Magnesium Sulfate Versus Diazepam Infusion in Eclampsia

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Abstract: The anticonvulsant has key role in management of eclampsia but the choice is still controversial.

Objectives: To compare the efficacy of magnesium sulfate and diazepam infusion as good anticonvulsant.

Study Design The study was conducted at Obst/Gynae Unit –II, Punjab Medical College, DHQ Civil Hospital, Faisalabad from 1st May, 2007 To 30th December,2007.

Material and Methods: There were total 3506 deliveries in *8 months* among *45 cases* of antenatal eclampsia were selected. The cases of postpartum eclampsia, gestational age less than 28 weeks, and dead fetuses were excluded. 25 patients were allocated $Mgso_4$ and 20 patients treated with Diazepam infusion regardless of prior therapy. The dosage of both was monitored clinically. Morbidity was defined in terms of maternal and fetal measures.

Results: MGSO4 was the better anticonvulsant than diazepam infusion in terms of total morbidity, the value ($P < 0.05$), recurrence of fits (16% versus 30%), maternal deaths (Null versus 5%), respiratory depression (Null versus 10%). Mgso4 was associated with better outcomes in terms of total fetal morbidity (28% versus 90%) and perinatal deaths (4% versus 15%) than diazepam the value ($P < 0.05$). Fewer babies in Mgso4 group had low apgore score at 1 minute (12% versus 25%), at 5 minute (Null l% versus 10%), required less intubations (8% versus 25%) and required less admission in special care unit (4% VS 15%) than diazepam group.

Key Words: Magnesium sulfate (Mgso4), Diazepam infusion, Eclampsia.

Introduction

Only 1:2000 women have an eclamptic convulsion but associated maternal mortality is 2%.[1] By WHO, the world wide approximately 60,000 women dies each year from pre eclampsia, among all maternal death fewer than ½ are associated with eclampsia.[2]

The successful prevention of eclampsia is difficult so it is important to discuss the treatment. Traditionally fits were controlled with different regimen like, lytic cocktail, paraldehyde, but favorites are diazepam infusion, magnesium sulfate and phenyton sodium.[3] The choice is still not clear. The purpose of the study is to compare Mgso4 versus diazepam as good anticonvulsant.

Material and Methods

The study was conducted at Obstetric & Gynaecology Unit-II, Punjab Medical College, DHQ Hospital, a tertiary care hospital in Faisalabad from 1st May 2007 to 30th January 2008. Total 55 patients were admitted with established diagnosis of ante partum eclampsia. 10 cases of postpartum eclampsia, gestational age less than 28 weeks and dead fetus were excluded from the study. 25 patients were given $Mgso_4$ and 20 patients were treated with diazepam infusion regardless of prior therapy. The dose of $Mgso_4$ was 4 grams intravenous slow over 10 minutes followed by 2 grams infusion per hour.[4] The dose was monitored clinically by tendon reflexes, urine out put more than 30 ml per hour and breathing more than 16 per minute. 10 mg diazepam was given to terminate the fit followed by 40 mg in 5% dextrose water slow so that patient remained sedated.[5] Both drugs were continued for at least 24 hours after the delivery of fetus.

The maternal mortality and morbidity was defined as maternal death, recurrence of convulsion, diminished renal out put, respiratory tract infection , pulmonary edema and admission to intensive care unit. The perinatal mortality and morbidity was defined as perinatal death, low apgore score at 1 minute and at 5 minutes, requiring intubations and admission to special unit with length of stay for > 5 days.

The student t test was applied, hypothesis as null that magnesium sublimate better than diazepam infusion.

Results

The results are summarized in Table No. 1 and 2.

As the number of Observed Cases is less than 30, so that "The student t test" was applied. X_1 was 0.36& X_2 was 0.8 for diazepam. The pooled variance was recorded 1.645. The SP value was calculated as 1.2825. The Probability-value was |1.1435| at 5% level 0f significance $\alpha = 0.05$ so $\alpha/2 = 0.025$ as P-value, the critical region in t-distribution was $-2.021 < t < +2.021$ confirming the hypothesis that magnesium sulphate was better than diazepam infusion.

At level of 1% significance, $\alpha = 1\% = 0.01$, the critical region is | 2.423 |. Under 1% level of significance we will accept the above hypothesis, it means that, only 1% are the chances of being magnesium is not better than diazepam.

As the No. of observation is less than 30(N_1&N_2<30) in both products so for effectivestatistical elaboration of outcomes, student t-test was applied. The X_1 was 0.28 for $Mgso_4$ and X_2 was 0.9 for Diazepam infusion. The Pooled Variance (sp) is calculated 1.2095.The value of t is calculated by prescribed formula that is "$t = X_1\text{-}X_2 / (sp)\ (1/N_1 + 1/N_2)$" found to be 1.8793. At 5% level of significance = α =0.05 so

α /2 =0.025 as p- value, the critical region was -2.021 < -1.8793 < +2.021 in t distribution curve so t value falls in acceptance region, supporting null hypothesis that $Mgso_4$ is better than Diazepam in fetal outcomes.

Discussion

Traditionally many remedies were tried in eclampsia to control convulsion like purging, son off regimen, paraldehyde Phenobarbital,[2] but now a days, the popular one are magnesium sulfate and diazepam infusion. Diazepam was favored in the UK. It is cheap, easy available, easy to give, and does not require any monitoring But its popularity as anti convulsant is under question.

In the study, total maternal morbidity was less in Mgso4 group (36% vs. 70%) than Diazepam (P-value < 0.05) with one maternal death in Diazepam as compared to Mgso4 group. She was primigravida, with recurrent convulsions; reached hospital after 48 hours and she had pulmonary edema with severs respiratory depression.

The convulsions recurred in both groups but less in $Mgso_4$ (16% VS 30%) than diazepam. The recurrence rate of 12 %[6], 10%[7] and 5.2%[8] is mentioned in literature in Mgso4 is comparable to our study. The Collaborative eclampsia trial group in 1992 demonstrated a reduction in the risk of recurrent convulsion of between 37 and 79% with Mgso4 as compared to Diazepam and non-significant reduction in maternal mortality.[9] This group established the efficacy of $Mgso_4$ in preventing convulsion following eclampsia.

Table 1: *Maternal Outcomes.*

Maternal Morbidity	$Mgso_4$ (N = 25)	Percentage (%)	Diazepam (N = 20)	Percentage (%)
Recurrence of fits	4	16	6	30
Respiratory depression	0	Nil	2	10
Pneumonia	1	4	3	15
Diminished renal out put Requiring stimulation	4	16	4	20
Maternal death	0	Nil	1	5
Total	9	36 (27.68%)	16	70 (43.6%)

Table 2: *Fetal Outcomes.*

Fetal Morbidity	Mgso4 (N = 25)	Percentage (%)	Diazepam (N = 20)	Percentage (%)
Still Birth	Nil	0	1	5
Early Neonatal death	1	4	2	10
Apgore Score < 5 at 1 minute	3	12	5	25
Apgore Score < 5 at 5 minute	Nil	0	1	10
Intubations	2	8	5	25
Admitted to Nursery	1	4	3	15
Total	7	28	18	90

This is further established by UKOSS study in UK in 2005[10]. The Mgso4 was used in 99% of women in eclampsia as routine after 1992 in UK. The incidence of eclampsia has reduced 4.9% per 10,000 births to 2.7% per 10,000 births, Proportion of women with severe associated morbidity from 35% to 10% Recurrence of convulsion from 41% to 25% in 2005 comparable to our study.

The exact mode of action Of Mgso4 is not known but it has membrane stabilizing and Vasodilator effect byreducing the brain schema [11]. The recurrence rate with Diazepam is as 2%[5], 7%[12], 26.5%[13], and 27.9% [8] almost equal to the study but A little higher due to less no, of cases. The risk of maternal mortality and fetal mortality is increased as number of fits is increased so the control of fits is therefore important in reducing maternal morbidity and mortality.[14] Magpie trial further establishes it that Mgso4 has shown to half the risk of eclampsia if used in severe Pre eclipse as Compared to placebo.[15] There was no significant difference in both groups in terms of other morbidity like respiratory tract infections, renal output But respiratory depression was more with diazepam (10% VS nil). Diazepam crosses the placenta and also causes depression of respiratory center of the fetus .It also causes fetal hypothermia and hyperbilirubinemia by red cell destruction. Yasmeen, Alee et al founded Mgso4 effective in 87.7% of patients for controlling fits.[7]

Eclampsia is major cause of maternal and perinatal mortality and morbidity world Wide casing 15% of all direct maternal deaths in the United Kingdom and 24% of all deaths in India. In non-industrialized countries, it causes almost up to 40% of Prenatal deaths.[16,17]

The perinatal morbidity occurred in both groups but less in magnesium sulphate (p value < .05) including perinatal deaths (4% versus 15%). The perinatal mortality has not changed significantly in Eclampsia being 54/1000 births

in 1992 to 59 /1000 births in 2005 in UK with The use of $Mgso_4$ (UKOOS). The only explained risk factor is prematurity. In study main risk factor was premature birth and respiratory depression by diazepam. The constant rate for perinatal mortality needs further research work in this field. The fetal morbidity was significantly reduced with the use of magnesium, like a few babies has low apgore score, less number of babies required intubations for resuscitation, and admission in special care unit as compared to diazepam infusion.[18]

There are certain limitations of the study. The most of the patients had already some form of therapy before reaching hospital as well as less number of cases in the study. The dose of both drugs were monitored clinically, blood level monitoring was not possible due to non availability .In summary Mgso4 was found to be very effective in terms of maternal motility and morbidity for controlling convulsions. It is suggested that the use of $Mgso_4$ in eclampsia as slandered protocol at national level in obstetric at primary health care. It is further suggested that $Mgso_4$ therapy in severe preeclampsia to reduce the risk of eclampsia.

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