Exchange Transfusion versus Intravenous Immunoglobulins in Treatment of Isoimmune Hemolytic Neonatal Jaundice

Thesis

Submitted for partial fulfillment for Master Degree in Pediatrics

By

Rehab Nadeem Abd El-Shafey M.B., B.Ch, (2003)

Under Supervision of

Prof. Dr. Laila Hussein Mohamed

Professor of Pediatrics
Faculty of Medicine, Cairo University

Prof. Dr. Ismail Bahie El-Din El-Hawary

Professor of Pediatrics
Faculty of Medicine, Cairo University

Dr. Mai Ahmed Khairy

Assistant Professor of Pediatrics
Faculty of Medicine, Cairo University

Faculty of Medicine Cairo University 2011



سورة البقرة آية (٣٢)



To my dear **Father**; who taught me how to love, scarify and how to be a genuine person

To my dear country, **EGYPT**, to which I am proud to belong

To everyone scarified his soul for our rights...we will never forget you

To my dear family...who provided me with love and support

Acknowledgment

First and foremost, I fell always indebted to **Allah**, the most kind and the most merciful.

I would like to express my sincere thanks to **Prof. Dr. Laila Hussein Mohamed,** Professor of Pediatrics, Faculty of Medicine, Cairo University for her supervision, guidance, valuable advice and helpful directions.

My extreme thanks and gratefulness to **Prof. Dr.**Ismail Bahie El-Din El-Hawary, Professor of Pediatrics, Faculty of Medicine, Cairo University, for his keen interest, beneficial advice, constant support and scientific opinions.

I also wish to offer my warmest and deeppest appreciation to **Dr. Mai Ahmed Khairy**, Assistant Professor of Pediatrics, Faculty of Medicine, Cairo University, for her unlimited, endless help and continuous encouragement.

Abstract

Key words: (hemolytic jaundice- exchange transfusion-intravenous Immunoglobulins)

Progressive hemolytic jaundice is conventionally treated with phototherapy and exchange transfusion. Recent studies have demonstrated that the use of intravenous immunoglobulins is promising in its management. In Our study 40 neonates with neonatal jaundice due to ABO and Rh incompatibility were studied. They were divided into 2 groups; one treated with immunoglobulins and other treated with exchange .We concluded that immunoglobulins decreases the level of serum bilirubin as exchange transfusion and in addition it shortens the period of hospitalization and phototherapy with no side effects detected.

Table of Contents

Introduction	1
Aim of the Work	3
Review of Literature	4
Patients and Methods	62
Results	67
Discussion	84
Summary and conclusion	92
Recommendations	94
References	95

List of Tables

		Page No.
Table (1):	Drugs that cause significant displacement of bilirubi	
Table (2):	Congenital Nonhemolytic Unconjugate Hyperbilirubinemia	
Table (3):	Characteristic Difference between Rh and ABO Hemolytic Disease of Newborn.	
Table (4):	Risk factors for development of seven hyperbilirubinemia in infants of 35 or more week gestation	's
Table (5):	Management of hyperbilirubinemia in the health term newborn	
Table (6):	Management of hyperbilirubinemia in pretern newborns (sick and well)	
Table (7):	Immunomodulatory action of IVIG	52
Table (8):	Comparison between the two studied group according to sex, mode of delivery and family histor of other jaundiced sibling	y
Table (9):	Comparison between the two studied group according to birth weight in (gms)	
Table (10):	Comparison between the two studied group according to gestational age in (wks)	
Table (11):	Comparison between the two studied group according to day of admission	
Table (12):	Comparison between the two studied group according to hospital stay and duration of phototherapy	of
Table (13):	Comparison between the two studied group according to complete blood picture and correcte reticulocytic count.	d

Table (14):	Comparison between the two studied groups according to blood group of the mother and blood group of the baby	 75
Table (15):	Comparison between Total serum bilirubin levels in group I (IVIG) on successive days	 76
Table (16):	Comparison between Total serum bilirubin in group II (Exchange transfusion) on successive days	 78
Table (17):	Comparison between the two studied groups according to Total serum bilirubin	 80
Table (18):	Adverse effects reported in Exchange transfusion group:-	 83

List of Figures

		Page No.
Fig (1):	Neonatal bile pigment metabolism	9
Fig (2):	Algorithm for the suggested evaluation of a ternewborn with hyperbilirubinemia	
Fig (3):	Hour-specific bilirubin Nomogram	37
Fig (4):	Guidelines for phototherapy in hospitalized infants 35 or more weeks' gestation.	
Fig (5):	Guidelines for exchange transfusion in infants 35 more weeks' gestation.	
Fig. (6):	Normal Bilirubin Metabolism and Bilirub Metabolism during Phototherapy.	
Fig. (7):	Immunoglobulin	49
Fig. (8):	Mechanism of maternal-fetal immunization and IVI antibody blockage	
Fig. (9):	Comparison between the two studied groups according to birth weight in (gms).	•
Fig. (10):	Comparison between the two studied groups according to gestational age in (wks)	ng 70
Fig. (11):	Comparison between the two studied groups according to day of admission.	•
Fig. (12):	Comparison between the two studied groups according to hospital stay and duration of phototherapy.	•
Fig. (13):	Comparison between Total serum bilirubin levels group I (IVIG) on successive days.	

Fig. (14):	Comparison between Total serum bilirubin in group II (Exchange transfusion) on successive days	. 79
Fig. (15):	Comparison between the two studied groups according to Total serum bilirubin	. 82

List OF Abbreviations

AAP : American Academy of Pediatrics

ALT : Alanine TransaminaseAST : Aspartate TransaminaseATP : Adenosine Triphosphate

 $\mathbf{B}_{\mathbf{F}}$: Free Bilirubin

CHT : Congenital hypothyroidismCNS : Central Nervous System

CO : Carbon monoxide

CPD : Citrate phosphate dextroseELBW : Extremely low-birthweight

ETCO: End Tidal carbon monoxide in Breath

Fab : Fragment, Antigen Binding
Fc : Fragment, Crystallizable

FFA: Free fatty acids

G6PD: Glucose -6- phosphate-Dehydrogenase Deficiency

GGT : G-Glutamyl Transferase

Hb : Hemoglobuin

HBV : Hepatitis B Virus

Hct : Hematocrite

HCV : Hepatitis C Virus

HDN : Hemolytic disease of newborn

HE : Hereditary ElliptocytosisHIDA : Hepatoiminodiacetic acid

HIV : Human Immunodeficiency Virus

I/T : Immature to total ratio

Ig : Immunoglobulin

IgA : Immunoglobulin A

IgD : Immunoglobulin D

IgE : Immunoglobulin E

IgG : Immunoglobulin G

IgM : Immunoglobulin M

IPT : Intraperitoneal transfusion

IUT : Intrauterine transfusion

IVIG : Intravenous Immunoglobulins

IVT : Intravascular transfusion

MRI : Magnatic Resonant Imaging

NADPH : Nicotinamide adenine dinucleotide phosphate

NAIT : Neonatal alloimmune thrombocytopenia

NAN : Neonatal alloimmune neutropenia

NEC : Necrotising enterocolitis

NH : Neonatal hemochromatosis

PK : Pyruvate kinase

Plt : Platlets

PPARs : Peroxisme-Prolifitated Activated Receptors

RBC: Red blood cells

SGOT : Serum Glutamic Oxaloacetic Transaminase

SGPT : Serum Glutamic Pyruvic Transaminase

TCB : Transcutaneous Bilirubinometry

TLC : Total leucocytic count
TSB : Total serum bilirubin

UCB : Unconjugated bilirubin

UDPG-T: Uridine-Diphosphoglucuronyl Transferase

WBC: White blood cells

Introduction

Neonatal hyperbilirubinemia is a commonly seen neonatal problem, approximately 60-70% of term infants and 80% of preterm infants develop jaundice in the first week of life. Although transient, the condition accounts for up to 75% of hospital readmission in the first week after birth (*Shapiro*, 2006).

Neonatal jaundice secondary to isoimmune hemolytic anemia (Rh-ABO incompatibility) is a cause of high serum bilirubin level due to hemolysis of red blood cells secondary to transplacental passage of antibodies.

Sensitization in Rh incompatibility occurs when an Rh D-negative mother may first encounter the D antigen while being pregnant with Rh D-positive child, or by receiving a blood transfusion of Rh D-positive blood. Once the mother has been sensitized her immune system produces IgM isotope that do not cross the placenta, later it produces IgG isotope that transverse the placental barrier (*Urbaniak and Gresis*, 2000).

The O positive mothers have Ig anti-A or anti-B antibodies, 10% to 15% of them are IgG producers. When an A or B positive newborn is born to an O positive mother, the O positive red cells with high titers of anti-A or anti-B cross the placental barrier and reach the fetal circulation and cause hemolysis. ABO incompatibility causes less severe anemia and jaundice than Rh incompatibility (*Bhat*, 2005).

The degree to which the fetus is affected correlates with the amount of maternal antibody that crosses the placenta (*Koeing*, 2000).

This leads to increased risk of acute bilirubin encephalopathy and kernicterus (*Murray and Roberts*, 2007).

Exchange transfusion is sometimes needed besides the conventional therapy (phototherapy) as it corrects anemia associated with hemolysis and is effective in removing sensitized red blood cells before they are hemolyzed. It also removes about 60% of bilirubin from the plasma, resulting in a clearance of about 30% to 40% of total bilirubin as it equilibrates with the extravascular tissue. Exchange transfusion is not without a risk. It carries a 5% risk of major morbidity and the risks associated with blood exposure. Infants receiving exchange transfusion have increased risks of infection, necrotizing enterocolitis, acidosis, hypocalcaemia, hypoglycemia, electrolyte abnormalities and air embolism (*Patra*, 2004).

In recent years, intravenous immunoglobulins (IVIG) have been successfully used in isoimmune hemolytic anemia (Rh-ABO incompatibility) (*American Academy of Pediatrics*, 2004).

It has been found that after IVIG administration there was a significant fall in total serum bilirubin level and no exchange transfusions were required (*Walsh et al.*, 2008).

None of the studies of IVIG use for Hemolytic Disease of the newborn reported any serious side effects; they are very rare but include hypersensitivity and anaphylaxis (*Gottstein and Cooke*, 2003).

Intravenous immunoglobulins (IVIG) were found to decrease hemolysis leading to reduction in serum bilirubin level. The immunoglobulin could act by occupying the Fc receptors of reticulo-endothelial cells preventing them from taking up and lysing antibody coated RBCs (Walsh and Molloy, 2009).

Aim of the Work

- 1. To assess the effectiveness of IVIG in reducing the need for exchange transfusion, the duration of phototherapy and hospital stay.
- 2. To compare between the efficiency of exchange transfusion and IVIG in lowering level of TsB in neonates suffering from indirect hyperbilirubinemia due to Rh and ABO incompatibility.