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Research Article

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Effect of magnesium sulphate versus phenytoin on the hospital length of stay of patients of eclampsia and severe preeclampsia

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ABSTRACT

Among the hypertensive disorders preeclampsia and eclampsia are important causes of mortality and morbidity. Magnesium sulphate is the anticonvulsant of choice for treating eclampsia; more effective than diazepam, phenytoin, or lytic cocktail. Although it is a low cost effective treatment, magnesium sulphate is not available in all low and middle income countries; scaling up its use for eclampsia and severe preeclampsia will contribute to achieving the Millennium Development Goals. Duration of hospital stay is one of the main indicators of the economic impact of any disease process .In the present study we studied the impact of two different modalities of treatments that is magnesium sulphate vs phenytoin for the management of eclampsia and severe preeclampsia(for control of seizures) on the hospital length of stay of the these patients. In our study there was a significant difference in the hospital length of stay in the subgroup treated with magnesium sulphate in comparison to subgroup treated with phenytoin for the control of seizures in eclampsia (p-0.006) and severe preeclampsia(p-0.001).

INTRODUCTION

Hypertensive disorders complicates 5-10% [1] of all pregnancies and form one of the deadly triads,along with haemorrhage and infection , that results in much of morbidity and mortality related to pregnancy.Among the hypertensive disorders preeclampsia and eclampsia are important causes of mortality and morbidity[1].Preeclampsia complicates 5-7% [2] of all pregnancies out of which 3.3% develop severe preeclampsia [3] and <1% land into eclampsia [2] which is the 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].

Over half a million women die each year from pregnancy related causes, 99% in low and middle income countries. In many low income countries, complications of pregnancy and childbirth are the leading cause of death amongst women of reproductive years. The Millennium Development Goals have placed maternal health at the core of the struggle against poverty and inequality, as a matter of human rights. Preeclampsia can lead to problems in the liver, kidneys, brain and the clotting system. Risks for the baby include poor growth and prematurity. Although outcome is often good, preeclampsia can be devastating and life threatening. Overall, 10% to 15% of direct maternal deaths are associated with preeclampsia and eclampsia. Where maternal mortality is high, most of deaths are attributable to eclampsia, rather than preeclampsia. In low and middle income countries many public hospitals have limited access to neonatal intensive care, and so the mortality and morbidity is likely to be considerably higher than in settings where such facilities are available. The only interventions shown to prevent preeclampsia are antiplatelet agents, primarily low dose aspirin, and calcium supplementation. Treatment is largely symptomatic. Antihypertensive drugs are mandatory for very high blood pressure. Plasma volume expansion, corticosteroids and antioxidant agents have been suggested for severe preeclampsia, but trials to date have not shown benefit. Optimal timing for delivery of women with severe preeclampsia before 32 to 34 weeks' gestation remains a dilemma. Magnesium sulphate can prevent and control eclamptic seizures. For preeclampsia, it more than halves the risk of eclampsia (number needed

to treat 100, 95% confidence interval 50 to 100) and probably reduces the risk of maternal death. A quarter of women have side effects, primarily flushing. With clinical monitoring serious adverse effects are rare. Magnesium sulphate is the anticonvulsant of choice for treating eclampsia; more effective than diazepam, phenytoin, or lytic cocktail. Although it is a low cost effective treatment, magnesium sulphate is not available in all low and middle income countries; scaling up its use for eclampsia and severe preeclampsia will contribute to achieving the Millennium Development Goals[6].Six trials (897 women) have compared magnesium sulphate with phenytoin[7]. Magnesium sulphate was associated with a 70% reduction in the relative risk of recurrent convulsions, compared to phenytoin (RR 0.31, 95% CI 0.20–0.47) (Fig. 5). On average, for every eight women treated with magnesium sulphate rather than phenytoin, one recurrence of convulsions will be prevented (95% CI 6–13 women). The trend in maternal mortality also favoured magnesium sulphate, but the difference did not achieve statistical significance (RR 0.50,95% CI 0.24–1.05). In addition, the use of magnesium sulphate, rather than phenytoin, was associated with a reduction in the risk of pneumonia (RR 0.44, 95% CI 0.24–0.79), the need for ventilation (RR 0.66, 95% CI 0.49–0.90) and admission to an intensive care unit (RR 0.67,95% CI 0.50–0.89)[8].

Duration of hospital stay is one of the main indicators of the economic impact of any disease process .In the present study we studied the impact of two different modalities of treatments that is magnesium sulphate vs phenytoin for the management of eclampsia and severe preeclampsia on the hospital length of stay of the these patients.

EXPERIMENTAL SECTION

This prospective randomized double blind study was conducted on 100 patients admitted in various units of Lalla Ded Hospital attached to Government Medical college Srinagar Kashmir India.Among these 50 patients had eclampsia (Group I) and 50 had severe preeclampsia (Group II).The patients in each group were than randomly subdivided into subgroup A and B of 25 patients each. Written informed consent and approval from hospital ethics committee was taken.

All the patients were managed by standard protocol of management of eclampsia and severe preeclampsia, except for the use of anticonvulsant drug, as follows:-

Prevention or control of convulsions
Control of blood pressure
Decision for termination of pregnancy
Maintaining the fluid balance
Subgroup A-was managed with magnesium sulphate
Subgroup B-was managed with phenytoin.
The impact on the hospital length of stay of the two drug regimens was then compared.

Inclusion criteria in the study were, all patients with the diagnosis of
1.Eclampsia
2.Severe preeclampsia regardless of age,parity,gestational age, singleton or multiple pregnancy, whether she had delivered or not, whether any medication had been given before trial entry.
Exclusion criteria were
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.

Subgroup A patients were given magnesium sulphate as anticonvulsant.Following protocol for eclampsia was followed:
Loading Dose – 4gms of 20 % of magnesium sulphate (prepared by mixing 8 ml of 50 % magnesium sulphate with 12 ml of Distilled water) was administered in 200 ml of saline intravenously over 20 – 30 minutes followed by 10 gms of 50 % magnesium sulphate given intramuscularly half in upper outer quadrant of each buttock by 3 inch long 20 gauge needle. To decrease the local discomfort, 1 ml of 1 % xylocaine was added to magnesium sulphate just before giving intramuscular injection.

Maintenance dose- 5 gms of 50 % magnesium sulphate intramuscularly was given every 4 hourly after ensuring that patellar reflex was present, urine output was > 100 ml in past 4 hours or > 25 ml per hour, respiratory rate was > 14 per minute. Therapy was continued for 24 hours post partum or after last convulsion whichever was later.

For recurrent convulsions-If convulsions occurred within 20 minutes,no treatment was given:if recurred after 20 minutes, additional 2-4 gms of 20 % magnesium sulphate was given intravenously over 5 minutes.

Following protocol for severe preeclampsia was followed:Loading dose and maintenance dose same as in eclampsia.Therapy was continued till premonitory symptoms subsided or 24 hours postpartum.

Subgroup A patients were monitored clinically by recording pulse and blood pressure every 15 minutes ; recording respiratory rate,conscious level, urine output and reflexes hourly. In case of toxicity , 10 ml of 10 % calcium gluconate was supposed to be given intravenously over 3-5 minutes.

Subgroup – B patients were given phenytoin.Phenytoin is available as 2 ml ampoule containing 50 mg of phenytoin per ml.Following protocol for eclampsia was followed:

Loading dose – 1000 mg of phenytoin in 200 ml of normal saline (15-25 mg per kg of body weight) was given intravenously slowly over 20 minutes.

Maintenance dose – 100 mg intravenously was given 6 hourly.Therapy was continued 24 hours post partum last convulsion whichever was later.

Following protocol for severe preeclampsia was followed:

Loading dose – 1000 mg of phenytoin in 200 ml of normal saline was given intravenously over 1 hour infusion.

Maintenance dose – 500 mg of sustained release capsule 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.

Subgroup B patients were monitored clinically by recording vital signs every 15 minutes and hourly neurological assessment.

RESULTS

The present study is based on the statistical analysis of data by using statistic t test.Chi square test and Fischer's exact test. The tests were referred to p values for significance .The analysis of data was done by using Statistical Package for Social Sciences for windows (SPSS Ver 10) by Chicago , USA.p value of < 0.05 was considered significant. The following results were obtained:-

In the two subgroups of both the groups I and II ,difference in the age wise distribution was not statistically significant as depicted in the table no. 1

The difference in the distribution of the patients according to their residential area(rural vs urban)in two subgroups was not statistically significant as depicted in the table no. 2.

Majority of patients in both subgroups of group I were unbooked (IA-92%,IB-100%).The difference in the two subgroups was not statistically significant (p-0.254).In group II , the majority of patients were booked in both subgroups(II A-88%,II B -80 %).The difference in two subgroups was not statistically significant (p 0.351).(Table 3).

The mean duration of hospital stay in subgroup I A was 4.28±2.11 days and that in subgroup I B was 5.32±2.10 days.Majority (68%)of patients in subgroup IA had less than 4 days duration,while majority (72%) in subgroup IB had hospital stay of 4-8 days duration.The difference in two subgroups was statistically significant (p-0.006).In group II ,mean duration of hospital stay in subgroup II A was 5.16±5 days and that in subgroup II B was 6.88±3.15 days.Majority (72%) of patients in subgroup II A had hospital stay less than 4 days duration while majority (56%) of patients in subgroup II B hospital stay of 4-8 days duration.The difference in two subgroups was statistically significant (p 0.001).(Table 4).

DISCUSSION

Duration of hospital length of stay in eclampsia and severe preeclampsia indicates the morbidity associated with this disease and has a direct implication on the economic impact of this disease.In our study there was a significant difference in the hospital length of stay in the subgroup treated with magnesium sulphate in comparison to subgroup

treated with phenytoin for the control of seizures as depicted in table 4.Henceforth the magnesium sulphate as a treatment modality has direct impact on the economic burden of eclampsia and severe preeclampsia. Although it is a low cost effective treatment, magnesium sulphate is not available in all low and middle income countries; scaling up its use for eclampsia and severe preeclampsia will contribute to achieving the Millennium Development Goals[6].In October 1998 ,Marian H Ascarelli et al[1] conducted a study on 168 postpartum preeclamptic patients to investigate the safety of treating preeclampsia with magnesium sulphate with clinical determinant used for drug discontinuation.They showed that patients with mild preeclampsia required significantly less magnesium sulphate than with those with severe preeclampsia or HELLP syndrome,with this protocol there was no eclampsia and recovery room time was reduced by 50%.

With well guarded magnesium sulphate therapy ,the incidence of intrapartum and post partum complications and hence morbidity is less.This correlates with the reduced hospital stay among the eclamptic and severe preeclamptic subgroups allocated magnesium sulphate.This corresponds with the observations of Marian H Ascaorelli et al[1].

The advantage of magnesium sulphate over phenytoin in reducing hospital stay as revealed by this study provides the obstetrician with cost effective, safe and better anticonvulsant for preeclamptic – eclamptic patients.

Table 1

Group	subgroup	Age Mean±SD(years)	P value	Remarks
I	IA IB	28.98±3.58 29.04±3.72	0.942	Not significant
II	IIA IIB	29.16±3.42 29.36±3.20	0.830	Not significant

Table 2

Group	Subgroup	Rural Patients(%)	Urban Patients(%)	P value	Remarks
I	IA IB	80 92	20 8	0.209	Not significant
II	IIA IIB	64 40	36 60	0.089	Not significant

Table 3

Group	Subgroup	Booked cases(%)	Unbooked Cases(%)	P value	Remarks
I	IA IB	8 0	92 100	0.254	Not significant
II	IIA IIB	88 80	12 20	0.351	Not significant

Table 4

Group	Subgroup	No.of patients with hospital stay<4 Days(%)	No.of patients with hospital stay 4-8 Days(%)	No.of patients with hospital stay>8 Days(%)	P value	Remarks
I	IA IB	68 24	32 72	0 4	0.006	Significant
II	IIA IIB	72 20	12 56	16 24	0.001	Significant

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