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ORIGINAL ARTICLE

An Experience of Use of Zuspan Regimen for Severe Preeclampsia and Eclampsia at a University Hospital

Girija S[1], Manjunath AP[1], Vanita P[2], Al Dughaishi T[1], Al Riyami N[3] and Suhas AM[4]*

[1]*Department of Obstetrics & Gynecology, Sultan Qaboos University Hospital, Muscat, Oman*

[2]*Warwick University Hospital, NHS, UK*

[3]*Department of Obstetrics & Gynecology, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman*

[4]*SDM College of Medical Sciences & Hospital, Dharwad, India*

***Corresponding author:** *Dr. Manjunath AP, Professor, Department of Obstetrics & Gynecology, The Oxford Medical College Hospital and Research Institute, Yadavanahalli, Attibele, Behind La Classic Hotel, Bangalore 562107, India; Department of Obstetrics & Gynecology, Sultan Qaboos University Hospital, Muscat, Oman, Tel: +971-506267268*

Abstract

Objective: Preeclampsia and eclampsia remain major contributors to maternal morbidity and mortality worldwide. Magnesium sulfate ($MgSO_4$) is a key treatment in managing these conditions. This study evaluates the outcomes of intravenous $MgSO_4$ therapy in women with preeclampsia and eclampsia at a tertiary care university hospital in Oman.

Methods: This retrospective cohort study covers four years, from January 2007 to December 2010 and included all women who received intravenous $MgSO_4$ treatment for preeclampsia and eclampsia as per departmental protocol (Zuspan regimen). Data were sourced from delivery registries and hospital electronic patient records. The study also noted the use of adjunct antihypertensive therapies. Delivery mode was determined after patient stabilization. Maternal demographics and $MgSO_4$ administration parameters, including duration, complications and labor outcomes were collected. $MgSO_4$ toxicity was monitored clinically with serum magnesium levels measured as necessary. Data analysis was performed using the IBM SPSS.

Results: A total of 82 women received $MgSO_4$ for preeclampsia and eclampsia, with an incidence of 0.76%. Only 1.2% of the woman experienced eclampsia, while 99% had severe preeclampsia. Hemolysis, Elevated Liver enzymes, Low Platelets (HELLP) syndrome was present in 12.2% of cases. The mean age of the women was 31.4 ± 6.54 years with 46.3% being primigravida. Magnesium sulfate was started alongside labor induction and continued for 24 hours postpartum in 45.5% of women and 54.4% of the women received it in the postpartum period. The mean duration of $MgSO_4$ therapy was 31.3 ± 10.7 hours. No women required calcium gluconate for $MgSO_4$ toxicity and no intravenous $MgSO_4$ related side effects were observed. Majority of women (85.3%) needed up to two antihypertensive medications to control their blood pressure, while only 12.4% required more than two antihypertensive medications.

Conclusion: The low incidence of eclampsia at our institution highlights the effectiveness of timely $MgSO_4$ regimen administration. The Zuspan regimen is well-tolerated among Omani women with preeclampsia and eclampsia, demonstrating full adherence to the protocol without associated side effects or complications.

Keywords

Eclampsia, Magnesium sulfate, Preeclampsia, Clinical protocols

Abbreviations

HELLP: Hemolysis Elevated Liver enzymes Low platelets; $MgSO_4$: Magnesium Sulfate; WHO: World Health Organization; PROMPT: Practical Obstetric Multi-Professional Training

Introduction

Preeclampsia and eclampsia remain significant contributors to maternal morbidity and mortality worldwide, accounting for approximately 10-15% of direct maternal deaths [1]. Magnesium sulphate ($MgSO_4$) has been a cornerstone in the management of these conditions for over a century and is currently the preferred drug for preventing and controlling eclamptic

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seizures [2,3]. Robust evidence from large multi-center randomized controlled trials and systematic reviews supports the efficacy of $MgSO_4$ therapy in treating eclampsia [2-8].

Internationally, two primary $MgSO_4$ regimens are employed for the prophylaxis and treatment of preeclampsia and eclampsia: the intramuscular (IM) Pritchard regimen [9] and the intravenous (IV) Zuspan regimen [10]. The choice between these regimens often depends on the availability of infusion pumps for IV administration or lack of access to a vein or contraindications for IM injection (HELLP syndrome).

Despite the global success of $MgSO_4$ in managing these conditions, there is a paucity of literature on the management of hypertensive disorders of pregnancy in Omani women. This study aims to analyze the outcomes of women who received the IV $MgSO_4$ regimen for severe preeclampsia and eclampsia at a tertiary care university hospital in Oman.

Methods

This retrospective cohort study spans four years, from January 2007 to December 2010. It included all women with preeclampsia and eclampsia who received intravenous $MgSO_4$. Preeclampsia was defined as multisystem disorder with new onset hypertension (> 140 and/or > 90 mmHg) after 20 weeks gestation accompanied by one or more of the following features; maternal symptoms & signs (features of cerebral irritability: Hyperreflexia with sustained clonus, persistent headache, persistent visual disturbances), abnormal laboratory tests, proteinuria, HELLP syndrome or maternal complications including, disseminated intravascular coagulation, renal failure, pulmonary edema, cerebrovascular accident, features of placental dysfunction (fetal growth restriction) [11,12]. Eclampsia was defined as the occurrence of seizures in a woman with preeclampsia [11,12]. The magnesium sulphate regimen consists of a four-gram intravenous loading dose administered over 15 minutes, followed by a maintenance infusion of one gram per hour until 24 hours after birth or last seizure [10]. Intravenous magnesium was administered using a syringe driver with an infusion pump, monitored by a trained nurse or midwife. Data were collected from the delivery registry and hospital electronic patient records. Demographic profiles, labor parameters and details related to $MgSO_4$ administration were retrieved, including the timing of treatment initiation (antenatally, intrapartum period or postnatally), total duration of use and any side effects.

All patients receiving $MgSO_4$ were monitored either in high-dependence units or delivery suites, or intensive care units, providing one-to-one care with constant monitoring. Drug toxicity was monitored using clinical parameters such as patellar reflex, hourly urinary output measurements, and respiratory rate. Serum magnesium levels were checked when necessary. Maintenance therapy continued for 24 hours after delivery or the last convulsion. Calcium gluconate was used as an antidote if needed. Data analysis was performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., 2012).

Table 1: Maternal demographics & pregnancy characteristics (N = 82).

Gestational age at delivery (weeks)	**N**	**%**
≤ 28	7	8.5%
29-34	20	24.4%
35-36	24	29.3%
≥ 37	31	37.8%
Gravida	**N**	**%**
1	28	34.2%
2	18	22.0 %
3	7	8.5%
4	7	8.5%
≥ 5	22	26.8%
Mode of delivery	**N**	**%**
Spontaneous vaginal delivery	36	43.9%
Vacuum/kiwi/ Forceps	1	1.2%
Cesarean section	45	54.9%

Results

A total of 82 women received IV $MgSO_4$ for preeclampsia and eclampsia, with no breaches in the protocol. All women completed the Zuspan regimen as per departmental protocol. The incidence of preeclampsia was 0.76% among 10822 deliveries during this period. Among them only, one (1.2%) woman had eclampsia, while 81 (98.8%) had preeclampsia. HELLP syndrome was observed in 10 (12.2%) women.

The mean maternal age was 31.4 years (SD = 6.54; range 19-47) and 28 (34.2%) were primigravida. The mean birthweight was 2142.7 grams (SD = 826.1; range 740-2600). Table 1 provides detailed maternal demographics and pregnancy characteristics.

The most common clinical feature observed was brisk reflexes, present in 50 (61.0%) cases, followed by headaches, which occurred in 45 (54.9%) cases. Notably, 25 (30%) women were asymptomatic despite having severe features of preeclampsia. It is important to note that each patient could exhibit one or more signs or symptoms. Table 2 provides a detailed overview of the signs and symptoms recorded before initiating the Zuspan regimen.

The mean highest recorded systolic and diastolic blood pressures were 166.9 mmHg (SD = 18.9; range 140-230) and 103.07 mmHg (SD = 13.4; range 84-190) respectively. Heavy proteinuria was observed in 21 (25.6%) women, and nephrotic range proteinuria in 30 (36.6%) women, based on the protein creatinine ratio [13].

Table 2: Signs & symptoms complex before starting Magnesium sulphate.

Signs & Symptoms	N	%
Brisk reflexes	50	61.0%
Headache	45	54.9%
Asymptomatic	25	30.5%
Epigastric pain	24	29.3%
Blurring of vision	20	24.4%
Edema	16	19.5%
Vomiting	7	8.5%
Clonus	2	2.4%
Right upper quadrant pain	2	1.2%

Table 3: Antihypertensive medications to control blood pressure.

No of antihypertensive medications	N	%
One	37	45.12%
Two	33	40.24%
Three	10	12.19%
Four	1	1.21%

Magnesium sulfate therapy was started antenatally along with labor induction in 45.5% of the women and was discontinued 24 hours after delivery, while 54.4% of the women received the drug postnatally. Notably, 20 women (14.6%) received the drug from 24 hours after delivery up to 6 days postpartum. Regarding the total duration of $MgSO_4$ therapy, it was administered for 24 hours in 43 cases (56%) and for more than 24 hours in 39 cases (48.2%). The mean duration of $MgSO_4$ therapy was 31.3 hours (SD = 10.72), with a range of 24 to 72 hours.

No women required calcium gluconate for $MgSO_4$ toxicity and no side effects from intravenous $MgSO_4$ were observed. Additionally, no women experienced eclamptic seizures while on $MgSO_4$ therapy and there were no maternal deaths. The number of antihypertensive medications needed to control hypertension varied among the women; however, in most cases (85.3%), blood pressure was controlled with either one or two medications, as shown in Table 3. The most commonly used medications were labetalol, nifedipine, methyldopa and hydralazine.

Discussion

Preeclampsia and eclampsia are serious and potentially life-threatening conditions. Over decades, $MgSO_4$ has emerged as the treatment of choice for these conditions. Although magnesium sulphate was one of the earliest drugs used as an anticonvulsant in the treatment of eclampsia in the 1920s in Europe and the US, diazepam became popular in subsequent years, particularly in developing countries, due to its affordability and availability. In the 1980s, phenytoin was advocated for its anticonvulsive action without sedative effects. The search for the best anticonvulsant for women with eclampsia continued for decades [8]. This debate was finally resolved when a large randomized trial demonstrated that $MgSO_4$ reduced the risk of further seizures and maternal death compared to diazepam or phenytoin [2]. Regarding pre-eclampsia, anticonvulsants have also been advocated for women with severe features to prevent the onset of eclampsia. The 2002 landmark Magpie Trial, involving about 10,000 women, demonstrated that magnesium sulphate halved the risk of eclampsia compared to placebo [3]. This finding has been confirmed by systematic reviews [5-7]. Magnesium sulphate was found to be superior to phenytoin [5,6], diazepam [7] and nimodipine [5] for the prevention of eclampsia in women with pre-eclampsia.

The WHO recognizes $MgSO_4$ as a lifesaving drug, recommending its availability in all healthcare facilities and endorsing it as an essential, effective, safe and low-cost treatment for severe pre-eclampsia and eclampsia [14,15].

Our study shows that no women developed convulsions during $MgSO_4$ administration and no side effects necessitating calcium gluconate due to $MgSO_4$ toxicity were observed. This aligns with the findings of the Magpie Trial [3], which reported that only 0.3% of women required calcium gluconate for $MgSO_4$ toxicity, with no significant difference in serious morbidities between the treatment and placebo groups.

The adherence to the $MgSO_4$ administration protocol in our study was 100%, likely due to the availability of resources and established systems at our hospital. Our quality department's inventory control methods, along with departmental protocols for effective $MgSO_4$ administration and monitoring, contributed to this high adherence. Moreover regular training for our doctors, nursing and midwifery staff through the PROMPT (Practical Obstetric Multi-Professional Training) courses further ensured preparedness for emergencies. These evidence-based, multi-professional training programs enhance non-technical skills like effective communication and teamwork, boosting healthcare providers confidence and competence in administering $MgSO_4$ for preeclampsia and eclampsia [16,17]. Additionally, our departments pre-filled eclampsia treatment kits ensure readiness for emergency obstetric care. Another article emphasizes the role of simulation in training residents and junior doctors for managing pre-eclampsia and eclampsia. It highlights that the participants found the simulation immensely valuable for managing eclampsia, particularly because none of them had prior exposure to this condition [18].

In contrast, many resource-poor settings face challenges such as system issues, gaps in policy practice [19] and lack of drug availability and trained staff [20]. The IV $MgSO_4$ regimen requires infusion pumps and constant monitoring, posing risks of toxicity if a

regular gravity-fed infusion set is used. The Pritchard regimen, which involves IM administration of $MgSO_4$, is easier to implement and can be administered by lower cadre health workers. WHO recommends the IM administration in low-resource settings and suggests using a loading dose followed by immediate transfer to a higher-level healthcare facility for severe preeclampsia and eclampsia cases [21].

Our study also highlights a low threshold for $MgSO_4$ administration, likely due to the definition of preeclampsia with severe features, which includes less severe hypertension with symptoms indicative of imminent eclampsia, such as hyperreflexia and clonus [3]. These severe symptoms also guided the extended $MgSO_4$ regimen of more than 24 hours in our protocol. While $MgSO_4$ is effective for both severe and non-severe preeclampsia, treating non-severe cases requires a higher number needed to treat to prevent one seizure and incurs higher costs [22]. In well-resourced settings, this has led to recommendations for administering $MgSO_4$ to all women of preeclampsia with severe features and considering it for those with non-severe disease. In under-resourced settings, WHO makes similar recommendations, though $MgSO_4$ may not be available for all women [21].

Limitations

This study's limitations include its small sample size and the specific population presenting to a tertiary center. Further research is recommended, involving multiple centers in Oman and larger sample sizes to enhance the generalizability of the findings.

Conclusion

The incidence of eclampsia in our setup was very low due to the timely use of zuspan regimen and low threshold for use of $MgSO_4$. The Zuspan regimen was well tolerated among Omani women with preeclampsia and eclampsia, with no observed side effects or complications.

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Authors' Contributions

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Disclosure

The authors declare no conflicts of interest related to this research.

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