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THE ROLE OF MGSO4 IN REDUCING THE RISK OF SEVERE PREECLAMPSIA (PEB) PATIENTS BECOMING ECLAMPSIA

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Abstract

The writing of this review article aims to determine the benefits of MgSO4 for patients with severe preeclampsia, so that it does not become eclampsia. Preeclampsia is an increase in blood pressure in pregnant women starting at more than 20 weeks of age. Patients with preeclampsia are given MgSO4 as a preventive therapy for eclampsia, where MgSO4 acts as an anticonvulsant that is safe and commonly used in pregnant women. Oktatin's research found that all patients who used MgSO4 prophylaxis at RSUD dr. Soetomo Surabaya did not experience eclampsia seizures and without symptoms of side effects or drug interactions. In Hariyanti's research through a retroprespective cohort approach at Fatmawati General Hospital, it was found that the reduction in eclampsia cases in patients with MgSO4 administration was higher than that in patients without MgSO4 administration. Apart from being an anticonvulsant, MgSO4 also plays a role in protecting the fetus.

Keywords: Preeclampsia, Eclampsia, MgSO4.

INTRODUCTION

Preeclampsia is a syndrome in which there is an increase in blood pressure and urine protei from the gestational age entering the second trimester or more than 20 weeks of gestational age (Yeyeh R et al., 2021)(Olda et al., 2022). International Soeciety for the Study of Hypertension in Pregnancy (ISSHP) preeclampsia when systole blood pressure > 140 mmHg or diastole blood pressure > 90 mmHg with measurement intervals of 4-6 hours with urine protein (> 300 mg / day) and organ dysfunctions such as renal insufficiency, liver dysfunction, disorders of the nervous system, pulmonary edema, uteroplacental dysfunction, and thrombocytopenia. Preeclampsia and eclampsia are emergencies, and contribute to maternal death. Every day in 2017, 810 women worldwide died from illness or complications from pregnancy and childbirth. 75% of maternal deaths are caused by hypertension in pregnancy (Suleman et al., 2021). Mothers are at risk of ongoing hypertension and at risk of death from cardiovascular disease. For fetuses at risk of IUGR (*intra-uterine growth restriction),* premature birth, oligohydramnios, placental abrupti, fetal distress and fetal death (Fox et al., 2019).

Preeclampsia is one of the most serious obstetric complications and affects 5-8% of pregnant women. Preeclampsia is a state of arterial hypertension with proteinuria identified after the 20th week of gestation. It may be followed by multiple organ dysfunction with symptoms such as headache, visual acuity, abdominal pain, pulmonary edema, brain disorders

in the form of headaches, seizures and scotoma or changes in laboratory test results such as thrombocytopenia, elevated liver enzymes, and hypercreatinine (Amalia,2020).

Other factors that increase the risk of preeclampsia in pregnant women are nulliparous, multiparous, gamelli, excessive body mass index (BMI) and a previous history of preeclampsia and comorbid conditions such as diabetes mellitus. According to experts, preeclampsia is a systemic disorder. Blood flow to each of the mother's organs is reduced due to vasoconstriction and microthrombus formation and results in multiorgan disorders. At the same time, fetal complications and growth retardation occur secondary to placental hypoperfusion (Amalia,2020).

The writing of this review article aims to determine the benefits of MgSO4 for patients with severe preeclampsia, so that it does not become eclampsia.

METHOD RESEARCH

This research is made in the literature review research method which provides output to existing data, as well as the elaboration of a finding so that it can be used as an example for research studies in compiling or making a clear discussion of the content of the problem to be studied. The author looks for data or literature material from journals or articles and also references from books so that it can be used as a strong foundation in the content or discussion. From this research, the content is related to the use of systematic literature review research methods In the use of research in sociology, search and collect several journals and draw several conclusions and then examine in depth in a detailed way so that there is a good final result and in accordance with what is expected.

RESULT AND DISCUSSION

Preeclampsia (PE) is hypertension that occurs at 20 weeks of pregnancy (M. I. A. Akbar et al., 2020). Hypertension in pregnancy accounts for 14% of maternal deaths in the world. The prevalence of eclampsia is 1 to 400 per 10,000 live births, with case fatality rates reaching 10% in developing countries (Verschueren et al., 2020). Preeclampsia is one of the pregnancy problems that causes mortality and morbidity in developing countries. Indonesia, the fourth most populous country in the world with a population of 267 million, is a middle-income country with a PE incidence of 5-7%. Maternal (2.2%) and perinatal (12%) PE mortality rates remain high.

Most Indonesians still face poverty, lack of access to health services, and often receive inadequate care in primary health care centers. Faulty financial incentives under Indonesia's current universal health insurance system are partly to blame for late referrals. Maternal effects of preeclampsia such as eclampsia, stroke, placental abruption, disseminated intravascular coagulation, HELLP syndrome, liver hemorrhagy/rupture, pulmonary edema/aspiration, adult respiratory distress syndrome, acute renal failure, death, chronic hypertension, diabetes mellitus, chronic renal failure, coronary artery disease, neurological deficits (Tsabitah et al., 2020). Figure 1 shows the effects of preeclampsia.

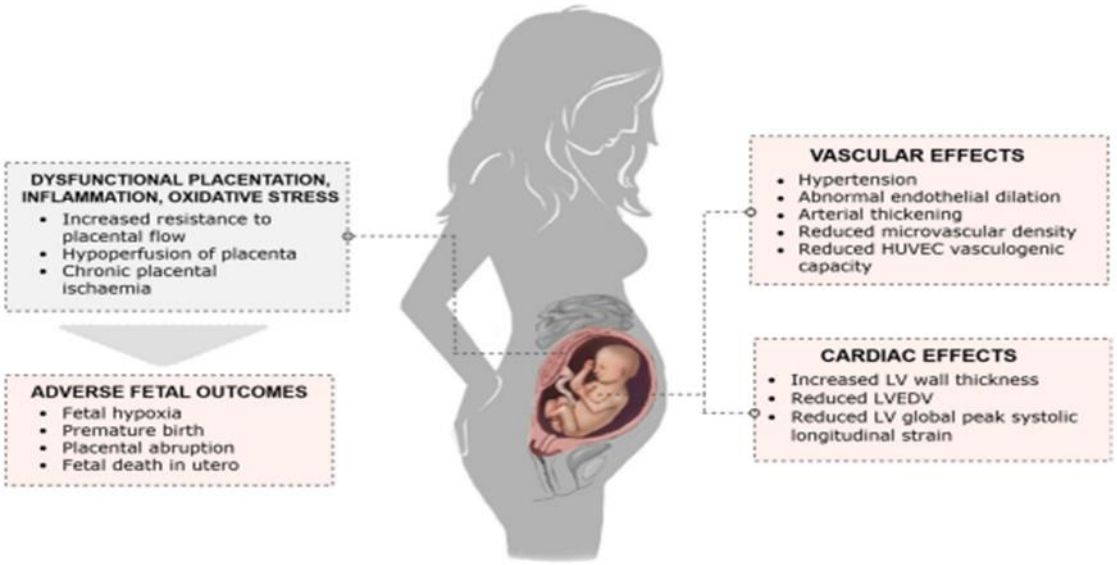

Figure 1. Effects of preeclampsia (Fox et al., 2019)

Eclampsia is a complication of preeclampsia, so it is important to understand the pathogenesis of preeclampsia. The placenta plays an important role in the pathophysiology of preeclampsia. After the placenta is born, some patients have their symptoms subsided.

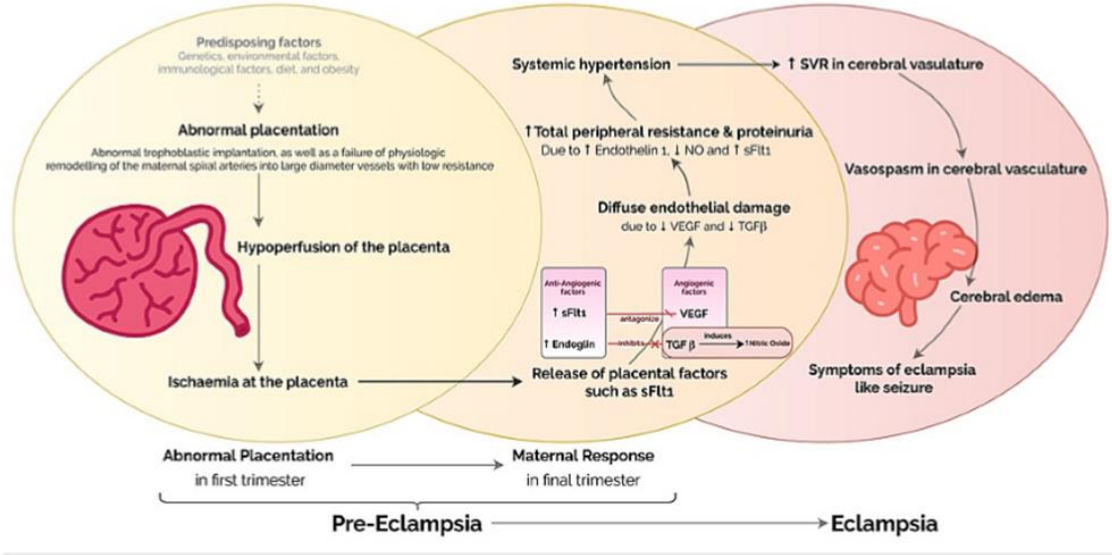

Figure 2. Pathophysiology of eclampsia and preeclampsia.

VEGF: vascular endothelial growth factor; NO: nitric oxide; sFltl: soluble FMS-like tyrosine kinase; TGFβ: transforming growth factor-beta; SVR: systemic vascular resistance.the image was created by the author (Lanson B. Colaco, MBBS)

Magnesium sulfate (MgSO4) is recommended by all major guidelines as the agent of first choice for preventing eclampsia seizures and is used worldwide (M. I. A. Akbar et al., 2020). MgSO4 is used to prevent maternal seizures in preeclampsia (PE) and protect the fetal

brain in preterm labor. MgSO4 also reduces the risk of neontal cerebral palsy, its benefits regarding periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and mortality are controversial (Richter et al., 2020).

MgSO4 is given intamuscular (IM) or intravenous (IV). Pritchard's regimen involves administering two doses of MgSO4, consisting of a slow IV dose of 4 g over five to ten minutes, immediately followed by an IM dose of 10 g divided into 5 g on each buttocks. This is then followed by a maintenance dose with 5 g IM to the buttocks alternating every four hours. In the Zuspan regimen, a single administered dose of 4 g is given as a slow IV infusion over five to ten minutes, followed by an hourly maintenance infusion of 1-2 g with a controlled infusion pump (Padda et al., 2021).

Table 1. Administration of the drug MgSO4.(M. I. Akbar & Putri, 2021)

Initial dose	Maintenance dosage
4g MgSO4 (10 ml 40% concentration or 20 ml 20% concentration) IV for 5-8 minutes (0.5-1 gr/min velocity). For 10 ml 40% concentration dissolved to 20 ml with aquadest	Continue with 15 ml of MgSO4 (40%) or 6 gr in ringer acetate solution / ringer lactate for 6 hours (1 g / hour). In case of repeated seizures, give MgSO4 2 gr IV for 5 minutes MgSO4 infusion of 1 gr/hour is given up to 24 hours post/after birth

Based on research conducted by Sujardi et al. Regarding the comparison of serum magnesium levels after magnesium sulfate therapy, the route was different in preeclampsia, namely the average magnesium levels of the two groups showed no difference. The IM group showed a higher average than group IV, but still in therapeutic levels (Biomedika et al., 2019) MgSO4 has an effect on the central nervous system (brain and spinal). Excessive administration can affect reflexes in the mother. Reflexes should be monitored 2-4 hours when administering MgSO4. MgSO4 is given to the mother for tocolysis in pregnancy. The mean duration in utero of exposure to MgSO4 was 9.6 weeks (range 8-12 weeks) and the estimated average total maternal dose administered was 3,700 grams (Rahman & Helali, 2014).

Magnesium sulfate is used in pregnancy, namely in women with preeclampsia, firs line *management of eclampsic seizures*, first line seizure therapy in pregnant women and neuroprotection of preterm infant. The effects arising from the administration of magnesium sulfate are secondary hypotension due to decreased vascular resistance, flushed face, visual impairment, redness at the injection site, chest pain and nasal congestion.(Polypharmacy, 2020)

The anticonvulsant mechanism of MgSO4 is associated with its action on the central nervous system (CNS) and vascular endothelium, while its effects are mediated through the neuromuscular junction (NMJ). CNS depression is common through voltage-dependent N-methyl-D-aspartate receptor (NMDA) blockade and NMJ blockade by decreasing calcium conductance, acetylcholine release, and motor endplate stimulation of acetylcholine release (Padda et al., 2021). It is thought to cause vasodilation by stimulating prostacyclin I2 and nitric oxide synthesis in vascular endothelial cells. In addition, it is known that the vasodilating effect of MgSO4 on intracranial blood vessels of smaller diameter serves to reduce cerebral ischemia when used in the prophylaxis and treatment of eclampsia(Padda et al., 2021). Because advances in technology allow ionized magnesium to be more easily measured, the question arises as to whether it is more appropriate to monitor total serum magnesium or the physiologically active

ionized form. Studies have shown little correlation between total and ionized magnesium levels, either at baseline before treatment or during MgSO4 treatment for preeclampsia.

Preeclampsia patients treated with a load dose of 4 g intravenously followed by an infusion of 2 g per hour, found that total and ionized Mg2-concentrations increased rapidly after infusion, but concentrations for total magnesium were 4.84-0.24 mg/dL, while for ionized magnesium was 2.04-0.14 mg/dL. Similar results have been found by other groups using the same infusion protocol. Interestingly, as MgSO4 infusion caused a significant increase in Mg ionized2-levels of serum ionized calcium (Ca2-) concentrations unchanged, suggesting that the effect of MgSO4 was not exerted through modulation of ionized calcium levels. Magnesium is a powerful vasodilator of the uterine and mesenteric arteries, and aorta, but has minimal effect on the cerebral arteries. In vascular smooth muscle, magnesium competes with calcium for the binding site, in this case for voltage-operated calcium channels (VOCC).

A decrease in the activity of calcium channels decreases intracellular calcium, causes relaxation and vasodilation. In the endothelium, magnesium has been shown to increase prostaglandin I2 production (via an unknown mechanism), which in turn decreases platelet aggregation. Magnesium also increases the production of NO, which causes vasodilation (Euser & Cipolla,2009).

Vascular Effects of Magnesium Sulfate.

Cellular Target	Mode of Action	Possible Mechanism(s)
Smooth Muscle Uterine +++ Mesenteric +++ Aorta +++ Cerebral +	Relaxation ↓ Vasodilation ↓ Decreased Vascular Resistance	Calcium Antagonism Decreased Voltage-operated Calcium Channel (VOCC) Activity Decreased $[Ca^{+2}]_i$ Release From Sarcoplasmic Reticulum
Endothelium	Decreased Platelet Aggregation	Increased Prostaglandin I_2 (PGI_2)
	Vasodilation	Increased Nitric Oxide (NO, Gestation Dependent)

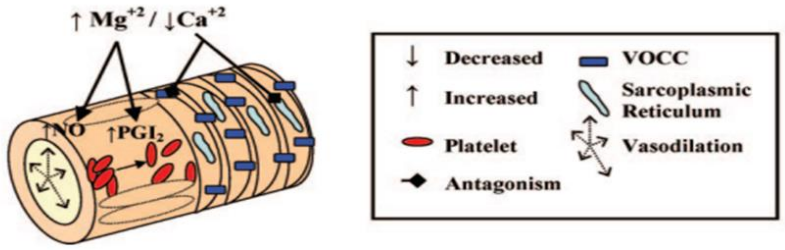

Figure 3. Vasodilation mechanism of magnesium sulfate.(Euser & Cipolla, 2009)

The use of MgSO4 as a seizure prophylactic in preeclampsia has been shown to be significant in numerous studies. Oktatin research (2016), found that all patients who used MgSO4 prophylaxis at RSUD dr. Soetomo Surabaya did not experience eclampsia seizures and without symptoms of side effects or drug interactions. In Hariyanti's research (2016) through a retroprospective cohort approach at Fatmawati Hospital, it was found that the results of reducing eclampsia cases in patients with MgSO4 administration were higher than patients without MgSO4 administration. Based on the results of Surjadi's research (2015) also found a significant effect of giving MgSO4 on reducing systolic blood pressure in preeclampsia patients (M. I. Akbar & Putri, 2021).

CONCLUSION

Administration of MgSO4 to preeclampsia patients has proven beneficial for the mother and her fetus. But it is necessary to carry out monitoring in the provision of therapy. Besides being beneficial for the mother, it is also beneficial for the fetus as a neuroprotector in the fetus.

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