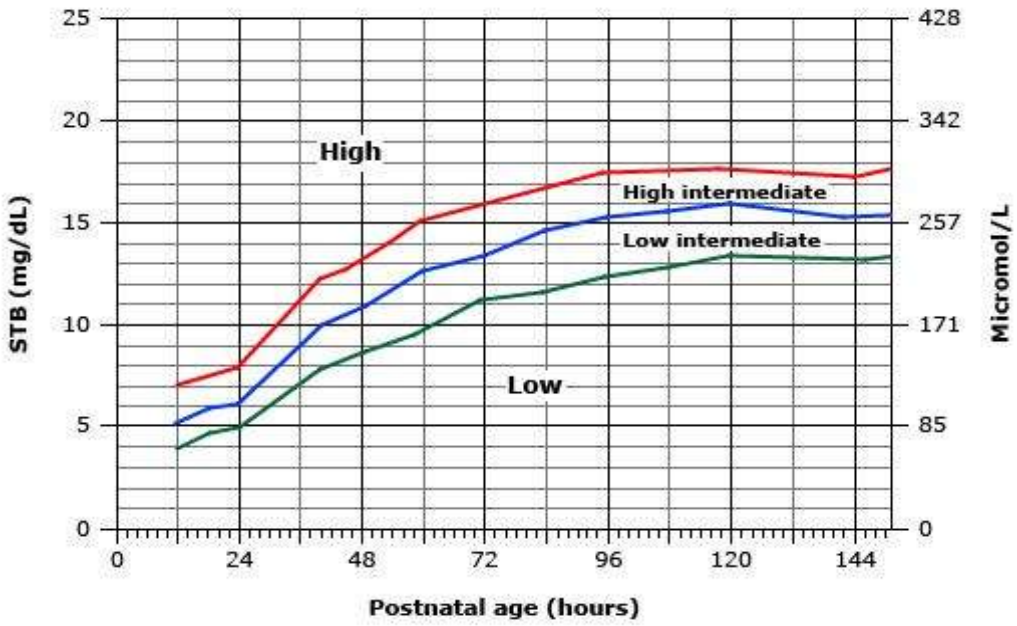

Figure 1: Hour specific nomogram *(adapted from AAP., 2004).*