Research Article

Maternal Outcomes with Twelve Hour versus Twenty Four Hour Maintenance Doses Of Magnesium Sulfate in Severe Postpartum Preeclampsia

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Abstract

Objective: To improve the quality of care for pregnant women with severe preeclampsia and provide data-driven solutions for healthcare system improvement.

Method: The study's inclusion criteria were pregnant women diagnosed with severe preeclampsia who were eligible for magnesium sulfate treatment. These women received the initial and maintenance doses of magnesium sulfate Zuspan. A clinical trial was carried out with 80 participants divided into two groups (control and trial), using randomized and double-blind methods. The study was conducted at multiple hospitals in Riau from October 2022 to February 2023. The data collected was analyzed to evaluate maternal outcomes for both groups. The study was approved by Ethical Review Board for Medicine and Health and registered with the Thai Clinical Trials Registry (TCTR 20230811008) once the data was assessed.

Results: The study did not report on the incidence of eclampsia or maternal mortality, and there was no significant difference in serum magnesium sulfate levels between the two groups ($p>0.005$).

Conclusions: Administering maintenance doses of MgSO4 for both 12 and 24 hours had similar effectiveness in preventing eclampsia, with the 12-hour group having better maternal outcomes.

Keywords: magnesium sulfate, maternal outcome, severe preeclampsia.

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INTRODUCTION

Preeclampsia is a dangerous complication that can occur during pregnancy, labor, or after delivery. It is one of the top three causes of maternal death, along with bleeding and infection. This condition affects over 70,000 women and contributes to the increasing rates of morbidity and mortality. According to the World Health Organization's 2019 data, 94% of maternal deaths occurred in low- to middle-income countries between 2010 and 2017 [1-3] Indonesia has the second-highest Maternal Mortality Ratio (MMR) among the Association of Southeast Asian Nations (ASEAN) countries, with an incidence rate of 305 per 100,000 live births according to the Indonesian Ministry of Health data.

Preeclampsia is a condition that is often difficult to manage. However, medical professionals are constantly improving their approach to ensure the best possible outcomes for both the mother and fetus[4,5-8]. This includes preventing seizures or eclampsia, controlling blood pressure, stabilizing cardiovascular function, and protecting the kidneys and other organs.[9,10] One study found that administering magnesium sulfate (MgSO4) can effectively control seizures in preeclampsia. MgSO4 is typically the preferred method for preventing seizures. It's worth noting that about one-third of seizures occur postpartum, with most happening within the first 24 hours and almost

all within 48 hours. However, it's important to consider the potential side effects and toxicity of MgSO4 before administering it.[5,11-14]

A research study investigate the incidence of magnesium (Mg) intoxication in severe preeclampsia women receiving MgSO4 therapy[15]. The study revealed that within the years 2014-2018, the reported incidence of Mg toxicity was between 0.6% and 1.5%. At the University of Mississippi, studies suggest that the administration of magnesium sulfate in postpartum preeclampsia women depends on clinical parameters[16] Studies at Universitas Airlangga reported an incidence of Mg toxicity of 0.6% to 1.5% within a period of 5 years (2014-2018)[15]. The study further showed that women with severe postpartum preeclampsia required an average maintenance dose of magnesium sulfate therapy for 16±5.9 hours. Comparing the clinical efficiency of MgSO4 in seizure prevention[17]. The study demonstrated that administration for 12 hours had the same clinical efficiency as 24 hours of administration. However, similar research has not been conducted in Indonesia. This study aimed to investigate the effectiveness of reducing the duration of the maintenance dose magnesium sulfate regimen to 12 hours from the standard 24 hours after the termination of pregnancy (postpartum). The study sought to determine if reducing the duration of magnesium sulfate therapy could improve maternal outcomes, and reduce adverse events and risk of toxicity, as well as the health care system.

METHODS

The study followed an analytical, double-blinding, and comparative design with a randomized controlled trial approach. It was conducted across multiple centers, including Arifin Achmad Hospital, Riau Province, Tengku Rafian Siak Sri Indrapura Regional General Hospital, Bengkalis Regional General Hospital, Dumai Regional General Hospital, and Selasih Hospital. The study took place in the Maternity and Care Room of SMF Obstetrics and Gynecology Arifin Achmad Hospital, Riau Province, and the Obstetrics and Gynecology Department education network hospital from October 2022 to February 2023. The research was approved by the Medical and Health Research Ethics Unit of the Ethical Review Board for Medicine and Health Research Faculty of Medicine, University of Riau with No. B/156/UN19.5.1.1.8/UEPKK/2022, and was registered with the Thai Clinical Trials Registry (TCTR 20230811008) once the data was assessed.

The study's inclusion criteria were pregnant women diagnosed with severe preeclampsia who were eligible for magnesium sulfate treatment. These women received the initial and maintenance doses of magnesium sulfate Zuspan. The exclusion criteria included severe preeclampsia with decreased consciousness, eclampsia, HELLP syndrome, renal failure, acute pulmonary edema, or a history of allergy to the trial drugs.

The study involved 80 participants who were fully informed about the research and given the opportunity to provide their consent. As part of the study, antihypertensive medication and trial drugs in the form of magnesium sulfate were administered to them using the Zuspan method. The magnesium sulfate was given through a double-blinded process, with a concentration of 40% and an initial dose of 4 g intravenously over a period of 15-20 minutes. This was followed by a maintenance dose of 1-2 grams/hour, which was delivered through infusion using a syringe pump. The participants were randomly assigned to two groups, namely, Group 12-hours and Group 24-hours. Group 12-hours received the maintenance dose of magnesium sulfate for 12 hours, while Group 24-hours received maintenance dose of magnesium sulfate for 24 hours (Figure 1).

Healthcare providers collect patient information using standardized coding kits. They use various measuring instruments to monitor maternal and fetal outcomes, serum magnesium levels, laboratory values before and after administering MgSO4, and any side effects that may occur. If the research shows poor results, it can be stopped at any time before reaching the target number of respondents. All activities are documented in the patient's medical records. The data collected is then recorded, compiled, and analyzed using SPSS software version 25.

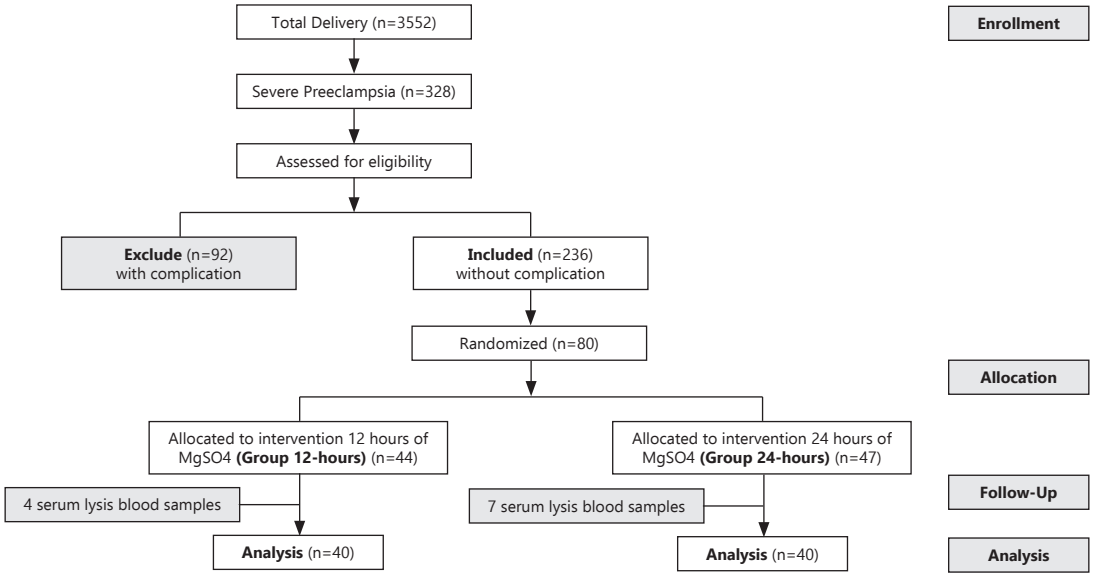

Figure 1. Protocol of the subject of study

RESULTS

The characteristics of the study subjects consisted of age, parity, gestational age, type of delivery, average systolic and diastolic blood pressure at the beginning of the patient's examination, and body mass index depicted in Table 1. Analysis of Table 1 data showed that based on age, parity, gestational age, mode of delivery, systolic and diastolic blood pressure, and Body Mass Index (BMI) in the two groups of study subjects, there was no significant difference ($p > 0.05$). The strength of this research was that it was carried out in a multicenter manner and was carried out using double blinding, the limitations of this research were only in patients with severe preeclampsia without warning's sign.

Table 1. Characteristics of the Research Subject

Characteristics	Group A MgSO4 12 hours (intervention) (n=40)	Group B MgSO4 24 hours (control) (n=40)	RR (CI 95%)
Age (Years)	31.20±5.50	30.77±6.60	2.01 (1.98-2.04)
Parity	31.25		1.82 (1.92-3.78)
Primigravida	68.75	35.50	
Multigravida		64.50	
Gestational Age (weeks) Mean±SD	33.92±2.99	32.82±2.69	2.22 (1.98-2.46)
Delivery methods			
Vaginal Delivery	27.50	25.00	1.66 (1.03-2.29)
Cesarean Section	72.50	75.00	1.06 (1.001-1.11)
Average Systolic Blood Pressure* (mmHg)	180.27±12.62	172.10±14.44	23.98 (11.23-36.11)
Average Diastolic Blood Pressure*(mmHg)	110.60±23.70	110±11.53	10.24 (10.01-10.47)
Body Mass Index (BMI) (kg/m^2)	25.71±3.48	26.67±2.14	23.78 (22.19-245.31)

The study aimed to evaluate various factors such as the occurrence of eclampsia, maternal mortality, duration of catheterization installation and mobilization start time, length of hospital stay, treatment costs, and blood serum magnesium levels. The data collected from the research has been presented in Table 2. The findings indicate that there were no cases of eclampsia or maternal death during the study. However, there was no significant difference ($p>0.05$) in the serum magnesium levels between the two groups.

Table 2. Primary Maternal Outcomes

Variable	Group 12 hours (n=40)	Group 24 hours (n=40)	*P-value*
Eclampsia	0 (0.0)	0 (0.0)	1.867
(48 hours postpartum)			
Mortality (maternal death)	0 (0.0)	0 (0.0)	1.092
Serum Mg Levels (mmol/L) Mean±SD			
T_{18}	2.68±0.09	2.70±0.04	0.060
T_{30}	2.45±0.21	2.64±0.28	0.340

Secondary outcomes in this study included assessments in comparing MgSO4 side effects, clinical symptoms of MgSO4 toxicity, and laboratory values before and after the trial drug (magnesium sulfate) in both groups of study subjects. The incidence of each side effect mentioned in Table 3 was higher in the 24-hour maintenance dose MgSO4 regimen group, although statistical analysis showed no significant difference between the two groups ($p>0.05$). The incidence of side effects in both groups was complaints of flushing (23.75%), vomiting (6.25%), drowsiness (23.75%), and no incidence of limb weakness (0%), oliguria (0%), or respiratory distress (0%). Clinical symptoms of toxicity assessed include loss of patellar reflexes, respiratory paralysis, or cardiac arrest.

Table 3. Comparison of MgSO4 Side Effects

Characteristics	Group 12 hours (n=40)	Group 24 hours (n=40)	*P-value*
Flushing	8 (20.0)	11 (27.5)	0.624
Vomit	2 (5.0)	3 (7.5)	0.442
Limb Weakness	0 (0.0)	0 (0.0)	0.871
Dizziness	9 (22.5)	10 (25.0)	0.793
Anuria/oliguria Urine Output (ml)			
<30	0 (0.0)	0 (0.0)	1.092
≥30	40 (100)	40 (100)	0.136
Respiratory distress	0 (0.0)	0 (0.0)	1.870

DISCUSSION

This study showed the general characteristics of pregnant women study subjects diagnosed with severe preeclampsia with an average age of 30.98±6.04 years. Although, this average age is higher compared to research conducted in India by Shaheen Anjum et al in their study showed that the age of women in the study participants had an average age of 23.8±3.4 years. This is estimated as a result of marriages in India in 2018-2022 having a faster graph, with an average age of 19.8 years [12,18]. The delivery method majority 73.75% by cesarean section and multigravida parity. The research data listed in Table 2 showed no incidence of eclampsia or maternal death reported in this study. Research conducted by Anjum (2015) also reported similar results to this study [12] Eclampsia is a major unexpected complication, although eclampsia is a complication that can be avoided with proper management [10,19-22]. Magnesium sulfate has been declared a first-line treatment for the prevention and treatment of eclampsia [1,20,23]. One of the main concerns of using magnesium sulfate is its potential toxicity, studies have shown that the duration of administration of magnesium sulfate is one of the significant toxicity factors of magnesium sulfate[15,24].

This study compared magnesium sulfate administration with a duration of 12 hours compared to a duration of 24 hours (standard) in patients with severe postpartum preeclampsia, then monitored maternal outcomes. Data showed no incidence of eclampsia or maternal death was reported in this study. The findings could represent a breakthrough in the management of patients with preeclampsia, especially in low-resource countries, where the incidence of preeclampsia disease remains high and places an

increasing burden on health care.

This study also showed an analysis of the results that there was a reduction in the time or duration of urinary catheter use and hospital treatment in the 12-hour group, compared to the 24-hour group, with statistical analysis showing a significant difference ($p < 0.05$). Early or faster release of the foley catheter significantly reduced patient morbidity, by allowing early mobilization and demonstrating better bladder function[1,12,16,25]. This study, reporting that foley catheters were removed earlier in the 12-hour group compared to the 24-hour group.

The average length of hospital stay in the 12-hour group was faster than the 24-hour group. This can serve as a new basis for postpartum treatment in severe preeclampsia patients, requiring a faster time than previous literature that required a minimum of 48 hours postpartum. This indirectly affected the average cost of hospital care in both groups, with statistical values showing a significant influence ($p<0.05$). A shortened hospital stay is beneficial for patients and the healthcare system, as it reduces the overall cost of care, reduces unnecessary ones such as exposure to nosocomial infections, and allows better utilization of available health resources. This reduction will be beneficial at the level of tertiary care centers, district hospitals, and primary health centers in many countries, especially with low resources. It will also reduce the burden on health workers and enable appropriate mother-child bonding [12,13].

Data from the study related to serum magnesium levels in statistical analysis showed no significant difference between the two groups after being given the test drug. The statistical analysis of the two groups did not show significantly different results ($p>0.05$). This indicates that using a maintenance dose of magnesium sulfate of 1-2 grams after receiving a loading dose of magnesium sulfate by the Zuspan Method, either for 12 or 24 hours, is able to maintain a therapeutic dose for 30 hours. This can be one of the research data points to counter previous studies that mention there are often subtherapeutic magnesium levels after being given a maintenance dose. [5,6,11,13,26].

Postpartum women with severe preeclampsia need a maintenance dose of magnesium sulfate therapy for an average of 20 ± 8.7 hours, provided that eclampsia does not occur.[1,17,20,27-29] Reported clinical efficacy with varying durations and routes of administration requires further research to determine the optimal effective duration with demonstrable clinical efficacy and low toxicity, which would be cost-effective for healthcare systems, especially in low-resource countries. [12,30,31]

The secondary output of the study showed a comparison of the incidence of side effects among the 2 study groups but statistically did not show a significant difference ($p>0.05$). The incidence of clinical symptoms of MgSO4 toxicity in this study showed no incidence of clinical symptoms of MgSO4 toxicity reported.[17]

CONCLUSION

Administering maintenance doses of MgSO4 for 12 hours and 24 hours was considered to have the same effect as eclampsia prophylaxis, with better primary and secondary maternal outcomes in the 12-hour group. The recent findings could be a significant breakthrough in managing preeclampsia, especially in countries with limited resources but high incidences of the condition. Reducing the incidence of side effects and risk of toxicity, and benefiting the health care system or reducing the burden on health workers.

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