ORIGINAL ARTICLE

Efficacy of Magnesium Sulphate Versus Phenytoin in Seizure Control and Prophylaxsis in Patients of Eclampsia and Severe Pre-eclampsia

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Abstract

This randomized controlled prospective study was conducted on 100 patients admitted in various units of Lalla Ded Hospital Govt. Medical college Srinagar Kashmir, India during period 2004-06. Among these patients 50 had eclampsia (Group -I) and 50 had severe preeclampsia (Group-II). The patients in each group were then randomly divided into two subgroupsA and B of equal numbers. Subgroup-A was managed with magnesium sulphate and subgroup B was managed with phenytoin. The efficacy in seizure prevention and control of drug regimens used in each subgroup was then compared.Among eclamptic patients treated with magnesium sulphate, there was no recurrence of convulsions, however among those treated with phenytoin, 6 patients (24%) had recurrence of convulsions out of which one had >3 convulsions while others had 1-3 convulsions. The difference in seizure recurrence rate in the two subgroups was found to be statistically significant (p= 0.033). Among severe preeclamptic patients managed with phenytoin, two patients progressed to eclampsia, where as no preeclamptic patient allocated magnesium sulphate progressed to eclampsia; the difference between two subgroups being statistically non significant.

Key Words

Eclampsia, Preeclampsia, Magnesium, Phenytoin

Introduction

Hypertensive disorders complicate 5-10% of all pregnancies, among which preeclampsia and eclampsia are important causes of maternal morbidity and mortality (1). Preeclampsia complicates 5-7%2 of all pregnancies out of which 3.3% develop severe preeclampsia (2) and <1% land into eclampsia (3) which is second most common cause of maternal and perinatal morbidity in underprivileged population (4). In eclampsia, maternal mortality is 10% and fetal mortality is 20-30% (5) .

Various therapeutic modalities have been used over past years in search of an ideal agent for treatment of preeclampsia and eclampsia. Various drugs like paraldehyde (1882), barbital (1903), magnesium sulphate(1906), phenobarbital(1912),phenytoin(1938), intravenous sodium thiopental(1950), lytic cocktail (chlorpromazine, promethazine,pethidine)(1961), diazepam(1968), etc. have been tried but choice remained controversial (6).

Magnesium Sulphate (MgSO4. 7H2O. USP) was first used intrathecally in1906 by Horn to prevent eclamptic seizures (6). In 1990 Sabai in a review of world literature concluded that magnesium sulphate is drug of choice to control eclamptic convulsions in North America and its efficacy and safety in the treatment of preeclampsia are well documented and evidence in literature indicates that it is the ideal anticonvulsant (7). It has advantage of being non sedative, has rapid onset of action, and has easily available antidote (calcium gluconate) (8). Therapeutic

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level of magnesium sulphate is 4-7 meq/l. Phenytoin was first synthesized in 1908 by Biltz, and it was first used as anticonvulsant in 1938.It is also non sedative and has an established anticonvulsant activity. Therapeutic serum levels are 40-100micromol/l (9). The aim of this study was to compare the efficacy of magnesium sulphate and phenytoin in control of seizures in eclampsia and seizure prophylaxis in severe preeclampsia.

Materials and Method

After approval from ethics committee this randomized controlled prospective study was conducted on 100 patients, among which 50 had eclampsia (Group -I) and 50 had severe preeclampsia (Group-II). The patients in each group were than randomly subdivided into subgroups A and B of 25 patients each.

Inclusion Criteria

Patients with diagnosis of eclampsia or severe preeclampsia regardless of age ,parity ,gestational age ,singletion or multiple pregnancy, whether delivered or undelivered .

Exclusion Criteria

1. Hypersensitivity to magnesium sulphate or phenytoin.
2. Hepatic coma with a risk of renal failure.
3. Myasthenia gravis.
4. Convulsions due to other causes like epilepsy, meningitis, intracranial space occupying lesions etc.
5. Significant heart disease.

All of them were managed by standard protocol of management of eclampsia and severe preeclampsia, except for the use of anti convulsant drug .

Subgroup A was managed with magnesium sulphate. Subgroup B was managed with phenytoin. The efficacy in terms of seizure control of drug regimens used in each group was then compared. Subgroup A patients were given magnesium sulphate as anticonvulsant. For eclampsia(IA) loading dose 4 gms of 20% magnesium sulphate was administered in 200ml of saline intravenously over 20-30 minutes followed by 10gms of 50% magnesium sulpahte given intramuscularly half in upper outer quadrant of each buttock by 3 inch long 20 gauge needle. To decrease local discomfort, 1ml of 1% Lidocaine was added to magnesium sulphate just before giving intramuscular injection. Maintenance dose of 5gms of 50% magnesium sulphate intramuscularly was given every 4 hourly after ensuring that:

- *Patellar reflex was present. (first sign of toxicity)*
- *Urine output was >100ml in past 4 hours or >25ml*
- *Respiratory rate was>14 per minute.*

Therapy was continued for 24 hours post partum or after last convulsion whichever was later. If convulsion recurred within 20 minutes, no additional treatment was given; if recurred after 20 minutes, additional 2-4 gms of 20% magnesium sulphate was given intravenously over 5 minute. If even then seizures recurred, short acting barbiturate like thiopental sodium 250mg was supposed to be given intravenously over 3 minutes (however, this was not required in any of the patients).

For severe preeclampsia patients (IIA) drug protocol was same as in eclampsia.Therapy was continued till premonitory symptoms subsided or 24 hours postpartum. Patients were monitored clinically by recording pulse and BP every 15 minutes; recording respiratory rate , conscious level , urine output and reflexes hourly.

Subgroup-B patients were given Phenytoin. For eclamptic patients(IB)loading dose of 1000mg of phenytoin in 200 ml of normal saline (15-25mg/kg body wt) was given intravenously slowly over 20 minutes (at infusion rate not more than 50 mg per minute) .Maintenance dose of 100mg Intravenously was given 6 hourly.Therapy was continued 24 hours post partum or last convulsion whichever was later.For severe preeclampsia(IIB) loading dose of 1000mg of phenytoin in 200ml of normal saline was given intravenously over 1 hour infusion.Maintenance dose of 500mg of phenytoin was given orally 10 hours later. Then oral phenytoin was continued as necessary for 24 hours postpartum or till premonitory symptoms subsided and then tapered off. Patients were monitored clinically by monitoring pulse ,BP every 15 minutes and conscious level hourly. The two subgroups were than compared with respect to seizure activity.

Statistical Analysis

The statistical analysis of the data was done by using statistic t-test, Chi-squire test and Fisher's exact test. The tests were referred to p-values for their significance. The analysis of the data was done by using statistical

Table-I: Distribution of Patients

Variable	Group –I			Group –II		
	IA N=25	I B N= 25	P value	II A N= 25	II BN=25	P Value
1. Age (yrs.) mean±SD	28.98±3.58	29.04±3.72	0.942	29.16±3.42	29.36±3.20	0.830
2. Rural patients population	20 (80)	23 (92)		16 (64)	10 (40)	
Urban patients population	5(20)	2 (8)	0.209	9 (36)	15 (60)	0.089
3.Socio- economic status						
Upper class	0(0)	0(0)		0(0)	0(0)	
Middle class	6(24)	2(8)	0.123	22(88)	18(72)	0.145
Lower class	19(76)	23(98)		3(12)	7(28)	
4.. Antenatal checkups						
Booked pts.	2(8)	0(0)	0.245	22(88)	20(80)	0.351
Unbooked pts.	23(92)	25(100)		3(12)	5(20)	
5.Period of amenorrhea						
>37 Weeks	14(56)	14(56)		20(80)	18(72)	
<37 Weeks.	6(24)	8(32)	0.675	5(20)	7(28)	0.371
Puerperium	5(20)	3(12)		0(0)	0(0)	
6.Parity						
P0	14(56)	13(52)		14(56)	14(56)	
P1	3(12)	3(12)	0.931	5(20)	6(24)	0.931
> P2	8(37)	9(36)		6(24)	5(20)	

Figures in parenthesis indicate percentage, N-Number of patients

Table-II: Distribution of Patients According to Seizure Activity Before Treatment in Group I

Number of seizures	Group I	
	IA	IB
	No. of Patients (%)	No. of Patients (%)
0-1	9(36)	5(20)
2-5	13(52)	15(60)
>5	3(12)	5 (200

P value - 0.409 Chi Square –1.79 NS (notsignificant)

Amenorrhea and parity wise distribution (Table I). Distribution of patients according to seizure activity before treatment in group I was also statistically non significant(Table II).In eclamptic patients, there was no recurrence of seizures after starting magnesium sulphate in subgroup IA. However, in subgroup IB (phenytoin group), 6 (24%) patients had recurrence of seizures after starting phenytoin out of which one patient had >3 convulsions while others had 1-3 convulsions. The difference in seizure recurrence ratio in two subgroups

Table- III: Distribution of Patients According to Seizure Activity After Treatment

Number of seizures	Group I		Group II	
	IA	IB	IA	IB
	No. of Patients (%)	No. of Patients(%)	No. of Patients (%)	No. of Patients(%)
0-1	25(100)	19(76)	25(100)	23(92)
2-5	0(0)	5(20)	0(0)	2(8)
>5	0(0)	1(4)	0(0)	0 (0)

P value - 0.033 Significant

P value - 0.245 Non Significant

package for social sciences for windows (SPSS, ver 10) by Chicago USA. P value of <0.05 was considered significant.

Results

Statistically, the two subgroups in both the groups I and II were similar in age, urban rural distribution, socio-economic status, antenatal checkups, period of

was found to be statistically significant (p-0.033) (Table -III).In severe preeclamptic group , no patient on magnesium sulphate prophylaxis (subgroup-IIA) progressed to eclampsia whereas 2 patients on phenytoin prophylaxis(subgroup-IIB) landed up in eclampsia out of which one had antepartum (2 convulsions) and other had intrapartum (one convulsion) eclampsia. However, the

difference in seizure activity after treatment in two subgroups was not statistically significant (p-0.245) (Table-III) .

Discussion

The most important step in the management of preeclampsia and eclampsia is preventing the occurrence of first convulsion (i.e. progression of preeclampsia to eclampsia and preventing the recurrence of convulsions in eclampsia). A variety of anticonvulsants are available but the most commonly used ones today are magnesium sulphate and phenytoin. The magnesium sulphate regimen was standardized at Parkland Hospital by Pritchard et al 10 and is widely used in America. Phenytoin regimen is popular in Britain but is now being replaced by magnesium sulphate. Various studies were conducted to compare the seizure prevention and control in the patients of preeclampsia eclampsia managed with magnesium sulphate and phenytoin. In our study, as far as seizure frequency in eclampsia group is concerned, 56% of patients had 2-5 convulsions before starting therapeutic intervention (Table-II). Among eclamptic patients treated with magnesium sulphate, there was no recurrence of convulsions, however, among those treated with phenytoin, 6 patients (24%) had recurrence of convulsions out of which one had >3 convulsions while others had 1-3 convulsions. Out of these six patients, two were shifted to magnesium sulphate because of recurrent seizures leading to deteriorating maternal and fetal condition and it was found that after switching over to magnesium sulphate, there was no recurrence of convulsions . The difference in seizure recurrence ratio in the two subgroups was found to be statistically significant (p-0.033). In preeclamptic group, two patients in subgroup allocated phenytoin progressed to eclampsia (One had antepartum eclampsia with two convulsions and other had intrapartum eclampsia with one convulsion), whereas no preeclamptic patient allocated magnesium sulphate progressed to eclampsia. The difference between two subgroups being statistically non-significant. These observations are similar to those observed by Pritchard *et al* (10) where no patient with preeclampsia convulsed and no patient with eclampsia had further convulsion after treatment initiation with magnesium sulphate. Dommisse *et al* (11) observed that none of 11 pre eclamptic patients on magnesium sulphate had recurrent seizures while 4 of 11 pre eclamptic patients on phenytoin had recurrent seizures and were shifted to magnesium sulphate regimen. Lucas *et al* (12) observed that 10 of 1089 preeclamptic women randomly assigned to the phenytoin regimen had eclamptic convulsions as compared with none of 1049 women randomly assigned to magnesium sulphate (p-0.0004). Patrich *et al* (13) also observed that magnesium sulphate compared to phenytoin is a superior drug in preventing the recurrence of seizures in eclampsia and in seizure prophylaxis in preeclampsia. In study conducted by Ascorelli *et al* (1), no preeclamptic patient progressed to eclampsia after treatment with magnesium sulphate. Sawhney *et al* (14), demonstrated recurrence of seizures in 10 out of 25 eclamptic patients (40%) treated with phenytoin and in 2 out of 25 eclamptic patients (8%) treated with magnesium sulphate, advocating better efficacyof magnesium sulphate as anticonvulsant.Further studies conducted by Manyemba *et al* (15), Sibai *et al* (16) and Duley *et al* (17) confirm the efficacy of magnesium sulphate in reduction of seizures in women with eclampsia and severe preeclampsia.In a review by Druzin *et al* (l8) evidence suggested that treatment of severe hypertension, seizure prophylaxis with magnesium sulphate and management by experienced healthcare professionals will improve maternal , fetal and neonatal outcomes.Omu *et al* (19) evaluated the use of magnesium sulphate therapy in women with severe preeclampsia and concluded that magnesium sulphate was effective in preventing recurrence of eclamptic fits . As each eclamptic seizure results in significant cerebral anoxia and brain damage, magnesium sulphate with low seizure occurrence and low seizure recurrence is deemed to be a better anticonvulsant than phenytoin in severe preeclampsia and eclampsia and our study corroborates with the evidence.

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