

Diazepam Versus Magnesium Sulfate ($MgSO_4$) in Treatment of Eclampsia

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SUMMARY

In this study the effect of anticonvulsants on maternal and perinatal morbidity and mortality was evaluated in 20 cases of antenatal eclampsia with gestational age more than 32 weeks with alive fetus during the period November 1994 to Nov. 1995 in the Department of Obst/Gynae, Quaid-i-Azam Medical College Bahawalpur (Bahawal Victoria Hospital Bahawalpur). The results of the study showed that diazepam was an effective anti-convulsant as compared to Magnesium sulfate (20% versus 10%) in respect of maternal mortality and morbidity (50% versus 40%). Diazepam showed poor fetal outcome as compared to $MgSO_4 \cdot 10H_2O$.

The purpose of the study is to discover the best anticonvulsant therapy for treatment of eclampsia.

INTRODUCTION

Eclampsia is a major source of maternal and perinatal morbidity and mortality in Pakistan as well as developed countries². Although the exact etiology of pre-eclampsia, and eclampsia remain enigmatic, trophoblastic tissue is necessary for inciting the pathophysiology. Depending upon when convulsions first appear, eclampsia is designated as antepartum, intrapartum and post partum. Nearly all cases of post partum eclampsia develop in the first 24 hours of delivery. When convulsion persist or develop more than 48 hours, after delivery post partum causes, other than eclampsia should be excluded³. Many treatment modalities are in practice. There is no consensus about the best anti-convulsant therapy for eclampsia¹.

Eclampsia is a multi-system disease and the extent of involvement of various organs is unpredictable. When cause of the disease is unknown, rational treatment is difficult and there is often multiplicity of remedies.

Conflicting opinion exist in the treatment of eclampsia. Historically, diminution of cortical activity by sedation and isolation of the patient has been tried with little effect. The other form of treatments such as, bleeding and purging, bed rest

with heavy sedation, morphine, chloralhydrate, chloroform, veratrum alkaloids, Benzodiazepines, lytic cocktail, magnesium sulfate, rectal ethanol hydralazine therapy, have all been used.

MATERIAL AND METHODS

Twenty cases of antenatal eclampsia, gestational age more than 32 weeks with alive fetus were admitted in emergency. All patients were randomly allocated to have diazepam infusion (10) and $MgSO_4$ (10) regardless of prior therapy. Serious maternal morbidity was defined as reoccurrence of convulsions, cardiopulmonary complications like pneumonia, respiratory depression, DIC, and acute renal failure. The other criteria were reoccurrence of convulsions after 1 hour therapy, diminished renal output and maternal death. The criteria for fetal outcome were, apgar score less than 5 at 1 minute and less than 5 at 5 minute, alive births, early neonatal deaths, needs for tracheal intubation and requiring admission into neonatology with more than 5 days stay in hospital.

Management

All patients were closely monitored with frequent blood pressure, pulse, respiratory rate,

conscious level and urine output. Fifteen were delivered vaginally and five by caesarean section which was performed for other obstetrical reasons. The general characteristics and investigation requested for all patients are summarized in Table 1 and Table 4. Ten patients received 10mg valium intravenously to terminate the fit followed by 40mg in 5% Dextrose water 500ml to keep the patient sedated. The infusion was continued 24 hours after delivery. The other 10 were given 4g of MgSO₄ 10H₂O (8ml of 50% solution of MgSO₄ + 12ml of water) intravenous slowly to terminate the fit, followed by 10 gm of intramuscular MgSO₄ solution into each buttock I/M magnesium sulfate was to prevent further convulsions up to 24 hours after delivery¹.

versus 30%, but in 10% cases they persisted in magnesium sulfate group 1 hour after the therapy. Renal out put (20%) was significantly depressed in MgSO₄ group. There was one maternal death (10%) in diazepam group due to intracranial haemorrhage.

Table 2: Investigations

| | |
|-------|--|
| Blood | Full blood count, platelet count, blood urea and creatinine, uric acid, fibrinogen level and serum electrolytes. |
| Liver | Serum bilirubin, SGOT, SGPT |
| Urine | Complete urine, microscopy, proteinuria on every specimen. |

Table 1: The characteristics of women in both groups diazepam versus magnesium sulfate (n= 10)

| | MgSO ₄ | | Diazepam | |
|---|-------------------|------|----------|-----|
| | No. | % | No. | % |
| Average maternal age | 21 years | | 25 years | |
| Parity | | | | |
| Primigravida | 6 | 60% | 8 | 80% |
| Between 1-3 | 1 | 10% | 2 | 20% |
| Previous diazepam therapy | 6 | 60% | 2 | 20% |
| Previous antenatal care | 2 | 20% | - | - |
| Median time from the start of convulsions to hospital admission | 8 hrs | | 8.5 hrs | |
| Blood pressure | | | | |
| Systolic | 160mmHg | | 170mmHg | |
| Diastolic | 110mmHg | | 115mmHg | |
| Proteinuria +1 | 1 | 10% | 5 | 50% |
| Proteinuria +2 | 1 | 10% | 3 | 30% |
| Gestational age | | | | |
| < 31 weeks | 0 | - | 1 | 10% |
| > 36 weeks | 10 | 100% | 4 | 60% |

Table 3: Maternal outcome is summarized (n= 10)

| | Magnesium sulfate | | Diazepam | |
|---|-------------------|-----|----------|-----|
| | No. | % | No. | % |
| Maternal Morbidity | 4 | 40% | 4 | 50% |
| Pneumonia | 2 | 20% | 2 | 20% |
| Respiratory depression | 2 | 20% | 3 | 30% |
| Coagulopathy | - | - | - | - |
| Acute renal failure | - | - | - | - |
| Recurrence of convulsions | 2 | 20% | 3 | 30% |
| Reoccurrence after 1 hr therapy | 1 | 10% | - | - |
| Diminished renal output less than 500ml in 24 hrs | 2 | 20% | - | - |
| Maternal death | 0 | - | 1 | 10% |

Fetal outcome

This is summarized in Table 4. Significantly fewer infants in MgSO₄ group (10%) had lower apgar score at 1 minute and at 5 minute as compared to diazepam group 50% and 20%. Two still births and one early neonatal deaths occurred in diazepam group due to respiratory anoxia and one early neonatal death in MgSO₄ due to prematurity 20% cases in MgSO₄ group required intubation versus 50% in diazepam group. Hundred percent cases in diazepam group required, hospital admission versus 50% in MgSO₄ group. The results showed more fetal demises in diazepam as compared to MgSO₄ group.

The maternal morbidity in both groups was almost equal, 40% versus 50%, pneumonia 20% versus 20% and respiratory depression 20% versus 30%. None of the patients developed coagulopathy and acute renal failure in both groups.

The convulsions reoccurred in both groups 20%

Table 4: (n = 10)

| | Magnesium sulfate | | Diazepam | |
|--------------------------|-------------------|-----|----------|----|
| | No. | % | No. | % |
| Apgar score | | | | |
| < 5 at 1 minute | 1 | 10 | 5 | 50 |
| < 5 at 5 minutes | 2 | - | 2 | 20 |
| Live birth | 10 | 100 | 8 | 80 |
| Still births | - | - | 2 | 20 |
| Early neonatal deaths | 1 | 10 | 1 | 10 |
| Intubated | 2 | 20 | 5 | 50 |
| Intensive care admission | 2 | 20 | 5 | 50 |
| Length of stay > 5 days | - | - | 2 | 20 |

DISCUSSION

There is no consensus about the choice of best anti-convulsant in eclampsia³. Eclampsia continues to be major source of maternal and perinatal morbidity and mortality¹. The present study shows diazepam to be as good an anticonvulsant as MgSO₄ solution in terms of morbidity and mortality (40% versus 50%). The overall maternal mortality from eclampsia varies from 1% to 20%². The frequency of morbidity in diazepam is estimated to be 52% and with MgSO₄ 29% in the literature³. Convulsions reoccurred in both groups (20% versus 30%) and persisted after one hour in 10% of the cases of MgSO₄ group. Twenty percent reoccurrence rate in MgSO₄ is higher in our study as compared to 10% and 12% in literature^{2,5}. 30% reoccurrence of convulsions, is higher in diazepam group as compared to 2%, 7% and 20% mentioned by various authors^{3,6,7}. This may be due to inadequate level of diazepam in the blood. The other reason being small number of cases in the study. The 10% mortality is almost equal to overall maternal mortality in eclampsia.

The respiratory depression due to diazepam is reported in previous studies but infrequently with MgSO₄ group. Cardiac arrest is a recognized problem with I/V Magnesium sulfate⁷. The dose should not be faster than 1 gram per minute. The maternal plasma level of 4-6meq/L of Magnesium is maintained by intramuscular regimen than intravenous administration⁸. Therapeutic level ranges between 4 to 6meq/L and severe respiratory arrest occurs at level of about 12meq/L⁸. The

treatment of overdose consist of oxygen inhalation and 1 gram calcium gluconate as 10% solution slowly intravenously.

There is no maternal death in MgSO₄ group in present study but 0.4-10%-14.6% has been reported in the literature⁹. The 10% mortality rate in diazepam group is higher than 3.3% reported previously¹. This may be due to heavy sedation and aspiration pneumonia in diazepam group.

The fetal outcome is better in MgSO₄ group versus diazepam group. The overall perinatal mortality rate in eclampsia ranges between 130-300 per 1000 birth. The 20% perinatal mortality rate in diazepam is greater than mentioned in literature. Ten percent early neonatal deaths occurred in both groups but 50% of infants in diazepam group required intubation and they remained hospitalized in neonatology unit for more than 5 days. The results showed higher fetal diseases with diazepam versus MgSO₄ solution. The other fetal side effect with diazepam were, bradycardia, changes in cardiac rhythms, hypotonia, hyperbilirubinemia and respiratory depression⁶.

CONCLUSION

The rational approach in the treatment of eclampsia is the use of combination of anti-hypertensive and anti-convulsant drugs. It is agreed that diazepam should be used for immediate control of fits as it is effective rapidly. It is inexpensive, readily available, easily administered and therefore suitable in outlying clinic before the patient are referred to special obstetric units. Magnesium sulfate therapy requires, frequent serum magnesium levels, close clinical monitoring of the patients. Furthermore MgSO₄ is not easily available in Pakistan.

Eclampsia is still a major problem in maternal medicine but many of its worst effect can be mitigated by early diagnosis. It is difficult to arrive at definite conclusion because of small study size and the fact that most women had already received diazepam before entry into the study. Until convincing clinical research has been achieved, the management of eclampsia includes.

- Immediate control of convulsion with diazepam given by bolus injection.
- The judicious and promote lowering of blood pressure with appropriate anti-hypertensive.

- c. Appropriate fluid and electrolyte therapy.
- d. Early delivery, ultimate mode of treatment wether vaginally or abdominal as indicated.

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