Efficacy of Enteral Lactoferrin and Oral Care with Bovine Colostrum in the Prevention of Invasive Fungal Infection in Preterm Neonates

Thesis

Submitted for Partial Fulfillment of
Master Degree in **Pediatrics**

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2018

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to **ALLAH** *the Most Beneficent and Merciful.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Hisham Abdel-Samie Awad****, Professor of Pediatrics, Faculty of Medicine, Ain-Shams University, for his meticulous supervision, kind guidance, valuable instructions and generous help.*

Special thanks are due to ***Ass. Prof. Nancy Mohamed Abou-Shady****, Assistant Professor of Pediatrics, Faculty of Medicine, Ain-Shams University, for her sincere efforts, fruitful encouragement.*

I am deeply thankful to ***Ass. Prof. Marwa Abd El Rasoul El Ashry****, Assistant Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her great help, outstanding support, active participation and guidance.*

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List of Abbreviations

Abb.	Full term
+PV	*Positive predictive value*
1,3 b-D glucan	*1,3 beta D glucan*
5-FC	*5-Flucytosine*
AAP	*American Academy of Pediatrics*
ABCD	*Amphotericin B colloidal dispersion*
ABLC	*Amphotericin B liposomal complex*
ACOG	*American College of Obstetricians and Gynecologists*
AmB	*Amphotericin B deoxycholate*
ATP	*Adenosine triphosphate*
AUC	*Area under the curve*
BC	*Bovine colostrum*
BDG	*Beta D glucan*
bLF	*Bovine lactoferrin*
BW	*Birth weight*
C.S	*Ceserean section*
CBC	*Complete blood count*
CNS	*Central nervous system*
CONS	*Coagulase-negative staphylococci*
CRP	*C-reactive protein*
CSF	*Blood and cerebrospinal fluid*
CT	*Computed tomography*
CVC	*Central venous catheter*
ELBW	*Extremely-low birth-weight*
ELISA	*Enzyme-linked immune-sorbent assay*
EMA	*European medicine agency*
EORTC-MSG	*The European Organization for Research and Treatment of Cancer-National Institute of Allergy and Infectious Diseases Mycosis study group*
EOS	*Early onset sepsis*

List of Abbreviations cont...

Abb.	Full term
ESCMD	*European Society of Clinical Microbiology and Infectious Diseases*
FBP	*Focal bowel perforation*
FDA	*Food and drug admnistration*
GA	*Gestational age*
GBS	*Group B streptococcal*
GGT	*Gama glutyl transferse*
GI	*Gastrointestinal*
GN	*Gram negative*
HCME	*Hematogenous candida meningeoencephalitis*
HGB	*Hemoglobin*
HIV	*Human immundeficieny virus*
HRC	*Heart rate characteristics*
HSS	*Hematologic scoring system*
IC	*Invasive candidiasis*
IFD	*Invasive fungal disease*
IFI	*Invasive fungal infection*
IFN-γ	*Interferon gamma*
IGFs	*Insulin-like growth factors*
Igs	*Immunoglobulins*
IL	*Inteleukin*
IPFI	*Invasive pulmonary fungal infection*
IV	*Intravenous*
L-AmB	*Liposomal amphotericin B*
LBW	*Low birth weight*
LF	*Lactoferrin*
LGG	*Lactobacillus Rhamnosus GG*

List of Abbreviations cont...

Abb.	Full term
LOS	*Late onset sepsis*
LTF	*Lactotransferrin*
MRI	*Magnetic resonance imaging*
NASBA	*Nucleic acid sequence-based amplification*
NEC	*Necrotizing enterocolitis*
NICU	*Neonatal intensive care unit*
NS	*Neonatal sepsis*
OFALT	*Oropharyngeal-associated lymphoid tissue*
Ors	*Odds ratios*
PCR	*Polymerase chain reaction*
PD	*Pharmacodynamic*
PK	*Pharmacokinetics*
PLT	*Platelet*
PMNs	*Polymorph nuclear leucocyt*
PPI	*Proton pump inhibitor*
-PV	*Negative predictive value*
SDA	*Sabouraud dextrose agar*
SNAP II	*Score for neonatal acute physiology II*
Spp	*Species*
Th2	*T helper*
TLC	*Total leucocytes count*
TPN	*Total parenteral nutrtion*
UTI	*Urinary tract infection*
VLBW	*Very low birth weight*
WBC	*White blood cell count*
WHO	*World health organization*

INTRODUCTION

Neonatal sepsis (NS) related morbidity and mortality is a concern in neonatal intensive care units (NICUs). Regardless of the recent improvements in the quality of neonatal assistance, infections cause 1.6 million neonatal deaths annually worldwide and more than 50% of these deaths occur in preterm or low birth weight infants in NICUs ***(Manzoni et al., 2011).***

Sepsis is a particular problem in very low birth weight infants (VLBW, birth weight < 1500 g); early onset sepsis (sepsis in infants < 72 hrs of life) occurs in about 1.5% and late-onset sepsis in about 21% of VLBW infants ***(Stoll, 2005; Stoll, 2002).***

Invasive fungal disease (IFD) is an important cause of late-onset sepsis in the neonatal intensive care unit (NICU), and is associated with severe co-morbidities and high rates of neurodevelopmental impairment.

The rising incidence of severe fungal infections has made the discovery of new compounds that have effective antifungal activity or that support the activity of currently used antifungal agents more important than ever. Natural products are a significant source of novel antimicrobial compounds, and an increasing number are being identified from mammalian sources including milk proteins. One example is the

multifunctional iron-binding glycoprotein, lactoferrin (Lf), and its various derived peptides ***(Fernandes and Carter, (2017)***.

Lactoferrin (LF) formerly known as lactotransferrin (LTF) is a glycoprotein from the transferrin family that has been attracting growing scientific interest since the late 1950's, due to its high concentration in human milk and its physiological functions, specially the antimicrobial, anti-inflammatory and immunomodulating functions on the gastrointestinal tract ***(Queiroz et al., 2013).***

Colostrum is the first milk that mammals produce after parturition, and its composition differs markedly from that of milk produced later in lactation. This fluid has evolved under selective pressure to care for highly sensitive mammalian neonates and is believed to contribute significantly to initial immunological defense in the neonatal period as well as to the growth, development, maturation, and integrity of the neonatal gastrointestinal (GI) tract ***(Rathe et al., 2014).***

Bovine colostrum (BC) has been found to be almost identical to human colostrum in terms of its beneficial components. It has also been found to be useful and produces no side effects ***(Godhia and Patel, 2013).***

The particular influence of early mother's milk exposure to the extremely premature infant's oropharynx is unique and important. Experts postulate that breastfed infants are protected