Effect of Magnesium Sulfate on Doppler Indices in Severe Preeclampsia.

Protocol of a thesis submitted for partial fulfillment
Of the Master Degree in Obstetrics and Gynecology
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List of Abbreviations

ACOG	:	American Collage of Obstetric and Gynecology
AFI	:	Amniotic fluid index
AFP	:	Alpha-fetoprotein
ALT	:	Aspartate aminotransferase
ANP	:	Atrial natriuetic peptide
AT-3	:	Antithrombin III
BMI	:	Body mass index
BP	:	Blood pressure
CI	:	Confidence interval
DOC	:	Deoxycorticosterone
EGA	:	Estimated gestational age
ET-1	:	Endothelin 1
HCG	:	Human chorionic gonadotropin
HIF-1 α	:	Hypoxia-inducible factor-1 α protein
HLA	:	Human leukocyte antigen
HS	:	Highly significant
IL	:	Interleukin
INF- α	:	Tumor necrosis factor α
IQR	:	Interquartile range
LDH	:	Lactate dehydrogenase
MCA	:	Middle cerebral artery
MOM	:	Multiple of the median
MPD	:	Mean paired difference
NICU	:	Neonatal intensive care unit
NK	:	Natural killer
NMDA	:	N-methyl-D aspartate
NS	:	Non significant
PAI	:	Plasminogen activator-inhibitor
PAPP A	:	Pregnancy-associated protein A
PI	:	Pulsatility index
PLGF	:	Placental growth factor
PRES	:	Posterior reversible encephalopathy
RI	:	Resistance index

List of Abbreviations (Cont.)

S	:	Significant
S/D	:	Systolic diastolic ratio
S_aO_2	:	Oxygen saturation
SD	:	standard deviation
sEng	:	Soluble endoglin
sFLT-1	:	Soulble Fms like tyrosine kinase receptor 1
TGF ß $_3$	:	Transforming growth factor beta 3
VEGF	:	Vascular entothelial growth factor
WHO	:	World Health Organization

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تأثير إعطاء عقار كبريتات الماغنسيوم علي مؤشرات الدوبلر في حالات تسمم الحمل

بحث رسالة

مقدم للحصول علي درجة الماجســـتير
في أمراض النساء والتوليـــــد

مقدمـــــه من :

الطبيبة/ شيمــاء عمر مبروك

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طبيب زائر نساء وتوليد بمستشفي الجلاء التعليمى

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Introduction

Worldwide, hypertension represents one of the most common complications of pregnancy. Its incidence varies from 2 to 8% of pregnancies in developed countries, reaching 10% or more in developing countries. It is associated with high rates of perinatal morbidity and mortality (5–20%) and is the third most common cause of maternal death worldwide **(Souza et al., 2009b)**.

Five to seven percent of all pregnancies are complicated by preeclampsia. Proteinuria and hypertension dominate the clinical picture, because the chief target organ is the kidney (glomerular endotheliosis). The pathogenesis of preeclampsia is complex; numerous genetic,immunologic, and environmental factors interact. It has been suggested that preeclampsia is a two-stage disease. The first stage is asymptomatic, characterized by abnormal placental development during the first trimester resulting in placental insufficiency and the release of excessive amounts of placental materials into the maternal circulation. This in turn leads to the second, symptomatic stage, wherein the pregnant woman develops characteristic hypertension, renal impairment, and proteinuria and is at risk for the HELLP syndrome (hemolysis, elevated liver function enzymes and low platelets), eclampsia, and other end-organ damage **(Hladunewich et al., 2007)**.

On the basis of the observation that the only definitive cure for preeclampsia is delivery of the placenta and that women who experience a molar pregnancy, in which a placenta develops without a fetus, frequently develop severe preeclampsia, it is reasonable to assume that the placenta plays a central role in the pathogenesis of the disease. Pathologic examination of placentas from preeclamptic pregnancies generally reveals placental infarcts and sclerotic narrowing of

arteries and arterioles, with characteristic diminished endovascular invasion by cytotrophoblasts and inadequate remodeling of the uterine spiral arterioles. Although gross pathologic changes are not always seen in the placentas of women with preeclampsia, placental profiles including abnormal uterine artery.

Doppler and placental morphology have been used to identify a subset from a cohort of high-risk women who go on to develop the syndrome. Uterine artery Doppler studies that assess the pulsatility index (PI) reveal increased uterine vascular resistance well before the clinical signs and symptoms arise. Moreover, mechanical constriction of the uterine arteries produces hypertension, proteinuria, and, in some species, glomerular endotheliosis, supporting an causative role for placental ischemia in the pathogenesis of preeclampsia **(Hladunewich et al., 2007)**.

The abnormal placentation that results from failure of trophoblast remodeling of uterine spiral arterioles is thought to lead to the release of secreted factors that enter the mother's circulation, culminating in the clinical signs and symptoms of preeclampsia. All of the clinical manifestations of preeclampsia can be attributed to glomerular endotheliosis, increased vascular permeability, and a systemic inflammatory response that results in end-organ damage and/or hypoperfusion. These clinical manifestations typically occur after the 20th week of pregnancy **(Hladunewich et al., 2007)**.

Severe pre-eclampsia was defined by the presence of any of the following signs or symptoms : systolic pressure > 160 mmHg or diastolic > 110 mmHg, proteinuria > 2 g / l in 24 hours of tape or proteinuria 3 + or more, signs of impending eclampsia, oliguria, creatinine > 1.2 mg%, acute pulmonary edema or cyanosis, characteristic laboratory findings of HELLP syndrome, fundus findings of papilledema or retinal exudates. Superimposed pre-eclampsia was defined as the presence of

chronic hypertension associated with the surge in blood pressure and / or proteinuria or evidence of any organ dysfunction, with symptoms or laboratory tests. The imminence of eclampsia was defined as the presence of the following signs and symptoms in patients with hypertensive syndrome in pregnancy: continuous headache, scotomata, blurred vision, epigastric pain and pain in right hypochondrium **(Souza et al., 2008)**.

Eclampsia and pre-eclampsia are important causes of morbidity and mortality during pregnancy childbirth and puerperium. The prevention of seizure activity in pre-eclampsia and recurrent seizures in eclampsia is an essential aspect of management. A number of different anticonvulsants are used to control eclamptic fits and to prevent future seizures **(Noor et al., 2004).**

Treatment of eclampsia using anticonvulsant began in the early 20th century and magnesium sulfate was the first drug used. Currently, multicenter clinical trials and systematic reviews to ensure effectiveness and safety of magnesium sulfate to significantly reduce the risk of seizures and maternal death **(Souza et al., 2009 a)**.

Magnesium sulfate has established itself as an important measure adopted therapy in patients with eclampsia and pre-eclampsia.. Magnesium sulfate has widely studied and recognized as the drug of choice not only for prophylaxis but also for the treatment of eclamptic seizures **(Souza et al., 2008)**.

Magnesium is the most abundant and important intracellular divalent cation, responsible for various functions. Is credited with the important role this cation in blood pressure regulation by modulating the reactivity of vascular tone and total peripheral resistance **(Souza et al., 2008)**.