REBOUND HYPERBILIRUBINEMIA AFTER PHOTOTHERAPY

Thesis

Submitted For Fulfillment of MSc Degree in Pediatrics

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﴿قالُوا سُبْحَانكَ لاَعلِمَ لَنَا إِلاّمَا
عَلّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ﴾

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الملخص :

صفراء حديثى الولاده مشكله شائعه تحدث فى حوالي ٦٠٪ من الأطفال الرضع كاملي النمو و ٨٠٪ من الخدج في الأسبوع الأول من الحياه. وكان الهدف من هذه الدراسه تحديد ما إذا كان يحدث إرتفاع في نسبة الصفراء في الدم في غضون ٢٤ ساعة بعد توقف العلاج الضوئى في حديثي الولاده. وأجريت الدراسه على١٣٣ طفل حديث الولاده من كاملى النمو والخدج تم علاجهم بالعلاج الضوئى. تم عمل إختبار لنسبة الصفراء بالدم لجميع الأطفال بعد ٢٤ (± ٦) ساعات من توقف العلاج الضوئى. وكانت نتيجة البحث حدوث إرتفاع في نسبة الصفراء بالدم فى ٢١,٨٪ من حديثى الولاده بعد انتهاء العلاج الضوئى. تم تحليل الانحدار المتعدد اللوجستيه لعوامل الخطر لإرتفاع نسبة الصفراء بعد العلاج الضوئى، وتبين أهميه لإنحلال الدم (نسبة الأرجحيه ١,٢٤١) وإيجابية إختبار كومبس المباشر (نسبة الأرجحيه ٦,٣٩٢).

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ABSTRACT

Introduction: Neonatal hyperbilirubinemia is a common problem. Approximately 60% of term infants and 80% of preterm infants develop jaundice in the first week of life. Despite hyperbilirubinemia being a common morbidity among neonates, few studies have systematically studied the phenomenon of post-phototherapy rebound, data about the phenomenon of bilirubin rebound is lacking.

Objectives: The aim of this study was to determine whether a rebound in serum bilirubin level occurs within 24 hours after discontinuation of phototherapy in neonates with hyperbilirubinemia and to identify aetiological factors for hyperbilirubinemia that could be used to select infants at risk for rebound.

Study design: A prospective clinical survey was performed on 133 term and preterm neonates treated with phototherapy. Neonates were tested for T.S.B 24(±6) hours after discontinuation of phototherapy, with additional testing as clinically indicated. The main outcome measure, significant bilirubin rebound, was defined as a post-phototherapy T.S.B ≥15 mg/dl. Phototherapy was not reinstituted in all cases of rebound, but rather according to clinical indications.

Results: A total of **29** (21.8%) neonates developed significant rebound, mean (±SD) T.S.B was 16.45 (±0.99) mg/dl. Multiple logistic regression analysis for risk factors for significant bilirubin rebound showed significant risk for aetiological risk factors including hemolysis (odds ratio 1.241, 95% CI 1.117 to 2.496) and positive direct Coombs test (odds ratio 6.392, 95% CI 1.530 to 26.706). **Sixteen** of those (55.2%) were retreated with phototherapy, mean (±SD) T.S.B was 16.9 (±1.1) mg/dl. Multiple Logistic regression analysis for risk factors for re-admission for phototherapy showed significant risk for aetiological risk factors including hemolysis (odds ratio 1.121, 95% CI 1.048 to 2.307) and positive direct Coombs test (odds ratio 7.162, 95% CI 1.571 to 32.658). Also there was a trend for re-admission for phototherapy with weight < 2kg (odds ratio 5.976, 95% CI 0.818 to 43.685).

Conclusion: Post-phototherapy neonatal bilirubin rebound to clinically significant levels may occur, especially in cases of hemolysis, direct Coombs test positivity and low birth weight < 2kg. These risk factors should be taken into account when planning post-phototherapy follow up.

Key words: Neonatal hyperbilirubinemia – Bilirubin rebound.

List of Contents

List of Abbreviations

ADCC	**Antibody Dependent Cell mediated Cytotoxicity**
AHT	**Allogenic Hepatocyte Transplantation**
ATP	**Adenosine Tri-Phosphate**
BIND	**Bilirubin Induced Neurologic Disorders**
CN	**Crigler-Najjar**
CO	**Carbon mono-Oxide**
CT	**Computed Tomography**
DAT	**Direct Antiglobin Test**
DWI	**Diffusion-Weighted Imaging**
ET	**Exchange Transfusion**
FFA	**Free Fatty Acids**
GA	**Gestational Age**
G6PD	**Glucose-6-Phosphate Dehydrogenase**
HDN	**Hemolytic Disease of the Newborn**
HO	**Heme Oxygenase**
HS	**Hereditary Spherocytosis**
IgG	**Immunoglobulin G**
IgM	**Immunoglobulin M**
IVIG	**IntraVenous ImmunoGlobulin**
LBW	**Low Birth Weight**
LEDs	**Light-Emitting Diodes**
MRI	**Magnetic Resonance Imaging**
NICU	**Neonatal Intensive Care Unit**
N.J	**Neonatal Jaundice**
NMR	**Nuclear Magnetic Resonance**

OD	**Optical Density**
PK	**Pyruvate Kinase**
RBCs	**Red Blood Cells**
Rh	**Rhesus**
SBR	**Significant Bilirubin Rebound**
TcB	**Transcutaneous Bilirubin**
T.S.B	**Total Serum Bilirubin**
UDPGT	**Uridine Di-Phosphate Glucuronyl Transferase**
UVC	**Umbilical Vein Catheter**
WHO	**World Health Organization**
2,3-DPG	**2,3-Di-Phospho Glycerate**

List of Figures

List of Tables

INTRODUCTION & AIM OF THE WORK

INTRODUCTION

Neonatal hyperbilirubinemia is a common problem. Approximately 60% of term infants and 80% of preterm infants develop jaundice in the first week of life ***(Gomella et al., 2009)***.

Jaundice is a common cause of readmission to hospital after early discharge of newborn babies, but fortunately only few babies have an underlying disease ***(Gale et al., 2001)***.

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. Fortunately, phototherapy is an effective method for the prevention or treatment of neonatal hyperbilirubinemia ***(Luchtman-Jones et al., 2006)***.

Phototherapy is the primary treatment in neonates with unconjugated hyperbilirubinemia and is now arguably the most widespread therapy of any kind (excluding prophylactic treatments) used in newborns. Phototherapy often averts the need for exchange transfusion and is generally regarded as safe method, the reported side effects have been subjected to extensive and controversial debate ***(Vreman et al., 2004)***.

Decreasing hospital length of stay is an objective sought by physicians and administrators alike and it is recommended that infants need not be kept in the hospital after discontinuation of phototherapy. However they should be followed-up to measure rebound bilirubin levels following the discontinuation of phototherapy ***(Maisels and Kring, 2002)***.

Data available are inadequate to formulate recommendations for or against post-phototherapy bilirubin testing. Many reports on the subject have been flawed by comprising retrospective chart reviews, analysis of rebound by determining the mean bilirubin value rather than peak post-treatment values. Lack of preset definitions for rebound or indications for retreatment are issues for further investigations ***(Bansal et al., 2010)***.

AIM OF THE WORK

The aim of this study was to determine whether a rebound in serum bilirubin level occurs within 24 hours after discontinuation of phototherapy in neonates with hyperbilirubinemia and to identify aetiological factors for hyperbilirubinemia that could be used to select infants at risk for rebound.