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Original Article

Eclampsia

Pak Armed Forces Med J 2021; 71 (2): 598-601

EFFICACY OF MAGNESIUM SULPHATE ON MATERNAL MORBIDITY AND MORTALITY IN ECLAMPSIA

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ABSTRACT

Objective: To study efficacy of Magnesium Sulphate in reducing maternal morbidity and mortality in patients presenting with eclampsia.

Study Design: Prospective observational study.

Place and Duration of Study: Gynae/Obs Department, Combined Military Hospital Bannu, from Jan 2018 Sep 2019.

Methodology: A total of 134 patients fulfilling inclusion criteria were included in the study. Patient management was multi-disciplinary. Convulsions were controlled by 4gram magnesium sulphate intravenously over 20 minutes as a loading dose, followed by 1gram per hour of maintenance infusion. Blood pressure was controlled with injection Labetalol 10 milligram followed by injection Hydralazine repeated after every 20 minutes till the blood pressure was controlled.

Results: A total of 134 patients had eclampsia constituting 6.8% of obstetric admissions. Case fatality was 14 (10.4%) while 120 (89.55%) of the cases responded well to treatment and survived the event. Mean age of patients was 22 years. Thirty patients 22.4% were booked and 104 patients 77.6% were un-booked. Mostly patients 122 (91%) came from rural area and only 12 (9%) were from urban areas with booked pregnancies having regular antenatal visits. One hundred and twenty six (94%) patients with eclampsia presented in antenatal period and only 8 (6%) presented in post natal period. Mode of delivery was cesarean section in 87 (64.9%) and 47 (35.1%) delivered vaginally. Frequency of patient requiring ventilator support, acute renal failure, disseminated intravascular coagulation, adult respiratory distress syndrome, HELLP (hemolysis, elevated liver enzymes, low platelet) syndrome was 11 (8.2%), 46 (34.3%), 43 (32.1%), 35 (26.1%), 7 (5.2%) respectively. In our study case fatality due to complications of eclampsia was 8 (6%) due to pulmonary edema while 5 (3.7%) was due to intra-cranial bleed.

Conclusion: Magnesium sulphate is a safe and cost effective drug in reducing maternal morbidity and mortality in patients presenting with eclampsia.

Keywords: Eclampsia, Magnesium sulphate, Maternal morbidity, Maternal mortality, Pulmonary edema.

INTRODUCTION

Eclampsia is an acute life threatening complication of pregnancy[1]. It accounts for about 50,000 maternal deaths a year worldwide[2]. Eclampsia is a pregnancy specific multi organ disorder. The main features are hypertension, proteinuria, generalized edema and tonic clonic fits with or without coma occurring after 20 weeks of gestation till 6 weeks postpartum. The earliest evidence was recorded by Hippocrates, who identified headache, altered conscious level and fits as certain abnormal features seen in some pregnancies. Eclampsia is a Latin term, 1st appeared in Johannes Varandaeus in treatise on gynaecology (1620).

There are variety of presentation and the classic features may not be present always. Pre-eclampsia and eclampsia occur mostly in primi-gravida[3]. The cause of eclampsia is a pregnancy specific multi-organ disorder involving vascular endothelial damage, intravascular coagulation and vasoconstriction leading to end organ ischemia and convulsions[4].

Eclampsia remains an important cause of maternal and perinatal mortality and morbidity worldwide. Many studies have indicated that over one tenth of maternal deaths in Asia, Africa and about one quarter of maternal deaths in Latin America occur due to eclampsia[5].

In developed countries its incidence is declining but in developing countries like Pakistan it is a significant contributor to maternal morbidity and mortality[6]. Pakistan is among the six countries where more than 50% world's maternal deaths occur[5]. According to WHO and UNICEF every year 18% of maternal deaths are caused by pre-eclampsia and eclampsia and only 40% of births take place in health facilities in developing countries[7]. The 2007 Health Survey has revealed thateclampsia caused 11% direct maternal deaths and is the third leading cause of maternal mortality after hemorrhage and infection[3].

In USA its incidence is 4.3/10,000 deliveries and in UK it is 4.9/10,000 deliveries8. According to one

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Received: 10 Apr 2020; revised received: 25 Jun 2020; accepted: 30 Jun 2020

study prevalence of pre-eclampsia and eclampsia in Pakistan is around 19%[6,4].

Deaths due to eclampsia are secondary to acute renal failure, cerebrovascular hemorrhage, aspiration pneumonia, pulmonary edema, hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, disseminated intravascular coagulation (DIC), adult respiratory distress syndrome(ARDS) and cardiac failure[3].

Perinatal morbidity and mortality varies from 5-11% in developed countries and up to 40% in developing countries[1]. It is due to prematurity, low birth weight, birth asphyxia and intra uterine growth retardation[8].

Magnesium sulphate was introduced in 1925 to control convulsions but it was a Collaborative Trial in 1995 (Magpie trial) that confirmed the efficacy of magnesium sulphate as an anticonvulsant of choice in severe pre-eclampsia and eclampsia[9]. MgSO4 is a potent cerebral vasodilator and acts competitively in blocking the entry of calcium into synaptic endings thus altering neuromuscular transmission. Potential hazards of magnesium sulphate include maternal hypotension, oligouria, loss of patellar reflexes, respiratory depression and cardiac arrest[9]. In developing countries there is limited use of Magnesium sulphate due to apprehension regarding it's side effects. The rationale of study was to determine the efficacy of MgSO4 in reducing maternal morbidity and mortality in patients presenting with eclampsia.

METHODOLOGY

This was a prospective observational study. It was conducted in the Department of Obstetrics and Gynecology, Combined Military Hospital Bannu, from Jan 2018 to Sep 2019. A sample size of 134 patients was selected through non-probability consecutive technique. Informed consent was obtained from attendants of every patient presenting with eclampsia. The study protocol was approved by the Ethics Committee of the Hospital (IERC/OBS/ 2019/01). Inclusion criteria were the patients developing eclampsia in second half of pregnancy or within ten days after delivery. Exclusion criteria were patients with fits due to epilepsy, cerebral or any other meta-bolic causes as well as patients presenting more than ten days after delivery.

Management of eclampsia is a multidisciplinary approach, as it requires presence of trained midwife, ICU with fully trained staff along with availability of anesthetist as at times patient may require ventilation support. A detailed history was taken from the attendants regarding gestational age or time passed after delivery, number of fits, history of hypertension during pregnancy, proteinuria, swelling of feet, headache, visual disturbances, epigastric pain, vomiting, urinary problems, scotomas, or bleeding per vaginum. A thorough general physical and systemic examination was performed. Blood pressure, pulse, oxygen saturation or temperature was recorded. Edema, jaundice, pallor and reflexes were also checked. Obstetrical examination to determine lie and presentation of fetus, amount of liquor and fetal heart rate was recorded. Vaginal examination was performed to note cervical dilation, effacement and station of presenting part. Ultrasound examination and cardio-tocography was recorded to rule out fetal distress. Mode of delivery (cesarean section or vaginal delivery) was decided according to Bishop Score, maternal and fetal condition.

Convulsions were controlled with 4 grams loading dose of magnesium sulphate (intra-venous) over 20 minutes followed by 1 gram/ hour maintenance infusion. The maintenance infusion was continued for 24 hours after the last fit. Blood pressure was controlled with injection labetalol 10mg IV over 2-3 minutes, followed by injection hydralazine 5mg IV repeated after every 20 minutes till the blood pressure was controlled. Urinary output, respiratory rate, level of consciousness, presence of patellar reflexes and recurrence of fits was recorded during MgSO4 infusion. Calcium gluconate (10ml of 10% soln.) was kept in hand in case of MgSO4 toxicity.

Patient requiring ventilator support was assessed. Frequency of complications like disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS), HELLP syndrome, accute renal failure (ARF) and death due to intra cranial bleed and pulmonary edema was noted. Statistical analysis was performed with SPSS-22. For quantitative variables like age and parity mean was calculated. For qualitative variables like booking status, locality, ventilation support, ARF, DIC, ARDS, HELLP Syndrome frequencies were measured. Descriptive statistical analysis was done.

RESULTS

A total of 134 patients had eclampsia constituting 6.8% of obstetric admissions. Case fatality was 14 (10.4%) while 89.55% of the cases responded well to treatment and survived the event. Mean age of patients was 22 ± 4.51 years. Thirty patients (22.4%) were booked and 104 patients (77.6%) were un-booked. Mostly patients 91% came from rural area and only 9% were

from urban areas with booked pregnancies having regular antenatal visits (figure).

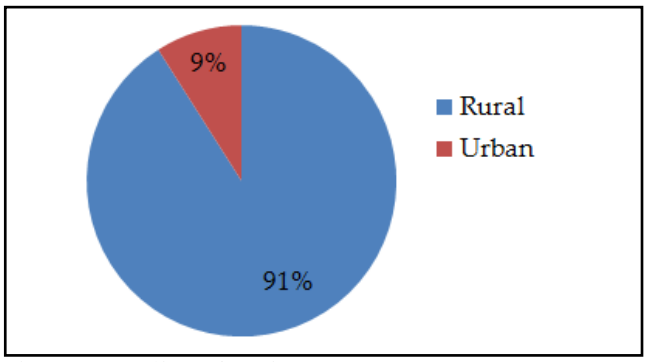

Figure: Locality of patients.

One hundred and twenty six patients with eclampsia presented in antenatal period and only 6 presented in post natal period. 64.9% underwent cesarean section and 35.1% delivered vaginally. Maternal mortality due to complications of eclampsia was 6% due to pulmonary edema while 3.7% was due to intra-cranial bleed. The frequency of other major complications in our patients is shown in table.

Table: Complications of eclampsia.

Complications	n (%)
Ventilator Support	11 (8.2)
ARF	46 (34.3)
DIC	43 (32.1)
ARDS	35 (26.1)
HELLP	7 (5.2)
Maternal Mortality	14 (10.4)

DISCUSSION

The pathogenesis of eclampsia is unknown, various proposed factors include maternal immunological intolerance, altered placental implantation, vascular endothelial growth factor (VEGF), placental growth factor (PlGF), genetic, nutritional and environmental factors as well as inflammatory changes.

Hypertensive disorders in pregnancy represent wide spectrum of conditions; pre eclampsia, high blood pressure and proteinuria ,while eclampsia is the occurrence of one or more generalized convulsions or coma in the presence of pre-eclampsia and in the absence of other neurological conditions. Eclampsia causes increased maternal morbidity and mortality. Once it occurs, hospital inpatient management is required for effective control of convulsions[11].

In the developing countries eclampsia is the major cause of seizures during pregnancy[5]. The main reason is non-availability of health care facilities especially in the rural areas. In our study the drainage area was mostly rural areas of Miranshah and South Waziristan. MgSO4 is effective in controlling eclamptic seizures and reducing maternal morbidity and mortality. WHO recommends that as soon as patients with eclampsia develops seizures the pregnancy should be terminated within 12-24 hours and has recommended MgSO4 to be effective, low priced and safe in the management of severe pre-eclampsia and eclampsia[8].

The Magpie trial which was initiated in 2002 by UK medical research council in collaboration with WHO was a three year study and included 10,000 pre-eclampsia patients from 33 countries all over the world[9]. In that study pre-eclampsia patients were managed with MgSO4 and it was concluded to have 58% decreased risk of eclampsia and 45% lesser risk of maternal mortality. However MgSO4 has not attainted widespread usage in developing countries like Pakistan as has been discussed in a study by Butt *et al*, the reason behind the decreased usage of MgSO4 is lack of public awareness of the drug, lack of adequate training of service provider due to non-availability of MgSO4 in these areas. Pakistan is a developing country with limited resources in health sector. It has also been mentioned in his study thatits low cost leaves little profit for pharmaceutical companies. Hence there is a supply shortage of this drug in our country[12].

MgSO4 was included in National Essential Drug List for treatment of eclampsia and severe pre-eclampsia. In 2007 the Drug List was revised at primary, secondary and tertiary levels for the treatment of eclampsia still Magnesium sulphate non availability as Basic Health Unit, Tehsil Headquarters and District Headquarters is a major issue.

In this study the factors contributing to maternal morbidity and mortality were un-booked status, lack of education, late referral, lack of transport, prolonged coma and multiple seizures prior to admission. This fact is favored by a study done in Madina Hospital, UMDC Faisalabad in 2010 where majority of patients were poor and illiterate[13]. They never had any antenatal visit and presented in coma or after having multiple seizures. In a study by Tabassum *et al* 65% patients with eclampsia presented late with major complications due to lack of health awareness, lack of training of traditional birth attendants and financial problems[13]. This fact has also been observed in the study conducted by Butt A that in Pakistan two third deliveries are still conducted by traditional birth attendants, so

their role cannot be ignored in reducing maternal morbidity and mortality[12]. Recent demographic and health survey conducted in Pakistan supports the same facts[14]. So education at basic health care level is required regarding efficacy, dosage, toxicity and antidote of MgSO4.

The reported data in Pakistan showed 18-23% maternal mortality[6]. In our study, it was 10.4% as compared to 24% in a study conducted by Shaikh and Rathore *et al*. Shaikh *et al* concluded 19.68% case fatality rate, which was mainly due to pulmonary edema (66%)[5]. Study conducted by Munro *et al* concluded cerebral hemorr-hage as the main cause of death[1].

The high perinatal mortality was mostly due to prematurity, which was also supported by other studies conducted in Lahore, Faisalabad, India and Africa[2]. Such neonates are prone to develop bronchopulmonary dysplasia, intra cranial hemorrhage, sepsis and respiratory distress secondary to surfactant deficiency[15]. Long term follow up for these babies is required to look for sequel of prematurity[16-20].

Need for strengthening of intensive care units, trained ICU team for central venous line insertion andfluid monitoring is required in hospitals. Further study and data collection is required to access the barriers to the use of magnesium sulphate in prevention and treatment of Eclampsia. Further study should be conducted regarding perinatal outcomes and follow up to detect long term sequel of pre maturity and birth asphaxialike cerebral palsy[21-25].

CONCLUSION

Eclampsia is a serious and life threatening cause of maternal morbidity and mortality in obstetrics. Magnesium sulphate is a safe, cost effective and time tested drug for prevention and treatment of eclampsia. Early booking and regular antenatal checkups should be encouraged. Prevention of eclampsia still remains a big challenge in developing countries like Pakistan.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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