

Ain shams university



Faculty of post graduate Childhood studies

Probiotics for the management of Neonatal hyperbilirubinemia

Thesis

Submitted for Partial Fulfillment of Master Degree in childhood studies of special needs

Presented By

Nasser Ramzy Rofail

M.B.B.Ch., ped. Diploma,
(Ministry of health)

Under Supervision of

Dr./Khaled Hussien Taman

Professor of Pediatrics
Faculty of post graduate childhood
studies Ain shams university

Dr./Rehab Abd-Elkader Mahmoud

Professor of Pediatrics
Faculty of post graduate childhood
studies Ain shams university

2018



سورة البقرة الآية: ٣٢



Thanks to ALLAH who offered me the ability to perform this work.

- I would like to express my sincere and deep gratitude to my *Dr. khaled Hussien Taman professor of pediatrics*, faculty of post graduate childhood studies, Ain shams university.

For his very valuable help, starting from choosing the subject and protocol till the end of the study.

I would like to thank him for his cooperation and kind suggestion and revision of the work, it is great honour to work under his guidance and supervision.

- I am also like to express my sincere and deep gratitude to my professor *Dr. Rehab Abd – Elkader Mahmoud. Professor of pediatrics*, faculty of post graduate child hood studies, Ain shams university.

For her valuable help, cooperation and kind suggestion and the time she spent during performing and revision of the work.

It is great honour to work under his guidance and supervision.

- I cannot forget the sincere cooperation offered by colleagues in the **ICU** incubator department in kenayat – hospital – in zagazig for their help in the practical and chlincal part of this work.

God bless all the lovely children participated in this study.

Contents

Title	Page
INTRODUCTION	3
REVIEW OF LITERATE	
Chapter 1	6
Chapter 2	48
SUBJECTS AND METHODS	67
RESULTS	7 6
DISCUSSION	88
SUMMARY	98
REFRENCES	103
ARABIC SUMMARY	128

A list of Abbreviations

TSB	Total serum Bilirubin
CBC	Complete Blood count
ABO	Blood groups A, B, AB, O
Rh	Rhesus factor
RBCS	Red Blood cells
G6PD	Glucose – 6- Phoshatc dehydro- genase.
CRP	Celluar – Reactive protein
NICU	Neonatal Intnesive care unit
VLBW	Very low Birth weight
PN	Parenteral Nutrition
NEC	Necrotizing Enterocolitis
B.GD.	Bata – Glucoronidase
UDPG.T	Uridine Diphosphate Glucoronidyl transferase
СВ	Conjugated Bilirubin
UCB	Un Conjugated Bilirubin
ECT	Exchange transfusion
СО	Carbon monoxide
FE	Ferrous
TORCH	Toxoplasmosis /Rubella/ cystomegalo virus/ Herpes
IGI	Immuno globulin A
IVIG	Intervanous immuno globulin
IL	Inter- leukin
EGF	Epidermal growth factor
IGG	Immuno globulin G
GA	Gestational Age
TCB	Trans cutaneous bilirubin

List of Tables

Table	Subject	Page
Table (1)	Drugs that cause significant displacement of bilirubin from albumin in vitro.	9
Table (2)	Factors that exacerbate physiological jaundice leading to high scrum bilirubin levels	16
Table (3)	Effects of Bilirubin toxicity in new borns.	38
Table (4)	Criteria to estimate clinical jaundice.	38

List of Tables

Table	Subject	Page	
Table (1)	Age distribution between groups		
Table (2)	Gestational age distribution between groups.		
Table (3)	Weight distribution between groups.		
Table (4)	Total bilirubin distribution between groups in/out	80	
Table (5)	Change assessment in each group	80	
Table (6)	Day before discharge distribution between groups	81	
Table (7)	Correlations of total bilirubin, days under treatment		
	gestatienal ago/and weight between groups.		
Table (8)	Type distribution between groups.	83	
Table (9)	Comparison among types in control groups.		
Table (10)	Comparison among types in intervention groups		
Table (11)	Total Bilirubin distribution between groups in hemolytic	85	
Table (12)	Total bilirubin distribution between groups in infection.		
Table (13)	Total bilirubin distribution between groups in physiological	87	

Graphes

Figure	Subject	Page
Graph (1)	Age distribution between groups.	77
Graph (2)	Gestational age distribution between groups	78
Graph (3)	Weight distribution between groups	79
Graph (4)	Total bilirubin distribution between groups IN /OUT	80
Graph (5)	Day needed distribution between groups	81
Graph (6)	Types distribution between groups	83
Graph (7)	Bilirubin in hemolytic	85
Graph (8)	Bilirubin in infection	86
Graph (9)	Bilirubin in physiological	87

Abstract

Background In recent years, the tendency to use drugs has been increasing in the treatment of neonatal jaundice. Several drugs have been used since then, but the effect of probiotics on serum bilirubin level (SBL) is not so clear. This study was conducted to evaluate the effect of probiotics on SBL and the duration of phototherapy in with term neonates hyperbilirubinemia. Objective/ the aim of the work: To evaluate and assess the therapeutic effects of the probiotic substance on neonatal jaundice. Subjects and Methods: - In this Experimental Randomized clinical trial study we studied (400) newborns with jaundice hospitalized for phototherapy in kenayate Hospital in zagazig during 5/2017 to 5/2018 - Eligible were Randomly divided into two groups: neonates Intervention (n = 200) 2) control (n = 200) Both groups receive standard conventional phototherapy but the intervention group received 250mg lactobacillus powder with milk as a probiotic substance until hospital discharge. The out come variable were. TSB and the duration of phototherapy.- the data were analyzed by (SPSS version 20.0) and p value was at (< 0.05) for significant, (< 0.01) for high significant. **Results** - TSB (out)/on discharge after hospitalization of intervention group was a mean: 9.39 ± 1.35 and of **control group** was a mean: 9.89 ± 0.9 , (TSB) was highly significant lower in intervention group / on discharge with a probiotic substance than the control Group/ on

without a probiotic substance. Duration discharge hospitalized days needed to stay under the phototherapy treatment are of intervention group is a mean of : 4.84 ± 0.62 and of control group is a mean of 5.785 ±0.801, duration of hospitalized days under phototherapy treatment of intervention group with a probiotic substance was highly significant lower than of control group. Without a probiotic substance. (TSB) out / on discharge was significantly lower in both groups in physiologic cases more than other two hemolytic and infectious cases and significantly lower in infectious than hemolytic cases. **Conclusion:** Probiotics lowered the serum bilirubin levels of neonates with jaundice and decrease the duration of hospitalized days under phototherapy treatment Recommendation: This study recommended that we can use a probiotic substance within a plane of management of neonatal hyperbilirubinemia. **Key words:** total serum bilirubin, phototherapy, probiotics.

INTRODUCTION

- Neonatal jaundice is defined as the yellowish discoloration of the sclera, mucuous membrane and skin caused by hyperbilirubinemia, which is one of the most common conditions confronting neonatologists daily. About 60% of term and 80% of preterm infants develop jaundice in the first week of life. (Annagur et al., 2014)

The incidence of neonatal jaundice remains high because of infections, genetic factors and premature birth. Depending upon the cause, jaundice may be present at birth or any time during the neonatal period. Jaundice due to either indirect (un-conjugated) or direct (conjugated) bilirubin within the first 24 hours of life should be taken seriously. (Rennie et al., 2011)

In rare instance, the TSB reaches levels that can cause kernicteurs, a condition characterized by bilirubin staining of neurons and neuronal necrosis involving primarily the basal ganglia of the brain and manifested in athetoid cerebral palsy, hearing loss, dental dysplasia, and paralysis of upward gaze. (Ambalvan and carlo, 2012)

For preventing the kernicterus and other complications of hyperbilirubinemia, jaundice should be managed by phototherapy or exchange transfusion (ECT) (Wallen stein et al., 2013)

Neonatal jaundice, which is common in clinical practice, can mainly be classified as **physiological** and **pathological** ones. The former does not need special treatment, But the latter, which originates from various factors, easily leads to bilirubin encephalopathy and even brain damage or death. (Utalah S, et al 2016)

The mature GIT contains a large quantity of microbiota. that play a role in protecting infant and promoting health functionality.

The normal development of the human GIT depends on the presence of complex gastro intestinal microbiota. (Yi- LiG et al 2017)

-Probiotic: a living friendly bacteria or micro - organism in the intestine. , Have health Benefit on the host. , It's a normal intestinal flora. and Controlls the growth of harmfull bacteria.

which, when administered in adequate amounts, confer a health benefit on the host, Most commonly available probiotic supplements contain Lactobacillus and/or Bifidobacterium, which are part of the normal human microbiotic. (Zahed pasha, et al.; 2017)

Current recommendations for the management of hyperbilirubinemia in preterm infants have focused on determining age - specific bilirubin levels for initiating phototherapy.(Maisels MJ, et al.,2012)

However, there is concern regarding Potential adverse effects. of aggressive phototherapy in preterm infants. Besides blue light phototherapy, and drugs, probiotics have also been used to enhance immunity mainly by regulating bacterial colonies. They can form a biological barrier by specifically binding intestinal epithelial cells

through teichoic acid. Therefore, particular attention has-been paid to the use of probiotics in treating neonatal jaundice. (**Tyson JE**, et al.2012)