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

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✍ *Ahmed Ayoub*

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List of Abbreviations

Abbreviation	*Title*
ACOG	**:** American College of Obstetricians and Gynecologists
ALT	**:**AlanineTransaminase
AST	**:** Aspartate Transaminase
BP	**:** Blood pressure
CNS	**:** Central nervous system
CW	**:** Continous Wave
DBP	**:** Diastolic Blood Pressure
HELLP	**:** Hemolytic anemia, elevated liver enzymes, low platelets.
HIF 1α	**:** Hypoxia inducible factor 1 α
HLA	**:** Human leukocyte antigen
HTN	**:** Hypertension
Hz	**:** Hertz
IL	**:** Interleukin
IM	**:** Intramuscular
INR	**:** International normalized ratio.
IU	**:** International unit
IUFD	**:** Intrauterine fetal death
IUGR	**:** Intrauterine growth restriction
IV	**:** Intravenous
Kg	**:** Kilogram
MCA	**:** Middle cerebral artery
MCA-PI	**:** Middle Cerebral Artery – Pulsatility Index
MCA-PSV	**:** Middle Cerebral Artery – Peak Systolic Velocity

MCA-RI : Middle Cerebral Artery – Resistance Index
mEq : Milli-equivalent
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
PI : Pulsatilityindex
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
SD : Standarddeviation
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

TGF-beta : Transforming growth factor- beta

U\L : Unit per liter

UA : Umbilical artery

UA-PI : Umbilical artery - Pulsatility Index

UA-RI : Umbilical artery - Resistance Index

UAV : Umbilical Artery Velocimetry

U/S : Ultrasound

VEGF : Vascular endothelial growth factor

VOCC : Voltage-operated calcium channels

VS : Versus

WHO : World Health Organization

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ABSTRACT

Backgroud: Magnesium sulfate (MgSO4) is used in women with severe preeclamptic toxemia for neuroprotection from seizures and can help to prevent serious complications

Objective: 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.

Patients and Methods: A total of 52 patients with severe preeclampsia admitted to Ain Shams University Maternity Hospital were evaluated. Before and after administration of magnesium sulfate, Doppler ultrasound scan was carried out to measure umbilical artery and fetal middle cerebral artery blood flow. Paired t-test was used for statistical analysis.

Results: After injection of magnesium sulfate, the mean resistivity index (RI)-umbilical, and pulsatility index (PI)-cerebral showed a statistically significant reduction ($P < 0.001$). The cerebroumbilical C/U ratio increased after the intervention ($P < 0.001$). The PI-umbilical ($P = 0.1$) and pre- and post-RI-cerebral ($P = 0.96$) did not have statistically significant changes.

Conclusions: Infusion of magnesium sulfate significantly decreases the flow in the fetus RI-umbilical and PI-MCA, and it increases C/U ratio indices in color Doppler ultrasound.

Key words: Doppler ultrasound, eclampsia, magnesium sulfate, preeclampsia

Introduction

Pre-eclampsia 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)**

Pre-eclampsia and eclampsia are among the common causes of death and disability in pregnant women and are associated with increased vascular resistance and decreased uteroplacental perfusion. It is characterized by vascular contraction, lesions in the placenta and umbilical arteries, high blood pressure, proteinuria, and seizure **(Roberts et al., 2003)**.

This disease can cause many fetal and maternal complications. Maternal complications include acute renal failure, liver damage, intracerebral hemorrhage, pulmonary edema, and death. Fetal complications are preterm birth or intrauterine growth restriction or intrauterine fetal death **(Roberts et al., 2002/ Sibai et al., 2002)**.

Magnesium sulfate ($MgSO_4$) is used in women with severe preeclamptic toxemia for neuroprotection from seizures and can

help to prevent serious complications **(Euser et al., 2009/ Witlin et al., 1998)**.

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)**, through one or more of the following mechanisms : Reduction of inflammatory cytokines or free radicles produced during hypoxic-ischemic reperfusion, prevention of excitotoxic calcium-induced injury, membrane stabilization by preventing the membrane depolarization, inhibition of the glutamate receptors involved in injury to preoligodendrocytes, stabilization of fluctuations in blood pressure that occur in neonates, and an increase in cerebral blood flow **(Conde-Agudelo et al., 2009/ Constantine et al., 2011/ Heybone et al., 2010/ Mercer et al., 2009)**. Other animal data suggest that $MgSO_4$ may serve an antiapoptotic role and prevent neuronal cell loss **(Burd et al., 2010)**.

During asphyxia, there is excessive release and reduced uptake of glutamate in the brain. Glutamate acts on the N-methyl-D-aspartate (NMDA) receptor, a postsynaptic ion channel,

allowing excessive calcium influx into the neurons and inducing neuronal injury **(Bhat et al ., 2009)**.Fetal and newborn brains seem to be more susceptible to damage from glutamate release **(Doyle et al., 2009)**. $MgSO_4$ is a naturally occurring NMDA receptor antagonist that blocks neuronal influx of calcium within the ion channels, preventing posthypoxic brain injury **(Bhat et al., 2009)**

Beneficial haemodynamic effects of magnesium sulphate have also been postulated, with potential increased cerebral perfusion and a stabilizing effect on neonatal blood pressure variability reported**(Macdonald et al., 2004/ Rantone et al., 2002).**

The large well designed randomized controlled trial (BEAM trial) which assess the neuroprotective benefit of MgSO4, provide strong evidence that in utero fetal exposure to MgSO4 in mothers at risk for premature delivery reduces the risks of developing cerebral palsy without affecting the rate of perinatal or infant death. Selecting the right patient candidate and identifying the ideal dosing regimen are still unclear and requires further research (**Rouse et al., 2008)**.

The French PREMAGmulticenter randomised trial that included women with no pregnancy associated vascular disease

and at risk of pretermdelivery before 33 weeks of gestational age. Its goal was toassess the effectiveness of a single MgSO4 infusion in preventing mortality and/or WMI (white matter injury) in new born **(Marret et al., 2006).**

In pregnancy, usually umbilical artery is tested by Doppler ultrasound but some recent studies also test maternal and fetal middle cerebral arteries (MCA) **(Bahlmann et al., 2002/ Ebrashy et al., 2005)**. In one study, the reference value of resistive index (RI) and pulsatility index (PI) have been investigated in Iranian patients **(NICE clinical guidelines)***. The ratio of middle cerebral artery/umbilical artery (C/U ratio) can be a good indicator of fetal prognosis and fetal well-being **(Tarzamni et al., 2009/ Kassanos et al., 2003).**

Doppler ultrasound is a useful tool for studying pathophysiological mechanisms that can affect the fetal hemodynamic status **(Rana et al., 2005/ Mihu et al., 2011/ Baschat et al., 2003)**. Assessing the changes in the arteries with Doppler ultrasound can show the adaptation of fetus to the situation **(Ebrashy et al., 2005/ Divon et al., 1996).**

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).**