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Short Report:

Should Magnesium Sulphate Prophylaxis be Used in all Cases of Severe Preeclampsia?

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Abstract:
A case control study, undertaken in the department of Obstetrics and Gynecology in a tertiary referral centre, was designed to administer standard dose of magnesium sulphate to 50 randomly selected severely preeclamptic women in labor (Group 1). 48 women who formed the control group did not receive the drug (Group 2). The admission – delivery interval, rate of Cesarean section showed no statistically significant difference. Four patients developed convulsions in Group 1 in contrast to twelve patients in Group 2. Efficacy of magnesium sulphate at preventing eclampsia was calculated as 68%. Mild respiratory depression occurred in two cases and oliguria in eight cases in Group 1. Both the conditions improved on suspending further doses of magnesium sulphate. No patient had post partum haemorrhage in Group 1 although 4% patients had it in Group 2. Neonatal outcome was comparable in both the groups. Hence magnesium sulphate may be regarded as a fairly safe and effective prophylactic agent for eclampsia when used in severe preeclampsia in labor.
Key Words: Preeclampsia; Prophylactic magnesium sulphate

Introduction:
Eclampsia is regarded as one of the most dangerous complications of preeclampsia and accounts for most of the maternal deaths in our country. Since the pathogenesis of eclampsia is not exactly known, the strategies for prevention are limited. Anticonvulsants are given to women with preeclampsia with the belief that they will prevent the onset of eclampsia and so improve the outcome for both mother and baby. Magnesium sulphate is a significantly better drug than either Diazepam or phenytoin for preventing recurrent seizures in eclamptic patients and is now considered as the drug of choice in treating eclampsia.(1) Magnesum sulpate has diverse cardiovascular and neurological effects. It alters calcium metabolism and crosses the placental barrier too. It has also to be kept in mind that even if eclampsia is prevented, it does not mean that other serious complications of preeclampsia can be avoided with this drug.(2) Hence the risk-benefit ratio has to be judged before routine administration of this drug in all women with preeclampsia. It is recommended that individual units determine their own protocols and monitor outcomes.(3)
Objective of the study: To determine the efficacy and safety of magnesium sulphate in preventing the development of eclampsia in the severely preeclamptic patients in labor.

Materials and Methods:
The study was undertaken from March 2009 to February 2010 in the department of Obstetrics and Gynecology of our institution which is a tertiary referral centre catering to four northern districts of West Bengal. The design of the study was an analytical case control type. Patients with severe preeclampsia, with blood pressure above 159/109mm of mercury were taken for the study. 50 patients were randomly selected to receive magnesium sulphate. We used Pritchard's protocol by which a loading dose of 4g was given intravenously followed by intramuscular dose of 5g in each buttock. 5g of intramuscular dose was repeated every four hours upto 24 hours after delivery. 48 women who formed the control group, did not receive this drug. Hypertension was controlled with IV labetalol in either group. Both the study and control group were monitored for the duration of labor, mode of delivery, maternal complications like convulsions, respiratory depression, oliguria, hematuria, postpartum hemorrhage, and fetal outcome was judged by the Apgar score at five minutes of birth and duration of stay at neonatal care unit (NICU).
Statistical analysis: All statistical analyses are done by the SPSS software version 17. Comparison between maternal demographic profiles and maternal and neonatal outcome between the two groups is done by Chi-Square test.
Results:
Table 1 shows that both the study and control groups were comparable as regards their age, gravida, gestational age on admission and duration of hypertension. Table 2 shows there doesn't seem to be any significant prolongation of labor in the study group in comparison to the control group, since the admission delivery interval are similar. 50% (25 out of 50) of wo-

men in Group 1 had a vaginal delivery out of which 20% (10 women) had forceps application. In contrast, in Group 2, out of the 45.2% (22 women) who had vaginal delivery, 4.2% (2 women) needed forceps applications. ($p<0.05$, Chi-Square = 5.66). This difference seems to be significant statistically. The incidence of Cesarean section was similar in both the groups – 50% in Group 1 and 54.2% in Group 2. Indication of operative delivery as labor dystocia, 22.85% in Group 1, which was more than Group 2, at 7.14% is not statistically significant (Chi-Square=2.32,$p>0.05$). Fetal distress occurred equally in both the groups (Chi-Square=0.75, $p>0.05$). Four patients developed convulsions in Group 1 which is significantly lower than in Group2 that had an incidence of convulsion in 12 patients (Chi-Square=5.79,$p<0.05$). Mild respiratory depression occurred in two cases and oliguria in 8 cases in the Group 1. The condition improved in all cases by suspending further doses of magnesium sulphate. The incidence of Apgar score 7-10 between Group1, at 40% and Group 2 at 47.9% is comparable (Chi-Square=o.62, $p>0.05$). Significantly more neonates were having an Apgar score 3-6 in Group 1 than in Group 2, 32% versus 10.4% respectively (Chi-Square=6.78,$p<0.01$).

Table 1: Comparison of socio-demographic and antenatal variables between Group 1 and Group 2.

	Group 1	Group 2	Total	P value
Age group				
15-20	30	29	59	Chi-Square= 0.25 p>0.05
20-25	17	15	32	
>25	3	4	7	
Gravida				
G1	38	40	78	Chi-Square= 0.24 p>0.05
G2	11	8	19	
G3	1	0	1	
Gestational age on admission				
28-36 weeks	20	18	38	Chi-Square= 1.08 p>0.05
37-40 weeks	27	28	55	
>40 weeks	1	0	1	
Duration of hypertension				
<2 weeks	2	3	5	Chi-Square= 3.06 p>0.05
2-4 weeks	30	25	55	
>4 weeks	2	0	2	
Unknown	16	20	36	

Table2: Comparison of the different obstetric outcome between Group 1 and Group 2.

	Group1 (n=50)	Group 2(n=48)	Total	P value
Admission delivery interval (hours)				
1-5	15	17	32	Chi-Square= 4.27 p>0.05
6-10	17	10	27	
11-20	0	2	2	
16-20	5	7	12	
>20	13	12	25	
Mode of delivery				
Spontaneous vaginal	15 (30%)	20 (41%)	35	Chi-Square= 1.45 p>0.05
Forceps application	10 (20%)	2 (4.2%)	12	Chi-Square= 5.66 p<0.05
Cesarean section	25 (50%)	26 (54.2%)	51	Chi-Square= 0.17 p>0.05
Indication of operative delivery (Forceps and Cesarean section)				
Indications	n= 35	n=28	Total	
Uncontrolled hypertension	15 (42.8%)	14(50%)	29	
Uncontrolled convulsion	2 (5.7%)	5 (17.8%)	7	Chi-Square= 2.32 p>0.05
Dystocia	8 (22.8%)	2(7.14%)	10	Chi-Square= 2.88 p>0.05
Fetal distress	10 (28.5%)	7 (25%)	17	Chi-Square= 0.75 p>0.05

Incidence of Apgar score <3 appears to be higher in Group 2 (41.6%) than in Group1 (22.2%) but not significantly (Chi-Square=0.08,$p>0.05$).

Efficacy of magnesium sulphate for preventing the incidence of convulsion [=(Incidence of convulsion among Group 2 - incidence of convulsion in Group 1) × 100/Incidence of convulsion in Group 2)] was calculated to be 68%. [(25-8)×100/25 = 68]

Table 3: Maternal outcome in Group 1 and Group 2

Maternal complications	Group1	Group 2	Total	P value
Convulsion	4 (8%)	12 (25%)	16	Chi-Square= 5.79 p<0.05 (for convulsion)
Oliguria	8 (16%)	5 (10.4%)	13	
Hematuria	3 (6%)	5 (10.4%)	8	
Respiratory depression	2 (4%)	0 (0%)	2	
Blurred vision	2 (4%)	1 (2%)	3	
PPH	0 (0%)	2 (4.1%)	2	
No complications	31	26	57	

Table 4: Neonatal outcome in Group 1 and Group 2

	Group 1 (n=50)	Group 2 (n=48)	Total	P value
Apgar score at five minutes of birth				
7-10	20 (40%)	23 (47.9%)	43	Chi-Square= 0.62 p>0.05
3-6	16 (32%)	5 (10.4%)	21	Chi-Square= 6.78 p<0.01
<3	12 (24%)	20 (41.6%)	32	Chi-Square= 1.77 p>0.05
Still birth	2 (4%)	0 (0%)	2	
Total	50	48	98	
Stay at NICU				
<24 hours	4	5	9	Chi-Square= 0.08 p>0.05
>24 hours	14	15	29	
Total	18	20	38	

Discussion:

Eclampsia remains a complex and partially understood disease and its prophylaxis is the area of greatest controversy. Although magnesium sulphate is a proven anticonvulsant in eclampsia, its role in prophylaxis is less certain.

The American College of Obstetrician and Gynecologists recommends the use of magnesium sulphate in every woman with a diagnosis of preeclampsia during labor and the post partum period.(4) Hence it is the practice in different institutions to administer prophylactic magnesium sulphate to all women with preeclampsia during labor and for 24 hours postpartum.(2,5,6) But many have expressed concern at the potentially lethal side effects exerted by magnesium sulphate at the high doses that are to be attained to prevent convulsions.(2) The four large randomized trials discussed by Sibai BM shows a lower rate of eclampsia in those assigned to magnesium sulphate (0.6% versus 2.0%). Thus the number of women needed to treat to prevent one case of eclampsia is 71.(7) Follow up data from Magpie Trial, where 9996 women were randomized in 33 countries to receive either magnesim sulphate, or placebo, shows a 58% lower risk of eclampsia in the group made to receive magnesium sulphate. The number of women with preeclampsia who needed to be treated to prevent one case of ecclampsia was 324 in high GNI countries but 43 in low GNI countries. Restricting this prophylaxis for severe preeclampsia would lower the expenditure considerably.(8,9) We had a much higher incidence of eclampsia in the severely preeclamptic mothers not receiving magnesium sulphate than the group receiving it (25% versus 8%). Efficacy of magnesium sulphate to control convulsion is found to be 68%. Maternal respiratory depression has been a serious concern.(7,10) Two women receiving the drug had respiratory depression but it was not significant when analyzed statistically. Although PPH has been reported to be associated with prophylactic magnesium sulphate use (11), we had no pa-

tient with PPH although 4% in the control group. Magnesium sulphate did not affect the outcome of labor like admission delivery intervals and rate of Cesarean section. This conforms with some of the previous studies.(11,12) While one study reports a high rate of Cesarean section (68.5%) done mostly due to fetal distress (38.6%) (13), we had a Cesarean delivery rate of 50% in the group receiving magnesium sulphate, mostly done for uncontrolled hypertension (42.8%) and fetal distress (28.5%). But the rate in the control group was similar with no statistically significant difference. Since magnesium sulphate crosses the placental barrier, there has been concern about its safety for the neonates. Some are of the opinion that the high cumulative doses of magnesium sulphate may be associated with infant mortality.(14) Even Sibai BM states that prophylactic magnesium sulphate has no significant benefit in perinatal outcome.(7) The overall neonatal outcome was better in our study group as regards the Apgar scores and duration of stay at NICU with only two still births (4%). This is in accordance to some previous studies.(8,11)

The Magpie Trial showed no substantitive harmful effects on babies born to mothers on prophylactic magnesium sulphate in the short term. Follow up study done on the same subjects has further proved no death or neurosensory disability at the age of 18 months for such babies.(15)

Conclusion:

Magnesium sulphate is a fairly safe and effective prophylactic agent for eclampsia when used during labor and 24 hours postpartum in women with severe preeclampsia. At the same time it should be accepted that even when given to women with the highest risk of eclampsia, it fails to prevent the onset of convulsion in all of them. Further studies are needed till we find the perfect antidote to this dreadful obstetric condition.

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