Different regimens of magnesium sulfate for management of women with severe pre-eclampsia

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CONTENTS

Page

LIST OF TABLES

LIST OF FIGURES

LIST OR ABREVIATIONS

ACOG : American College of Obstetrics and Gynecology
AFI : Amniotic Fluid Index
AFP : Alpha Feto-Protein
ALT : Alanine Transaminase
aPTT : activated Partial Thromboplastine Time
ANOVA : alalysis of variance
ANP : Atrial Natriuuretic Peptide
AST : Aspartate Transaminase
AT-3 : Anti-Thrombine III
BEAM : Beneficial Effects of Antenatal Magnesium Sulfate
BMI : Body Mass Index
BP : Blood Pressure
CBC : Complete Blood Count
CC : cubic centimeter
CNS : Central Nervous System
CS : Caesarian section
DNA : Deoxy Ribonucleic Acid
EDHF : Endothelial Derived Hypopolarizing Factor
EGA : expected gestational age
g : gram
HCG : Human Chorionic Gonadotropin
HELLP : Hemolysis, Elevated Liver enzymes, Low Platelet count
hr : hour
IL : Interleukin
IM : Intra-Muscular
IUFD : Intra-Uterine Fetal Death
IUGR : Intra-Uterine Growth Restrection
IV : Intra-Venous
Kg : Kilo gram
LDH : Lactate Dehydrogenase
L/S : lecithin-sphingomyelin
meq : mille-equivalent
mg : mille-gram

MgSO4 : Magnesium Sulfate
mmHg : millemeter Mercury
MOD : Mode of delivery
mmol : mille-mole
MICU : Maternal Intensive Care Unite
MLCK : Myosin light-chain kinase
NICU : Neonatal Intensive Care Unite
NHBPEP **:** National High Blood Pressure Education Group
NMDA **:** N-Methyl-D-Aspartate
NO **:** Nitric Oxide
PAI **:** Plasminogen Activator Inhibitor
PAPP **:** Pregnancy Associated Protein A
PE **:** Preeclampsia
PGI_2 **:** Prostacyclin
PLGF **:** Placental Growth Factor
PRES : posterior reversible encephalopathy syndrome
PT **:** Prothrombin Time
RH **:** Rhesus
RNA : Ribonucleic Acid
SD **:** Standard Deviation
sEng **:** Soluble Endolgin
sFlT-1 **:** Soluble Fms-Like Tyrosine Kinase 1
SaO2 : Oxygen saturation
TNF **:** Tumor Necrosis Factor
UA **:** Umbilical Artery
UC **:** Umbilical Cord
VD : Vaginal delivery
VEGF **:** Vascular Endothelial Growth Factor
vs : versus
WHO **:** World Health Organization
wk : Week
yrs : years

A B S T R A C T

Background: Magnesium sulfate remains the drug of choice for both prevention and treatment of women with eclampsia. Regimens for administration of this drug have evolved over the years, but have not yet been formally evaluated.

Objectives: To determine the minimal effective dose of magnesium sulfate in controlling cases of severe preeclampsia and prevention of eclampsia and to determine whether only loading dose of magnesium sulfate is effective in prevention of eclampsia.

Material and method :A randomized controlled study that compared three regimens for administration of MgSO4 used for the cases of severe pre-eclampsia that was performed in the Obstetrics & Gynecology Department, Kasr Al-Ainy Hospital, Cairo University during the period from May 2013 to the end of January 2014.The study included 240 pregnant women presenting to the casualty unit with criteria of severe preeclampsia and was divided into three categories:- Category A including 80 patients who took only loading dose of MgSO4 (6 grams of MgSO4 on 250 ml ringer solutions over 20 minutes) with no postpartum maintenance sulfate. Category B including 80 patients given abbreviated doses of MgSO4 (4 grams of MgSO4 on 250 ml ringer solution over 4 hours every 4 hours by IV drip only for 12 hours) in the postpartum period. Category C including 80 patients given full dose of maintenance MgSO4 (4 grams of MgSO4 on 250 ml ringer solution over 4 hours every 4 hours by IV drip for 24 hours) in the postpartum period.

Main results: Although strong evidence supports the use of magnesium sulfate for prevention and treatment of eclampsia, there was no significant difference between occurrence of eclampsia in the three groups after either administration of loading dose of MgSO4 only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients.

Conclusion: Considering the equal effectiveness, fewer side effects, ease of monitoring and cost-effectiveness of loading dose, single loading dose of magnesium sulfate in the management of pre-eclampsia is preferable to other regimes of administration requiring multiple doses.

Key words

Different regimens of magnesium sulfate for management of women with severe pre-eclampsia

INTRODUCTION

Preeclampsia is a multisystem disorder of pregnancy which is a major cause of maternal and fetal morbidity and mortality worldwide. The cardinal clinical features of the condition are hypertension and proteinuria occurring after 20 weeks gestation in women who were not previously known to be hypertensive. **(1)**

Pre-eclampsia often affects young and nulliparous women, whereas older women are at great risk of chronic hypertension with superimposed preeclampsia. (2)

Preeclampsia is considered severe if one or more of the following:

(1) Blood pressure of 160 mmHg systolic or higher or 110 mmHg diastolic or higher on two occasions at least 6 hours a part while the patient on bed rest.

(2) Proteinuria of 2 gm. or high in 24 hours urine specimen or +2 or great on two random urine samples collected at least 4 hours apart.

(3) Oliguria of less than 500 ml in 24 hours.

(4) Cerebral or visual disturbance.

(5) Pulmonary edema or cyanosis.

(6) Epigastric or right upper quadrant pain.

(7) Impaired liver function.

(8) Thrombocytopenia.

(9) Fetal growth restriction. **(3)**

In normal pregnancy the spiral arteries in the placental bed are invaded by trophoblast, which becomes incorporated into the vessel wall and replaces the endothelium, muscular layer and neural tissue. These physiological changes convert the spiral arteries from narrow muscular vessels to wide non-muscular channels independent of maternal vasomotor control. Pre-eclampsia is thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries. **(4)**

Magnesium sulfate is widely used in obstetrics and is a drug of choice in two important complications of pregnancy, preeclampsia and preterm labor . Magnesium sulfate, is used to prevent seizures in preeclampsia patients. **(5)**

The most common side effect is flushing .Others are far less common and include nausea, vomiting, muscle weakness, thirst, headache, drowsiness and confusion. Although magnesium sulphate can lead to respiratory depression and respiratory arrest, these hazards appear to be rare. Higher dose regimens may be associated with a great risk of

side effects and adverse effects. If magnesium sulphate toxicity does occur, intravenous calcium gluconate is an effective antidote.**(6)**

Magnesium sulfate remains the drug of choice for both prevention and treatment of women with eclampsia. Regimens for administration of this drug have evolved over the years, but have not yet been formally evaluated.**(7)**

In past, MgSO4 was given according to Pritchard regime in which 5 grams of magnesium sulfate was administered four-hourly for 24 hours after loading with 14 grams. It was observed that many patients did not receive maintenance therapy due to suspicion of toxicity but they did not convulse any further. On the basis of this observation, many studies were planned to compare the efficacy of loading dose of magnesium sulfate versus the standard regime in the management of preeclampsia to prevent fits. Ehrenberg and Mercer studied abbreviated post partum magnesium administration in 200 women with mild pre-eclampsia. None of these women and none of the other cohort given the 24 hour magnesium infusion developed eclampsia. **(8)**

Implementation of magnesium sulfate would be strengthened if guidelines and recommendations for practice could be based on reliable

evidence about the comparative effects of alternative regimens. It is therefore relevant to assess the pros and cons of alternative strategies for administration. As administration of magnesium sulfate requires regular supervision by trained staff, which is costly, and higher doses may be associated with a greater risk of side effects and adverse events, it is particularly important to assess the minimum effect dose and duration of treatment**.(9)**

In our study we tried to assess the comparative effects of three regimens for the administration of magnesium sulfate when used for the care of women with severe pre-eclampsia.

Aim Of Work

The aim of our study was to assess the comparative effects of three regimens for the administration of the magnesium sulfate when used for the care of women with severe preeclampsia to determine the minimal effective dose of magnesium sulfate in controlling cases with severe preeclampsia and prevention of eclampsia and to determine whether only loading dose of magnesium sulfate is effective in prevention of eclampsia or not.

PREECLAMPSIA

Hypertensive disorders complicate 5 to 10 percent of all pregnancies, and together they form one member of the deadly triad, along with hemorrhage and infection, that contribute greatly to maternal morbidity and mortality rates. Preeclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks' gestation and can present as late as 4-6 weeks postpartum. It is clinically defined by hypertension and proteinuria, with or without pathologic edema **(10).**

TERMINOLOGY AND CLASSIFICATION

The classification of hypertensive disorders complicating pregnancy by the Working Group of the **NHBPEP** - National High Blood Pressure Education Program - (**2000**) is shown in **Table 1**.

There are four types of hypertensive disease:

1. Gestational hypertension.
2. Preeclampsia and eclampsia syndrome
3. Preeclampsia syndrome superimposed on chronic hypertension
4. Chronic hypertension.