Effect of Magnesium Sulfate on Doppler Parameters of Fetal Middle Cerebral, Umbilical and Uterine Arteries in Women with Threatened Preterm Labour

Thesis

Submitted for partial fulfillment of Master Degree
in Obstetrics and Gynecology

By

Ammar Ali Mohamed
M.B., B.CH.2012
Faculty of Medicine
Ain Shams University

Supervisors

Prof. DR. Mohamed Ahmed EL kady
Professor of Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University

Assist. Prof. Laila Aly Farid
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine - Ain shams University

Faculty of Medicine
Ain Shams University
2018

سورة البقرة الآية: ٣٢

Acknowledgments

First and forever, thanks to ***Allah,*** *Almighty for giving me the strength and faith to complete my thesis and for everything else.*

I would like to express my sincere gratitude to ***Prof. Mohamed Ahmed Elkady,*** *Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, under his supervision, I had the honor to complete this work, I am deeply grateful to him for his professional advice, guidance and support.*

My deep gratitude goes to ***Assist. Prof. Laila Aly Farid ,*** *Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his invaluable efforts and tireless guidance and meticulous supervision throughout this work.*

I wish also to express my gratitude to ***Assist. Lecturer Khalid Afifi,*** *Assistant lecturer of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his great effort, kind advice, support and encouragement throughout the whole work.*

I wish also to express my gratitude to ***the whole members of fetal medicine unit****, at maternity hospital Ain Shams University, for their great effort, support and encouragement throughout the whole work.*

Last but not least, I like to thank my beloved father and brothers for their persistent assistance, kind care, help and encouragement.

Ammar Ali Mohammed

List of Contents

List of Abbreviations

Abbr.	Title
ACOG	**:** American College of Obstetricians and Gynecologists
ACTH	**:** Adrenocorticotropic hormone
AST	**:** Aspartate aminotransferase test
BMI	**:** Body mass index
BP	**:** Blood pressure
BPD	**:** Bronchopulmonary dysplasia
CAP	**:** Contractile associated proteins
CI	**:** Confidence interval
CP	**:** Cerebral palsy
CRH	**:** Corticotropin releasing hormone
CS	**:** Cesarean section
CT	**:** Computed tomography
DD	**:** Developmental delay
DM	**:** Diabetes mellitus
DV	**:** Ductus venosus
EDV	**:** End diastolic volume
ELBW	**:** Extremely low birth weight
FDA	**:** Food and drug administration
FGR	**:** Fetal growth restriction
FHR	**:** Fetal heart rate
g	**:** Gram
h	**:** Hour
HELLP	**:** Hemolytic anemia, elevated liver enzymes, low platelets.

HPA : Hypothalamic pituitary adrenal axis
HTN : Hypertension
IM : Intramuscular
IU : International unit
IUFD : Intrauterine fetal death
IUGR : Intrauterine growth retardation
IV : Intravenous
IVH : Intraventricular hemorrhage
LBW : Low birth weight
MCA : Middle cerebral artery
Mg : Milligram
MgSO4 : Magnesium sulfate
mmHg : Millimeter mercury
Mmol : Millimole
MRI : Magnetic resonance imaging
NEC : Necrotizing enterocolitis
NICE : National Institute of Clinical Excellence
NMDA : *N*-methyl-d-aspartate
NO : Nitric oxide
PG : Prostaglandins
PI : Pulsatility index
PIV : Pulsatility index for viens
PlGF : Placental growth factor
PPROMS : Preterm premature rupture of membranes
PSV : Peak systolic velocity
PT : Prothrombin time

PTL : Preterm labour
PVL : Periventricular leucomalacia
RADAR : Radio detection and ranging
RDS : Respiratory distress syndrome
REDF : Reversal of end diastolic flow
RI : Resistibility index
ROP : Retinopathy of prematurity
RUPP : Reduced uterine perfusion pressure
S\D : Systolic\diastolic ratio
SONAR : Sound navigation and ranging
TAMV : Time averaged mean velocity
TAPS : Twin anaemia polycythaemia sequence
TAV : Time averaged velocity
TCD : Transcranial Doppler
TGF-beta : Transforming growth factor- beta
TTTS : Twin to twin transfusion syndrome
U\L : Unit per liter
UA : Umbilical artery
VEGF : Vascular endothelial growth factor
VLBW : Very low birth weight
VOCC : Voltage operated calcium channels
WHO : World Health Organization

List of Tables

List of Figures

Introduction

Preterm birth remains the principle cause of early neonatal death. Infants born preterm which is defined as labour before 37 weeks of gestation often suffer significant immediate morbidity and need lengthy stay in neonatal intensive care units with significant risk of long term neurological morbidity in a proportion of the survivors. The earlier the preterm labour the more the risk especially when labour occurs before 32 weeks **(Crowther et al., 2014).**

Worldwide, around 15 million children were born preterm in 2010 which represents around 11% of live births. Around 85% of the children born before 37 weeks of gestation can be considered to be moderately or late preterm births (32-36 weeks), 10% very preterm (28-31 weeks), and 5% extremely preterm (before 28 weeks) **(Sentilhes et al., 2016).**

Numerous factors that can be identified during the periconceptional period are associated with the risk of preterm delivery. There are many maternal or fetal characteristics that have been associated with preterm birth, including maternal demographic characteristics, nutritional status, pregnancy history, present pregnancy characteristics, psychological characteristics, adverse behavior's, infection,

uterine contractions and cervical length, and biological and genetic markers **(Goldenberg et al., 2008).**

As a result clinicians use tocolytics for pregnancy prolongation for 48-hours to permit the administration of corticosteroids to enhance fetal lung maturity and reduce neonatal morbidity and mortality **(flenady et al., 2014).**

There is considerable variation in the type of tocolytic agent used in different parts of the world. Magnesium sulphate has been widely used as a tocolytic in the United States of America **(Grimes et al., 2006).**

Magnesium sulphate can be used as atocolytic and also in the management of pre- eclampsia, eclampsia and neuroprotective for neonates **(Rose et al., 2008).**

The precise mechanism by which magnesium sulfate exerts a neuroprotective benefit is not known, but it is speculated that it possess anti-inflammatory and anti-excitotoxic effects while also improving cerebral blood flow and stabilizing fluctuations in blood pressure in the newborn infant **(Berger et al., 2016).**

The exact mechanism of magnesium sulphate as a tocolytic agent is partially understood. It acts by decreasing the frequency of depolarisation of smooth muscle, by modulating calcium uptake, binding and distribution in

smooth muscle cells to inhibit uterine contractions **(Crowther et al., 2003).**

Reported side effects of magnesium sulphate include maternal side effects as flushing, sweating, sensation of warmth, nausea, vomiting, headache, palpitations and rarely pulmonary edema. Administration of a concentration above the recommended therapeutic range can lead to respiratory depression, respiratory arrest and cardiac arrest **(McDonnell et al., 2009).**

Neonatal side effects include hypermagnesaemia, hyporeflexia, poor sucking, and, rarely, respiratory depression needing mechanical ventilation **(Crowther et al., 2003).**

Contraindications to MgSo4 therapy include respiratory rate less than 16 breath/minute, absent patellar reflexes, urine output less than 100 milliliter during four hours , renal failure and hypocalcemia **(McDonnell et al., 2009).**

To assess the fetal circulation Doppler sonography is used to provide valuable information regarding neonatal prognosis and fetal well-being in compromised pregnancies. Doppler sonography has also been used for evaluation of

effect various drugs on Doppler blood waveforms **(Sayin et al., 2010)**.

In pregnancy, umbilical artery (UA),uterine artery (UtA) and fetal middle cerebral artery (MCA) Doppler parameters can be assessed carefully improving detection of disturbances in fetus wellbeing **(Figueira et al., 2016).**

The ratio of middle cerebral artery to umbilical artery (MCA/U) can be used as a good indicator of fetal prognosis and fetal well-being **(Tarzamni et al., 2009).**

Assessment of the changes in the arteries with Doppler ultrasound can show the adaptation of the fetal haemodynamics **(Mihu et al., 2011).**

Investigating the mechanism of action of Mgso4 on the fetus is an important issue. Studies are needed to evaluate the effect of Mgso4 on Doppler parameters of uterine, fetal middle cerebral and umbilical arteries in patients with threatened preterm labour (**Ebrashy et al., 2005).**