Effect of Enteral Lactoferrin Administration on Invasive Fungal Infections in Preterm Neonates

Thesis

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By

Menna Allah Maged El Tagoury
M.B, B.Ch

Under supervision of

Prof. Dr. Maha Hassan Mohamed
Professor of Pediatric Medicine
Faculty of medicine - Ain Shams University

Dr. Hebat Allah Ali Shaaban
Lecturer of Pediatric Medicine
Faculty of medicine- Ain Shams University

Dr. Marwa Saad Fathi
Assistant Professor of Medical Microbiology and Immunology
Faculty of medicine- Ain Shams University

Dr. Mohamed Salah Eldin Mohamed Abdelkader
Lecturer of Pediatric Medicine
Faculty of Medicine- Must University

Faculty of Medicine
Ain Shams University
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List of Abbreviations

Abb.	Full term
APO-LF	*Apo Lactoferrin*
ARDS	*Acquired respiratory distress syndrome*
BCG	*BaciilusCalmette-Guerin*
BLF	*Bovine lactoferrin*
BPD	*Bronchopulmonary dysplasia*
CBC	*Complete blood count*
CMV	*Cytomegalovirus*
CRP	*C reactive protein*
CSF	*Cerebrospinal fluid*
CVC	*Central Venous Catheter*
CXR	*Chest x ray*
DIC	*Disseminated intravascular coagulation*
DM	*Diabetes mellitus*
DNA	*Deoxyribonucleic acid*
ECHO	*Echocardiography*
E-Coli	*Escherichia coli*
ELBW	*Extremely low birth weight*
EOS	*Early onset sepsis*
EPO	*Erythropoietin*
ERE	*Estrogen response elements*
ETT	*Endotracheal tube*
EV71	*Enterovirus 71*
FE+3	*Ferric Ions*
GBS	*Group B streptococci*
G-CSF	*Granulocyte colony-stimulating factor*
GIT	*Gastrointestinal tract*
Hb	*Hemoglobin*
HBV	*Hepatitis B virus*
HCT	*Hematocrit*

List of Abbreviations (Cont....)

Abb.	Full term
HCV	*Hepatitis C virus*
HIE	*Hypoxic Ischemic Encephalopathy*
HIV	*Human Immunodeficiency virus*
HLF	*Human lactoferrin*
HLF	*Halo Lactoferrin*
HS	*Heparin sulphate*
HSV	*Herpes Simplex Virus*
IAP	*Intrapartum antibiotics prophylaxis*
IFIs	*Invasive fungal infections*
IFN	*Interferon*
IL	*Interleukin*
INT1p	λ phage integrase 1p
IRDS	*Infant respiratory distress syndrome*
IVH	*Intraventricular hemorrhage*
IVIG	*Intravenous Immunoglobulins*
KDa	*Kilodalton*
LBW	*Low birth weight*
LF	*Lactoferrin*
LGG	*Lactobacillus Rhamnosus GG*
LOS	*Late onset sepsis*
LPS	*Lipopolysaccharide*
LSCS	*Lower segment cesarean section*
MV	*Mechanical Ventilation*
NEC	*Necrotizing enterocolitis*
NICU	*Neonatal intensive care unit*
NK	*Natural Killer*
NPO	*Nil per Os*
NS	*Neonatal sepsis*
PDA	*Patent Ductus Arteriosus*

List of Abbreviations (Cont....)

Abb.	Full term
PIV	*Parainfluenza virus*
PLT	*Platelets.*
PMN	*Poly morphnuclear cell*
PPV	*Positive pressure ventilation*
PROM	*Premature Rupture of membranes*
Pulm hge	*Pulmonary hemorrhage*
PV	*PolioVirus*
PVHI	*Periventricular Hemorrhagic Infarction*
RCT	*Randomized controlled trial*
RDS	*Respiratory distress syndrome*
RNA	*Riboxynucleic acid*
ROP	*Retinopathy of prematurity*
RSV	*Respiratory Syncytial virus*
S. Ferritin	*Serum ferritin.*
SD	*Standard deviation*
SGA	*Small for gestational age*
SPP	*Species*
SPSS	*Statistical Program for social science*
SVD	*Spontaneous vaginal delivery*
UTI	*Urinary Tract Infection*
VLBW	*Very low birth weight.*
WHO	*World Health Organization*

INTRODUCTION

Preterm birth is defined as the birth of a living neonate before the 37th gestational week ***(Blencowe et al., 2012).***

Those preterm babies especially very low birth weight (VLBW) (< 1500 g) and ELBW (<1000 g) are more susceptible to the risk of invasive fungal infections (IFIs), this risk is inversely proportional to the gestational age and birth weight ***(Kaufman and Manzoni, 2010).***

Many risk factors contribute in the increase of IFIs in the preterm neonate such as:

- Invasive procedures, such as central vascular catheters and endotracheal tubes.
- Exposure to broad-spectrum antibiotics and parenteral nutrition.
- The occasional use of postnatal steroids and gastric acid inhibitors.

(Chitins et al., 2012 and Kaufman, 2012)

The most common organism causing nosocomial fungal infections is *Candida* which is the 2nd most common cause of infectious disease related death in the neonatal intensive care unit (NICU) ***(Testoni et al., 2012).***

Candida infection can spread vertically from maternal flora or horizontally from health care workers or contaminated sources ***(Testoni et al., 2012).***

Although, the VLBW infant with candidiasis can present with many of the nonspecific signs and symptoms associated with invasive bacterial infection, symptoms are often more subtle and indolent and the lab results are not readily available ***(Greenberg et al., 2012).***

Fluconazole has been shown to be safe and effective in a number of randomized controlled trials (RCTs) and it is recommended in settings of patients with high incidence of IFIs ***(Kaufman et al., 2010).***

Despite reassuring reports, some concerns still exist related to long-term safety and modification of the fungal ecology induced by this azole with emergence of resistant strains ***(Manzoni et al., 2008 and Kaufman and Manzoni, 2010).***

Hence comes the importance of the use of prophylactics against IFIs to decrease the financial burden on the health system related to long term sequelae of IFIs in addition to long hospital stay.

Lactoferrin (LF) has immersed as a new tool for prevention of IFIs, it is an iron binging glycoprotein that is naturally present in mammalian milk, colostrum, tears, saliva, CSF and vaginal secretions, it's considered as a cell-secreted mediator that bridges the innate and adaptive immune responses ***(Valentini and Antonini, 2005 and Siqueiros-Cendon et al., 2014).***

Many studies had shown its important role in the innate immunity by its anti-bacterial, anti-viral, anti-fungal, anti-parasitic, anti-cancer, anti-inflammatory, anti-oxidant, anti-allergic, iron absorption modulatory functions ***(Pierce et al., 2009 and Trend et al., 2015).***

Its antifungal activity in particular is due to its fungistatic effects, and the activity of the N-terminal, 11 aminoacidic peptide of LF called lactoferricin [hLF(1-11)] ***(Lupetti et al., 2007).***