Effect of Magnesium Sulfate on Doppler Parameters of Fetal Umbilical and Middle Cerebral Arteries in Women with Severe Preeclampsia

Thesis

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Nada Al-Toukhy

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List of Abbreviations

Abbr.	Title
ACOG	**:** American College of Obstetricians and Gynecologists
AEDF	**:** Absent end diastolic flow
APA$	**:** Antiphospholipid antibody syndrome
AST	**:** Aspartate aminotransferase test
BMI	**:** Body mass index
BP	**:** Blood pressure
CBF	**:** Cerebral blood flow
CBFV	**:** Cerebral blood flow
CI	**:** Confidence interval
CPR	**:** Cerebroplacental ratio
CS	**:** Cesarean section
CSF	**:** Cerebrospinal fluid
CT	**:** Computed tomography
dl	**:** Deci-liter
DM	**:** Diabetes milletus
DV	**:** Ductus venosus
EAAs	**:** Excitatory amino acids
EDV	**:** End diastolic volume
FGR	**:** Fetal growth restriction
FHR	**:** Fetal heart rate
g	**:** Gram
GOPEC	**:** The Genetics of Preeclampsia Collaborative
h	**:** Hour

HELLP : Hemolytic anemia, elevated liver enzymes, low platelets.
HLA : Human leukocyte antigen
HTN : Hypertension
Hz : Hertz
IM : Intramuscular
IU : International unit
IUFD : Intrauterine fetal death
IUGR : Intrauterine growth retardation
IV : Intravenous
LDL : Low density lipoprotein
LOX 1 : Lectin-like oxidized low-denisty lipoprotein receptor1
MCA : Middle cerebral artery
Mg : Milligram
MgSO4 : Magnesium sulfate
MHz : Mega Hertz
mmHg : Millimeter mercury
Mmol : Millimole
MRI : Magnetic resonance imaging
NHBPEP : National High Blood Pressure Education Program
NICE : National Institute of Clinical Excellence
NK : Natural killer
NMDA : *N*-methyl-d-aspartate
NO : Nitric oxide
PI : Pulsatility index
PIH : Pregnancy-induced hypertension
PIV : Pulsatility index for viens

PlGF : Placental growth factor
PPT : Partial thromboplastin time
PSV : Peak systolic velocity
PT : Prothrombin time
PVIV : Peak velocity index for viens
RADAR : Radio detection and ranging
REDF : Reversal of end diastolic flow
RI : Resistibility index
RUPP : Reduced uterine perfusion pressure
S\D : Systolic\diastolic ratio
sEng : Soluble endoglin
sFlt-1 : Soluble fms-like tyrosine kinase I receptor
SLE : Systemic lupus erythrematosis
SONAR : Sound navigation and ranging
TAMV : Time averaged mean velocity
TCD : Transcranial Doppler
TGF-beta : Transforming growth factor- beta
TRAP : Twin reversed arterial perfusion
TTTTS : Twin to twin transfusion syndrome
U\L : Unit per liter
UA : Umbilical artery
VEGF : Vascular endothelial growth factor
VOCC : Voltage-operated calcium channels
WHO : World Health Organization

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Introduction

Pre-eclampcia is defined as new hypertension presenting after 20 weeks with significant proteinuria which in turn is defined as urinary protein : creatinine ratio is greater than 30 mg/mmol or a validated 24-hour urine collection result shows greater than 300 mg protein (**(NICE) clinical guidelines, 2010).**

There is no single reliable, cost-effective screening test for preeclampsia, and there are no well-established measures for primary prevention. Management before the onset of labor includes close monitoring of maternal and fetal status. Management during delivery includes seizure prophylaxis with magnesium sulfate and, if necessary, medical management of hypertension. Delivery remains the ultimate treatment. Access to prenatal care, early detection of the disorder, careful monitoring, and appropriate management are crucial elements in the prevention of preeclampsia-related complications **(Lana et al., 2004)**.

Magnesium is a potent vasodilator of uterine and mesenteric arteries as well as the aorta. In vascular smooth muscle, magnesium competes with calcium for binding sites, in this case for voltage-operated calcium channels (VOCC). Decreased calcium channel activity lowers intracellular calcium, resulting in relaxation and vasodilation. In the endothelium, magnesium increases production of prostaglandin

I_2 which in turn decreases platelet aggregation. Magnesium also increases NO production causing vasodilation **(Euser et al., 2009)**.

Magnesium sulfate ($MgSO_4$) is used in women with severe preeclamptic toxemia for neuroprotection from seizures and can help prevent serious complications. The exact mechanism by which magnesium sulphate exerts a protective role in the prevention of neuronal injury in the fetal brain has not been elucidated. However there is evidence for various effects of magnesium sulphate, some or all of which likely play a role in the neuroprotective effect observed **(Marret et al., 2007).**

Doppler ultrasound is a useful tool for studying pathophysiological mechanisms that can affect the fetal hemodynamic status. Assessing the changes in the arteries with Doppler ultrasound can show the adaptation of fetus to the situation. An increase in umbilical artery resistance shows as a decrease in perfusion. If the situation continues, RI in the middle cerebral artery will decrease **(Mihu et al., 2011).**

There were many studies that were performed to evaluate the effect of magnesium sulfate intravenous administration on Doppler indices of middle cerebral artery and umbilical artery on women with severe preeclampsia. In 2016, **(Maged et al., 2016)** proved that intravenous

magnesium sulfate administration in pregnant women with severe preeclampsia resulted in a decrease in fetal middle cerebral artery and umbilical artery Doppler indices with reduced resistance to blood flow in these vessels.

The purpose of this study was to evaluate the effect of $MgSO_4$ in severe preeclampsia on fetal middle cerebral artery and umbilical artery using Doppler parameters.

Aim of the Work

To assess the effect of $MgSO_4$ before and after its administration on Doppler ultrasound parameters of fetal umbilical artery (UA) and middle cerebral arteries (MCA) in pregnant women with severe pre-eclampcia.

Preeclampsia

Hypertensive pregnancy disorders complicate 10% of all pregnancies and cover a spectrum of conditions, namely preeclampsia, eclampsia, and chronic and gestational hypertension. Pre-eclampsia, a human-pregnancy-specific disease defined as new hypertension presenting after 20 weeks with significant proteinuria which in turn is defined as urinary protein: creatinine ratio is greater than 30 mg/mmol or a validated 24-hour urine collection result shows greater than 300 mg protein **(NICE clinical guidelines 2010).**

In 2013, the American College of Obstetricians and Gynecologists removed proteinuria as an essential criterion for diagnosis of preeclampsia with severe features. They also removed massive proteinuria (5 grams/24 hours) and fetal growth restriction as possible features of severe disease because massive proteinuria has a poor correlation with outcome and fetal growth restriction is managed similarly whether or not preeclampsia is diagnosed (**American College of Obstetricians and Gynecologists**, **Task Force on Hypertension in Pregnancy 2013)**. Oliguria was also removed as a characteristic of severe disease.