Effectiveness of Conventional Phototherapy in Relation to Irradiance Measurement in the Treatment of Neonatal Hyperbilirubinemia in Abo El-Rish Neonatal Intensive Care Unit.

Thesis
Submitted for partial fulfillment for master degree in
Pediatrics

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Abstract

Introduction: Some 60% of normal newborns become clinically jaundiced sometime during the first week of life. Sufficiently elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps. Phototherapy and exchange blood transfusion are two major therapeutic strategies to prevent bilirubin-induced brain damage in neonates. The choice of therapy depends on the severity of hyperbilirubinemia, but phototherapy is the most frequently used treatment.

Objectives: Our aim was to assess irradiance levels to which babies are exposed to during conventional phototherapy for neonatal jaundice in the NICU and its effectiveness in reducing the bilirubin levels.

Patient and methods: This is an observational study included 122 full term neonates, with neonatal hyperbilirubinemia and undergoing conventional phototherapy treatment in Abu El-Rish neonatal intensive care unit.All neonates were subjected to complete clinical study, CBC, Serum bilirubin level at the beginning of conventional phototherapy and after 24 hour, blood group of the baby and the mother, reticulocytic count and Coombs' test, and irradiance measurements of the phototherapy unitusedwhich were divided into 2 groups (A) and (B).Included babies admitted to the study were assigned to the different phototherapy units alternatively in order to avoid bias.

Results: The mean gestational age was 38±0.7 weeks, while mean age on admission in days was 4.9±3.6 days and the mean time between onset of jaundice and admission was 2.9±3.2 days.The mean irradiance level of type (A) lamps was 5.3±0.5 µw/cm2/nm, while the mean irradiance level of type (B) lamps was 18.8±2.5 µw/cm2/nm.Themean serum bilirubin level at the start of conventional phototherapy of the babies randomly assigned to different lamps was 12.9±4.2 mg/dl for type (A) , and was 16.4±3.9 mg/dl for type (B), and this was statistically significant.The mean drop inTSB using type (B) was 4.2±3.2mg/dl versus 1.6±1.3mg/dl in type (A), and this was statistically significant.In addition, we found that the mean total durationof required conventional phototherapy treatment was significantly shorter among patients in group (B) compared to those in group (A) (2.34±1.3 days versus 3.87±2.2 days.

Conclusion: Phototherapy should not be provided as a placebo in the NICU. Measuring irradiance is essential for providing effective phototherapy, proper management of neonatal hyperbilirubinemia and prevention of kernicterus without the risk of exchange transfusion.

Key wards: Irradiance, neonatal hyperbilirubinemia, total serum bilirubin.

Acknowledgement

First of all, thanks to ALLAH the most beneficial and merciful for helping me to complete this study.

I would like to express my deepest gratitude and appreciation to Prof. **Dr. Manal El Sayed Abd El Meguid,** Professor of pediatrics, Cairo University, for her generous support and guidance to help me to complete this work. It was indeed an honor to work under her supervision.

It is my pleasure to express my unlimited gratitude and deepest thanks to Prof. **Dr. Iman Fathy Iskander,** Professor of pediatrics, Cairo University, for her faithful supervision, precious help and guidance she offered me to complete this study. No words of gratitude can equal her help and support.

I also wish to thank **Dr. Sameh Mostafa Reda,** Assistant Professor of Radiometry Lab, National Institute For Standard for his great help, guidance, support and valuable advice through this work.

I would like to thank all my patients and their parents who agree to participate in this study, and also wish to express my thanks to all the staff working in Abo El-Rish neonatal intensive care unit.

I would like to thank my husband, my mother, my father, my brother, my friends and my lovely daughter Reem, for their patience, support and great effort to help me finishing this work.

Contents

List of abbreviations

AAP	American Academy of Pediatrics
ABE	Acute bilirubin enchephalopathy
ABM	American Board of Medical Specialties
B/A	bilirubin/albumin ratio
BBB	blood brain barrier
BBS	Bronze baby syndrome
BIND	bilirubin-induced neurological dysfunction
CH	Congenital hypothyroidism
cMOAT	canalicular multi specific organic anion transporter
CNS	Crigler-Najjar syndrome
DAT	Direct antiglobulin test
ETCOc	end-tidal carbon monoxide
ETs	exchange transfusions
G6PD	Glucose-6- phosphate dehydrogenase
HDN	Hemolytic disease of newborn
HE	Hereditary elliptocytosis
HHP	Hereditary pyropoikilocytosis
H.M.P	Hexose Monophosphate
HS	Hereditary spherocytosis
IDM	infant of diabetic mother
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IVIG	Intravenous immune globulin
LED	light-emitting diodes
MCHC	mean corpuscular hemoglobin concentration
MRP2	multidrug-resistance associated protein

NADPH	nicotinamide-adenine dinucleotide phosphate
NEC	necrotizing enterocolitis
NNPT	neonatal phototherapy
OATP1B1	organic anion transporter polypeptide 1B1
PDA	patent ductus arteriosus
QTH	quartz-tungsten-halogen
RCT	randomized controlled trials
RDW	red cell distribution width
ROP	retinopathy of prematurity
TB	Total bilirubin
TcB	Transcutaneous bilirubin
TSB	Total serum bilirubin
UB	Unbound bilirubin
UDP	Uridinediphosphate
UGT1A1	uridine-diphosphateglucuronosyltransferase 1A1
UV	ultraviolet

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Introduction

Jaundice is one of the most common conditions needing medical attention in newborn babies. Jaundice refers to the yellow coloration of the skin and the sclerae (whites of the eyes) caused by the accumulation of bilirubin in the skin and mucous membranes. ***(NICE, 2010)***

Some 60% of normal newborns become clinically jaundiced sometime during the first week of life. Unconjugated (indirect) hyperbilirubinemia occurs as a result of excessive bilirubin formation and because the neonatal liver cannot clear bilirubin rapidly enough from the blood. ***(Maisels and Kring, 2006)***

Although most newborns with jaundice are otherwise healthy, they need to be monitored because bilirubin is potentially toxic to the central nervous system. Sufficiently elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps. Kernicterus is a common complication of hyperbilirubinemia associated with Rh erythroblastosis fetalis and, occasionally, ABO hemolytic disease. ***(Maisels et al., 2001)***

Phototherapy and exchange blood transfusion are two major therapeutic strategies to prevent bilirubin-induced brain damage in neonates. The choice of therapy depends on the severity of hyperbilirubinemia, but phototherapy is the most frequently used treatment. ***(Ip et al., 2004)***

It is now well established that effective phototherapy implies its use as a " drug" with specific wavelengths at (a) a light emission spectrum within the bilirubin absorption spectrum (400-520nm); (b) a peak emission of 450±20nm; (c) preferably in a precise bandwidth that is delivered at an irradiance foot print

which exposes at least one horizontal body surface plane or optimally the entire circumferential (360º) body surface area; (d) an irradiance level ≥30-35 µW/ cm^2/nm, as measured with an appropriate irradiance meter; and, (e) optimized duration of exposure ***(Maisels and McDonagh, 2008)***

The only way to ascertain the actual dose received is to measure the irradiance at the skin with a phototherapy radiometer. The irradiance level varies depending on where the measurement is taken. The irradiance should be measured in 3 places where the infant will be lying and an average of the measurements should be made. The irradiance decreases exponentially as the distance from the baby increases. The higher the irradiance the larger the rate of bilirubin decline***. (Maisels et al ., 2004)***

Aim of the work:

The aim of this study was to assess irradiance levels to which babies are exposed to during conventional phototherapy for neonatal jaundice in the NICU and its effectiveness in reducing the bilirubin levels.

REVIEW OF LITERATURE

Chapter 1

Neonatal Hyperbilirubinemia

BILIRUBIN METABOLISM

Bilirubin is the end product of heme degradation. The majority of bilirubin is derived from erythrocytes normally removed from the circulation and destroyed in the reticuloendothelial system. Hemeoxygenase is the rate-limiting enzyme that catalyzes the alpha-specific oxidative cleavage of the heme molecule to form equimolar amounts of biliverdin and carbon monoxide. Biliverdin undergoes reduction via NADPH-dependent biliverdin reductase to form bilirubin. Bilirubin, after formation, is released into the circulation. ***(Bhutani et al., 2008)***

Unconjugated bilirubin is fat soluble; it crosses cell membranes and is potentially neurotoxic. However, toxicity is generally avoided because most unconjugated bilirubin is bound to albumin. ***(Smitherman et al., 2006)***

Albumin transports bilirubin to its specific metabolic pathway in the liver, where bilirubin uptake is rapid. Intracellular transport of bilirubin from the hepatic plasma membrane to the endoplasmic reticulum, where conjugation occurs, is not well understood; however, cytosolic proteins (Y or ligandin Z or fatty-acid-binding protein) account for most of the intracellular bilirubin binding capacity. The conversion of bilirubin to mono- and di-glucuronide conjugates occurs in the endoplasmic reticulum.

(Bhutani et al., 2008)

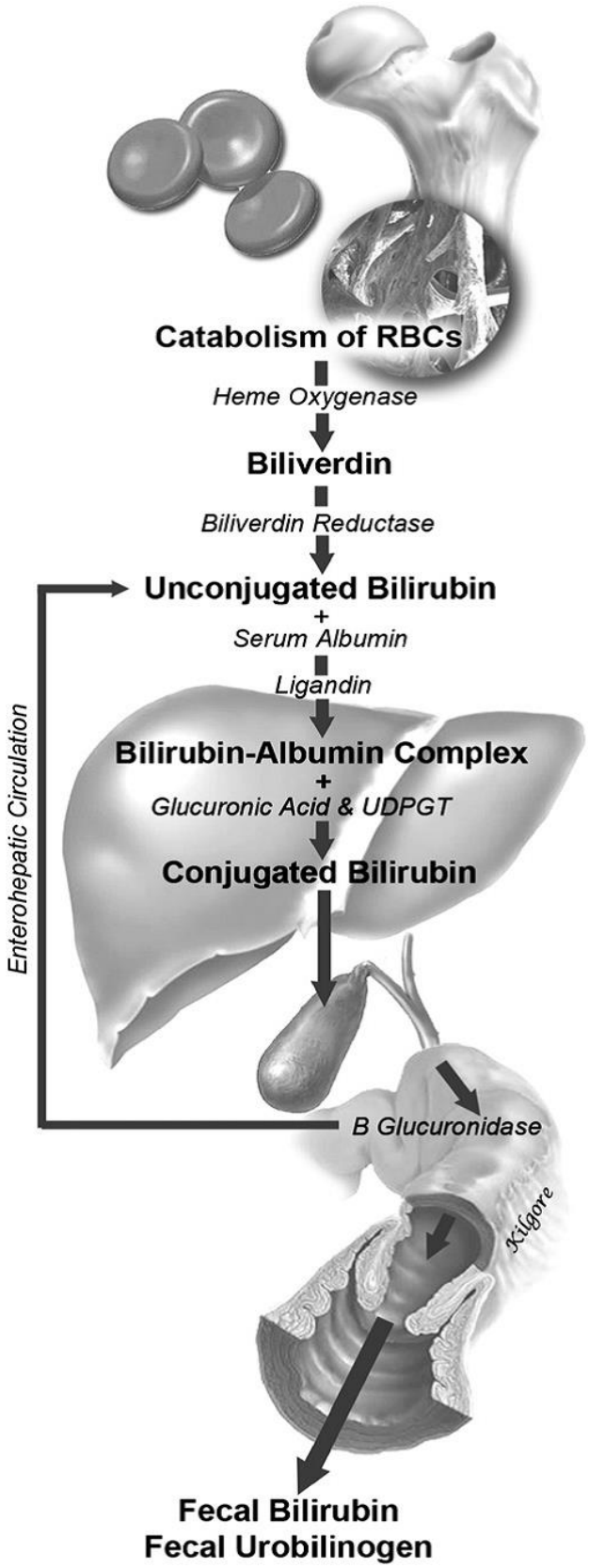

Figure (1): Neonatal Bile Pigment Metabolism (Colletti et al., 2007).