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A COMPARATIVE STUDY OF LOW DOSE MGSO4 VS STANDARD PRITCHARD REGIMEN IN INDIAN SCENARIO.

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KEYWORDS :

INTRODUCTION:
Hypertensive disorders complicate 5 to 10 % of all pregnancies, that contribute greatly to maternal morbidity and mortality.

As per ACOG, hypertension in pregnancy is defined as a diastolic blood pressure of 90 mmHg or higher or a systolic blood pressure level of 140 mmHg or higher, after 20 weeks of gestation in a woman with previously normal blood pressure. Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system. It is PIH associated with proteinuria, greater than 0.3 g/L in a 24-hour urine collection or 1+ by qualitative urine examination, after 20 weeks of gestation. Eclampsia is pre-eclampsia complicated by generalized tonic-clonic convulsions.

In 1955, Dr. J. A. Pritchard introduced Magnesium Sulphate for control of convulsions in eclampsia and is now used worldwide.

Pritchard's Regime:
-Loading dose: 4 g (20% solution) IV over 3–5 minute followed by 10g (50%), deep IM 5 g in each buttock.
-Maintenance dose: 5 g (50%) IM 4 hourly in alternate buttock for 24 hours after delivery or last episode of convulsion.

Mechanism of Action of MgSO4:
-It acts as a membrane stabilizer and a neuroprotector.
-It reduces motor endplate sensitivity to acetylcholine.
-Magnesium also blocks neuronal calcium influx.
-It induces cerebral vasodilatation, dilates uterine arteries, increases production of endothelial prostacyclin and inhibits platelet activation.

Aim:
The study was conducted from April 2016 - April 2017 with an aim:
1. To study the effectiveness of a lower dose of MgSO4 regime (Half of Pritchard's regime) & to compare it with Pritchard's regime in management of patients with eclampsia.
2. To assess the magnesium related toxicity
3. To analyze the maternal outcome
4. To validate the efficacy of low dose regime.

Considering a smaller built & a lower BMI of Indian women, several studies have been published communicating that low dose MgSO4 regime have been as effective as the standard higher dose Pritchard's regime.

MATERIAL AND METHODS:
It was a Prospective Randomized study conducted, A total of 50 patients with an informed consent were randomized & divided in two groups.

Group A:
25 patients who would be managed by a low dose regime that is half of Pritchard's regime.

-Loading dose: 2 g (20% solution) IV over 3–5 minute followed by 5 g (50%), deep IM 2.5 g in each buttock.

-Maintenance dose: 2.5 g (50%) IM 4 hourly in alternate buttock for 24 hours after delivery or last episode of convulsion.

Group B:
25 patients who would be managed by the standard high dose Pritchard's regime.

Inclusion Criteria:
Pregnant patients presenting after 20 weeks of gestation with:
1. h/o convulsions and without a h/o any seizure disorder in the past.
2. Patients who have not received any anticonvulsant treatment before admission.
3. BP > 140/90mmHg.
4. Proteinuria greater than 1+ by qualitative urine examination.

Exclusion Criteria:
Cases which are presenting with serious complications of eclampsia:
1) Renal Failure
2) Pulmonary Oedema With Respiratory Failure
3) Cerebrovascular Accident
4) HELLP syndrome
5) DIC
Patients not consenting to participate in the study.

RESULT:
As our setup is a major referral center, roughly 80% of the cases were referred cases.

The low dose regime showed a success of 100%. There was 1 failure by Pritchard's regime in spite of a repeat dose. The patient was diagnosed with liver capsule rupture & haemorrhage, which eventually led to a mortality (Post mortem findings).

Patients managed with low dose regime had a better general condition throughout the course of the treatment, had lesser complain of pain at the injection site and were ambulatory earlier. Also the total cost incurred by the patient was reduced.

The low dose regime was as effective as the standard Pritchard's regime with even lesser chances of toxicity.

Table 1: Maternal Age As A Risk Factor

Age	Low dose	Pritchard's
<25 (76%)	18 (72%)	20 (80%)
>25 (24%)	7 (28%)	5 (20%)

Almost two third of cases (76%) were less than 25years of age.

Table 2: Parity Of Current Pregnancy As A Risk Factor

Parity	Low dose	Pritchard's
Primi (74%)	19 (76%)	18 (72%)
Multi (26%)	6 (24%)	7 (28%)

Out of total 50 patients, 74% were Primigravida and 26% multipara.

Table 3: Gestational Age As A Risk Factor

Gestational age	Low dose	Pritchard's
>37 (26%)	6 (24%)	7 (28%)
28-37 (60%)	16 (64%)	14 (56%)
<28 (14%)	3 (12%)	4 (16%)

Most of the cases (70%)occurred between gestation age of 28-37 weeks.

Table 4: Booking Status As A Risk Factor

Booking status	Low dose	Pritchard's
Booked (32%)	7 (28%)	9 (36%)
Unbooked (68%)	18 (72%)	16 (64%)

Out of 50 cases, 68% were unbooked.

Table 5: Incidence As Per The Delivery Status Of The Mother:

Period when eclampsia occurred	Low dose	Pritchard's
ANC (86%)	22 (88%)	21 (84%)
PNC (14%)	3 (12%)	4 (16%)

Incidence of eclampsia was 86% in Antenatal period and 14% in postpartum

Table 6: Distribution Of Perinatal Outcome

Perinatal outcome	Low dose	Pritchard's
Live birth (90%)	22 (88%)	23 (92%)
Still birth/IUFD (10%)	3 (12%)	2 (8%)

Out of the 50 eclamptic patients, 90% were associated with good perinatal outcome (Live birth)

Final Results :

observation	Low dose	Pritchard's
Control of convulsion	25(100%)	24(96%)
Need for repeat dose	3(12%)	2(8%)
Failure of regime	0(0%)	1(4%)
No. of ampoules used	22	44
Cost of MgSO4	Rs.242	Rs.484

Control of convulsion and need for repeat dosing was approximately similar in both the groups. Failure of regime was seen in 1 patient given high dose Mgso4 (occurred due to liver capsule rupture).

Significant difference was seen in cost of treatment as number of ampoules used in low dose regimen was half of that used in high dose..

Distribution Of Dose Related Toxicity :

Toxicity	Low dose	Pritchard's
Loss of knee jerk	0(0%)	0(0%)
Decrease in RR	0(0%)	0(0%)
Decrease in U/O	0(0%)	0(0%)
Toxicity	0(0%)	0(0%)

No difference in Mgso4 related toxicity was seen in both the groups.

DISCUSSION:

Prevention of further fits in eclampsia is associated with a reduction in adverse outcomes (1). Magnesium is an ideal drug, with rapid onset of action, a non-sedative effect on mother and baby, a fairly wide safety margin and a readily available antidote in the form of calcium gluconate (2, 3).

The mechanism of action of magnesium sulphate is uncertain, but there is evidence from computed tomography and magnetic resonance angiographic studies implicating cerebral vasospasm and ischemia in the genesis of eclampsia (4-6). Magnesium seems to reverse and ameliorate the effects of cerebral ischemia (7). There may also be a moderate inhibitory effect on cortical discharge (8), with magnesium antagonizing the excitatory glutamate N-methyl-d aspartate receptor (9). Falling serum calcium levels following the administration of intravenous magnesium sulphate inhibit acetylcholine release at the motor end plate. The degree of inhibition is directly related and inversely proportional to the serum calcium level (10, 11). Magnesium also increases production of the endothelial vasodilator prostacyclin (12), inhibits platelet activation (13), and protects endothelial cells from injury mediated by free radicals (14). There is also evidence that magnesium dilates human uterine arteries (15).

Pritchard et al (16) in 1984 suggested that the dose of magnesium sulphate should be limited in women who are known to be or appear to be small. Women in India, especially from rural areas or from low socioeconomic strata tend to have smaller weights. Administering Pritchard regime might prove to be hazardous in these low weight women and there is a possibility of a most dreadful respiratory failure.

The present study was planned to find out the efficacy of low dose magnesium sulphate regime in controlling the convulsions in eclampsia and seizure prophylaxis in imminent eclampsia.

In Our study efficacy of low dose regimen was similar to the Pritchard regimen. Similar results were seen in R. Begum et al. (17). In another study of Sardesai Suman et al (18) suggested, Low dose magnesium sulphate protocol was very effective as seizure prophylaxis in imminent eclampsia in 474 patients (98.75%); only 6 patients (1.25%) had one convulsion inspite of prophylaxis.

In Our study, dose related toxicity was not noted in any of the group. Similarly in R. Begum et al. (17), No patient developed toxicity with the low dose 'Dhaka' regime. The earliest sign of toxicity would be loss of tendon reflexes, which will usually occur when serum levels of 10mg/dl are reached (19).

One patient from Pritchard regimen group was diagnosed with liver capsule rupture & haemorrhage, which eventually led to a mortality (Post mortem findings).

CONCLUSION:

Hypertensive disorders in pregnancy ranks second only to haemorrhage as a specific & a direct cause of maternal death.

MgSO4 is the Prima donna drug in the management of pre-eclampsia & eclampsia.

The success of MgSo4 therapy & a good prognosis depends on strict monitoring & avoiding MgSO4 toxicity.

Low dose MgSO4 regime has been proved by various studies to be as effective as other regimes.

The method we used is simple & effective as the dosage is half of the standard Pritchard's regime but follows rest of the protocol which obstetricians are well versed with.

The low dose MgSO4 regime could be the standard choice of protocol in the future, in the management of pre-eclampsia & eclampsia as it reduces the total cost, has lesser side effects like pain at injection site, etc and has lesser chance of Mgso4 toxicity without any increase in the mortality or morbidity.

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