Umbilical Cord Blood CD34 cells in Preterm and Full Term Neonates

Thesis
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Abbreviations

ADA……. Adenosine deaminase

ADHD……. Attention deficit hyperactivity disorder

AML…… Acute myeloid leukaemia

BFU-E ..... Burst-forming unit erythroid

BM..... Bone marrow

BMT ..... Bone marrow transplant

BPD ..... Bronchopulmonary dysplasia

CB..... Cord blood.

CBU..... Cord blood units.

CFU-GM..... Colony-forming unit granulocyte and macrophage/ monocytes

CFU-S ..... Colony-forming unit spleen

CMV..... Cytomegalo virus

CPD ..... Citrate phosphate dextrose

CS ..... Cesarean section

DCD ..... Developmental coordination disorder

ELBW ..... Extremely low birth weight

ES ..... Embryonic stem cells

GA ..... Gestational age

G-CSF ..... Granulocyte colony stimulating factor

GM-CSF ..... Granulocyte–macrophage colony-stimulating factor

GvHD ..... Graft-versus-host disease

HEGCs..... Human embryonic germ cells.

HES ..... Human embryonic stem cells

HIV..... Human immunodeficiency virus

HLA ..... Human leukocyte antigen

HSC..... Hematopoietic stem cell

HSCs ..... Haemopoietic stem cells

ISHAGE..... International Society for Cellular Therapy

LBW..... Low birth weight

LDMN..... Low-density mononuclear

LMP ..... Last menstrual period

MAIN ..... Morbidity assessment index for newborns

MSCs..... Mesenchymal stem cells

MNC..... Mononuclear cells

NEC..... Necrotizing enterocolitis

NICU ..... Neonatal intensive care unit

NK ..... Natural killer cells

NMDP ..... National Marrow Donor Program

NRBCS..... Nucleated red blood cells

NVD ..... Normal vaginal delivery

PBS..... Phosphate buffer saline

PDA..... Patent ductus arteriosus

PE ..... phycoerythrin

PPRM..... Preterm premature rupture of membranes

RDS ..... Respiratory distress syndrome

RLF ..... Retrolental fibroplasia

ROP..... Retinopathy of prematurity

SCF..... Stem cell factor

TNC..... Total nucleated cells

WHO World health organization

U.S. ……. United States

UCB..... Umbilical cord blood

UCBT ..... Umbilical cord blood transplantation

VLBW ..... Very low birth weight

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Introduction

Preterm birth is one of the major clinical problems in obstetrics and neonatology as it is associated with perinatal mortality, serious neonatal morbidity and in some cases childhood disability. It is reported that 60-80% of all neonatal mortality and morbidity is due to preterm birth. During the last two decades the survival for premature infants has significantly increased due to advancement in perinatal and neonatal treatment expertise and improvement in the care of high-risk mother. The survival rate of lower birth weight infant is reported to have increased from 10% to 50-60% ***(Goldenberg, 2002)***.

Stem cells are those, which have remarkable potential to develop into many different cell types in the body. Basically, these cells serve as a sort of repair system for the body; they can theoretically divide without limit to replenish other cells as long as the person or any other living being is still alive. The stem cells' ability to differentiate, or change, into other types of cells in the body, is a new discovery that holds tremendous promise for treating and curing some of the most common diseases such as heart diseases, cancers, stroke, Alzheimer's and many others ***(Broxmeyer et al., 1992)***.

Cord blood (CB) has been shown to contain pluripotent stem cells that have the potential to differentiate into non hematopoietic tissue, such as cardiac, neurologic, panceriatic and skin tissue ***(Cairo et al., 2007)***.

Aim of the Work

The aim of the study is the assessment of umbilical cord stem cells in preterm and full term neonates, and to correlate the effect of preterm delivery on the percentage of these cells. Also the relation between stem cell count and clinical outcome in preterm neonates will be studied.

Preterm Infants and Stem Cells

Preterm Birth

The standard length of a human gestation is 266 days. However, for convenience most timing is based on the last menstrual period (LMP), with conception being assumed to occur approximately 14 days after the LMP, making a standard term pregnancy 280 days or 40 weeks ***(Martin et al., 2004)***.

Premature or preterm birth is defined medically as childbirth occurring earlier than 37 completed weeks of pregnancy or before 259 days according to world health organization (WHO) in 1970. Approximately 12 percent of babies in the United States (U.S.) — or 1 in 8 — are born prematurely each year. Worldwide, prematurity accounts for more than 12.5 percent ***(Martin et al., 2004)***.

The exact worldwide rates of prematurity are more difficult to obtain as the lack of widespread professional obstetric care in developing regions makes determination of gestational age less reliable. The WHO in 2005 stated that more than 20 million infants worldwide, representing 15.5 per cent of all births are born with low birth weight (LBW) which is either

the result of preterm birth or due to restricted fetal (intrauterine) growth, 95.6 per cent of them are in developing countries. The level of low birth weight in developing countries (16.5 per cent) is more than double the level in developed regions (7 per cent). However, these estimates are biased for most developing countries because the majority of newborns are not delivered in facilities and more than half of infants in the developing world are not weighed, and those who are weighed represent only a selected sample of all births ***(Wardlaw et al., 2005)***.

Preterm birth is one of the major clinical problems in obstetrics and neonatology as it is associated with perinatal mortality, serious neonatal morbidity and in some cases childhood disability. It is reported that 60-80% of all neonatal mortality and morbidity is due to preterm birth. During the last two decades the survival for premature infants has significantly increased due to advancement in perinatal and neonatal treatment expertise and improvement in the care of high-risk mother. The survival rate of lower birth weight infant is reported to have increased from 10% to 50-60%. In the U.S. where many infections and other causes of neonatal death have been markedly reduced, prematurity is the leading cause of neonatal mortality at 25 % ***(Mathew and Macdorman, 2003)***.

The shorter the term of pregnancy, the greater the risks of complications. Infants born prematurely have an increased risk

of death in the first year of life (infant mortality), with most of that occurring in the first month of life (neonatal mortality) ***(Robert, 1999)***.

Although there are several known risk factors for prematurity, nearly half of all premature births have no known cause. When conditions permit, doctors may attempt to stop premature labor, so that the pregnancy can have a chance to continue to full term, thereby increasing the baby's chances of health and survival. However, there is no reliable means to stop or prevent preterm labor in all cases. Identification of women at risk of preterm birth is essential to ensure therapies are targeted appropriately. Risk assessments for prediction include previous obstetric history, previous episode of threatened preterm labour ***(Groom, 2007)***. Fetal fibronectin status and fetal cervical length measured by ultrasound between 18 and 34 gestational weeks can predict preterm birth (fetal fibronectin $\geq$ 50 ng/mL and fetal cervical length $\leq$ 25 mm with sensitivity of 63% and 75% respectively) ***(Schmitz et al., 2006)***.

The survivors of preterm birth, especially when born at <34 weeks of gestation, require to remain in newborn intensive care unit (NICU). They need to spend time in NICU till close to term to allow for sufficient multi-organ maturation resulting in prolonged hospital stay for both mother and infant. Therefore, the consequences of preterm birth often continue beyond the