ROLE OF EXCHANGE TRANSFUSION IN THE TREATMENT OF NEONATAL SEPTICEMIA

M.Sc. Thesis

Submitted for the partial fulfilment of
Master Degree in Pediatrics

By

HANAN MOHAMED EBRAHIM
M.B.B.CH.

Under the supervision of

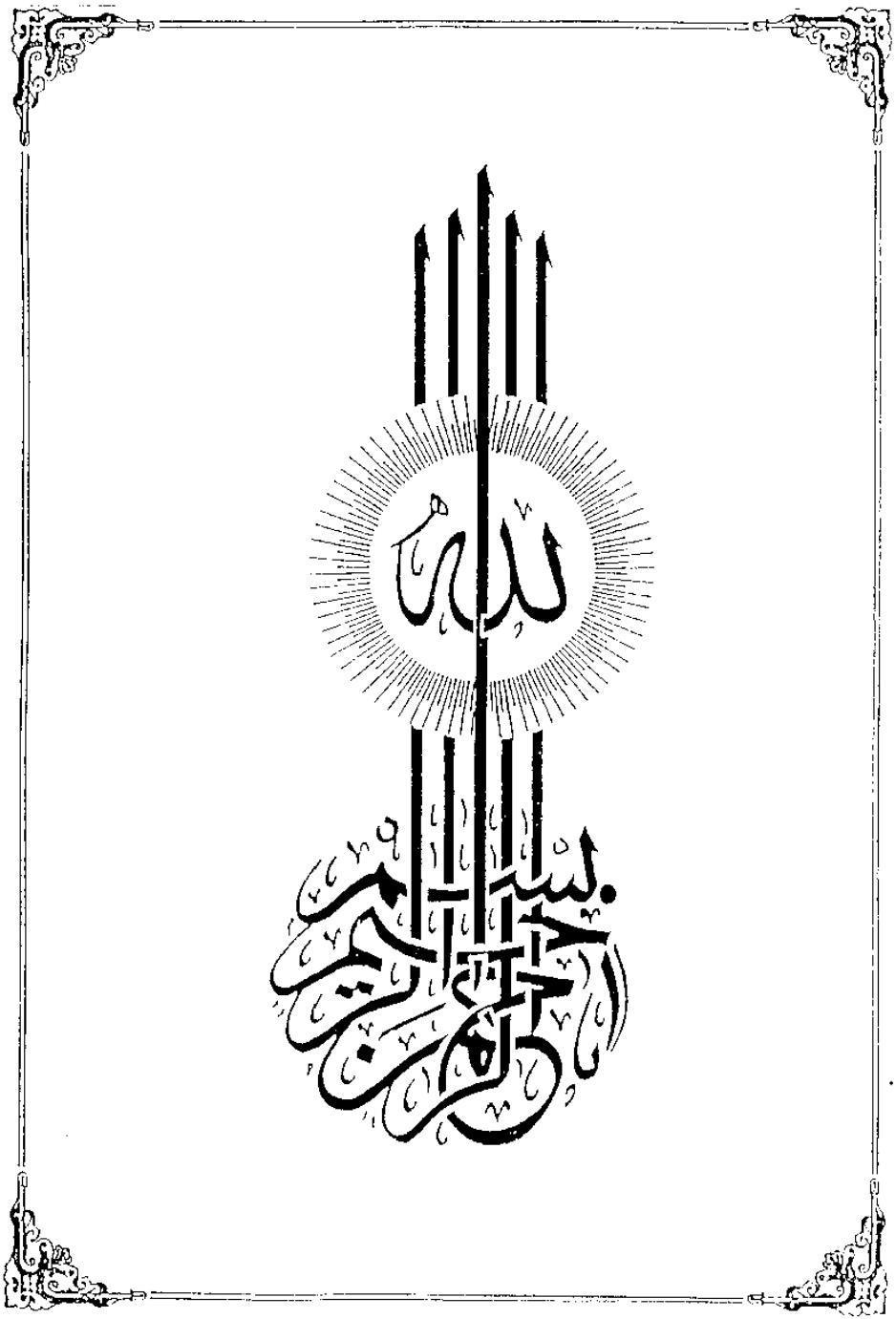
Prof. Dr. Saadia Mohamed Abdel Fattah
Professor of pediatrics
Faculty of Medicine
Ain Shams University

Dr. Hesham Abdel Samei Awad
Lecturer of Pediatrics
Faculty of Medicine
Ain Shams University

Dr. Tahany Aly El-Kerdany
Lecturer of Clinical Pathology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
1993


بسم الله الرحمن الرحيم



LIST OF TABLES

LIST OF ABBREVIATIONS

Ab : Antibody .

Ag : Antigen .

AGA : Appropriate gestational age .

APC : Antigen-persenting cells .

BUN : Blood urea nitrogen .

C : Complement .

CIE : Counter current immunoelectrophoresis .

CRP : C-reactive protein .

C.S.F : Cerebrospinal fluid .

DIC : Disseminated intravascular coagulation .

E coli : Escherichia coli .

FT : Fulltern .

GBS : Group-B streptococci .

Hg : Haemoglobin .

HpG : Haptoglobin .

H.I.E : Hypoxic ischemic encephalopathy .

HIV : Human immune deficiency virus .

H.S.M : Hepatosplenomegaly .

HSS : Hematologic scoring system .

I.D.M : Infant of diabetic mother .

Ig : Immunoglobulin .

IL-6 : Inter leukin 6 .

I.M : Intramuscular .

I.V : Intravenous .

IVIG : Intravenous immunoglobulin .

Contents

***

Introduction And Aim of The Work

*Introduction

Neonatal sepsis is a disease of infants who are less then (1) month of age are clinically ill and have positive blood cultures (***Siegel and McCracken, 1981***).

Multiple risk factors for perinatal infection have been identified . These factors can be generally divided between maternal and neonatal observations (***Cole,1991***).

The high frequency of infection in the newborn has been ascribed to the immaturity of the immune system at brith (***Stern ,1992***).

Systemic bacterial infections during the first month of life have remained a major cause of infant morbidity and mortality despite the development of broad spectrum antimicrobial agents and technologic advancements in life support therapy (***Yoder and Polin,1986***).

Reliable statistics are not available because sepsis of the newborn is poorly defined and is not a reportable disease. Estimates of incidence range from one to four per 1,000 live births (***Gotoff 1992 b***).

Future therapy of neonatal sepsis will depend on new non toxic methods for enhancing neonatal host defense (***Cairo,1989***).

Exchange transfusion using whole fresh blood have been used in neonatal septicemia to (1) remove bacterial toxins and /or decrease the bacterial burden , (2) improve peripheral and pulmonary perfusion and (3) booster the immune system of infected newborn infants.Furthermore fresh blood transfusion provide an alternative method of providing neutrophils to septic newborn infants with severe neutrophil storage pool (NSP) depletion (***Clohrty,1991***).

Aim of the work

To find out the effect of exchange transfusion in raising the immunity in cases of neonatal septicemia through evaluation of the phagocytic power before and after exchange transfusion being one of the most important host defense mechanisms.

Review Of Literature

Immune System

The immune response is made up of a complex sequence of events ; indeed , the primary function of immune response is to discriminate between self and non self and thereby to eliminate the latter . The immune response depends primarily on 3 major cell types : macrophages , thymus - derived lymphocytes (***T cells***) , and bone marrow - derived lymphocytes (***B cells***). These interact with one another , either directly or via interleukins. In addition , the immune system is integrally connected with complement , kinin , clotting and fibrinolytic systems , all of which are involved in inflammatory response (***Goodman ,1991***).

There are 2 levels of defense against invasion by external agents : Innate immunity and adaptive immunity. The principal differences between the two relate to specificity and immunologic memory , which are properties of acquired immunity only (***Kishimoto and Hirano, 1988***).

Innate immunity (***Natural immunity***) is present since birth and includes numerous non specific elements . Body surfaces , especially skin , form the first line of defense against penetration by micro-organisms . The enzyme lysozyme is widely distributed in secretions and can damage the cell wall of many bacteria (***Frank , 1991***) .

Similarly , the alternative complement pathway is directly activated by a variety of bacteria ; this may result in clearance of the bacteria via lysis or via facilitation of phagocytosis by macrophages which possess receptors for certain components of the complement system , and by polymorphonuclear neutrophils (PMNs) , for which activated complement components are chemotactic (***Terr, 1991***) .

Innate immunity against viruses as opposed to bacteria , is implemented by natural killer NK cells and by interferons . NK cells are distinguishable from cytotoxic T lymphocytes on the basis of surface antigens and their failure to exhibit immunologic memory . Alpha and beta interferons are produced by certain leukocyte and by virus - infected cells . Aside from their action on N K cells , interferons elevate the resistance of normal cells to viral infection and thus constitute a vital early defense mechanism against many viruses (***Goodman, 1991***).

Adaptive Immunity (***acquired immunity***) : If the defenses provided by the innate immune system fail to fully prevent infection , the adaptive response comes into play which is distinguished by a remarkable specificity for the offending immunogen and by its memory. In this adaptive immune response , the foreign agent or immunogen triggers a chain of events that lead to the activation of lymphocytes and the production of antibodies and effector lymphocytes which are highly specific for the immunogen . The principal players in adaptive immunity are antigen - presenting cells (APC), thymus - derived lymphocytes (***T cells***) , and bone marrow - derived lymphocytes (***B cells***) . T cells produce soluble molecules with many effects , and B cells eventually result in antibody formation (***Singer and Hodes,1983).***

Neonatal Immune Response

During the 9 months of gestation the fetus develops in a highly protective environment , whereas during the birth process and thereafter the infant is exposed to a wide variety of micro-organisms . Although the antimicrobial defense mechanisms begin to develop early in gestation , at time of delivery many of these mechanisms do not function as efficiently as in older children and adult (***Polmar, 1987***)

Neonatal host defense simulates a clinical state of immune deficiency that predisposes the preterm and term newborn to overwhelming bacterial infections (***Cairo, 1989***)

During neonatal period , the skin which is the greatest natural barrier to infection is functionally and anatomically immature.Skin permeability is increased , melanin production is decreased and an increased susceptibility to blister formation. (***Soloman and Esterly ,1973***).

Normally many substances coating body surfaces serve as local disinfectants and antimicrobial substances . The skin has high content of fatty acids , which are inhibitory to bacteria and fungi . Also the low pH of the skin is sufficient to kill many pathogens (***Mills and Drutz ,1991***).

The pH of the skin of the neonate is higher during the first few days of life than in the older children and adults .The skin surface lipids are similar to those in older children ; during the first 2 weeks of life , cholesterol is decreased and wax esters increased ; the skin's free fatty acids and triglycerides slowly decrease during the postnatal period (***Ramasastry etal, 1970***).

The two most important deficits that are seen to increase the risk of bacterial sepsis in neonates are quantitative and qualitative changes in phagocytic system and defects in antibody mediated immunity (***Cairo, 1989).***

Phagocytic system

The most primitive of the host defense mechanisms involves the ingestion and killing of bacteria and other micro-organisms by phagocytic cell . Although polymorphonuclear leukocytes (PMNs) are the most important phagocytic cells , monocytes and the non mobile phagocytic cell of reticuloendothelial system contribute substantially to the function of this system. (***Polmar, 1987***).

Cells whose major function is phagocytosis of foreign materials and killing of micro-organisms are frequently referred to as " Professional phagocytes , " to differentiate them from other cells , including epithelial cells that have some capacity to ingest foreign material .These include neutrophils, basophils , eosinophils and alveolar macrophages .Professional phagocytes also have surface FC and complement receptors that facilitate phagocytosis , and they contain enzymes in lysosomal granules that will kill eukaryotic and prokaryotic cells (***Mills and Druts, 1991***).

To adequately combat the invading micro-organisms ,the PMNs must arrive at the site of infection within a critical period (2 - 4 h) . PMNs are involved in (1) chemotaxis (migration), (2)phagocytosis and (3) killing .The process of cell movement involves a complex series of events .The first , chemotaxis is in response to chemotatic factors released by the bacteria or from the complement system (***McIntosh ,1992***).