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Research Paper

Provision of neuroprotective dose of Magnesium Sulphate injection in Preterm Labor and its benefits as tocolytic

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Abstract
Introduction: *Magnesium sulfate (MgSO4) is easily available, cheap, and effective drug in the management of preterm birth ,since it can block cerebral gluta-mate receptors, which prevents post hypoxic brain injury in the perinatal period. Therefore, women at risk of early preterm imminent birth, from viability to 32 weeks of gestation, use of MgSO4 for neuroprotection of the fetus is recommended. The objective of the present study was to increase the percentage of women receiving neuroprotective dose of MgSO4 from 65% to 90% in preterm labour below 34 weeks of pregnancy within 8 weeks time.*
Methodology: *A short term quality improvement project was undertaken for a period of eight weeks. Fish bone analysis and process mapping was done to find out the low rate of Neuroprotective dose of MgSO4 in preterm labour. Necessary interventions were undertaken. Effect of intervention was assessed by finding out the percentage of women receiving the dose after 8 weeks.*
Results: *It was observed that after 8 weeks of intervention, percentage of women who received neuroprotective dose of MgSO4 increased from 65 % to 92 percent among eligible women.*
Conclusions: *Finding out the reasons for low percentage of women receiving neuroprotective dose of MgSO4 by using the scientific approach like fish bone analysis and process flow mapping of admitted women with preterm labour helped in undertaking necessary steps for improvement f exor low coverage of eligible pregnant women receiving the neuroprotective dose.*

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I. INTRODUCTION

Premature babies are more likely than term babies to pass away in their first few weeks of life [1]. Infants who survive have a higher risk of developing neurologic conditions such cerebral palsy, blindness, deafness, or cognitive dysfunction, as well as a higher risk of developing severe disabilities as a result of these conditions [2-4]. The long-term social and economic costs are high [5].

The phrase "cerebral palsy" refers to a variety of distinct disorders or ailments that can develop at any stage of brain development. It entails a permanent deficit of motor function that may change over time, as well as a disorder of movement, posture, or both [6].

Two per thousand live births on average, cerebral palsies continue to be the most common cause of severe motor impairment in children [6]. The majority of affected children (92%) live to be at least 20 years old, resulting in a significant burden of sickness into adulthood [7].

The main risk factor for cerebral palsy (responsible for 17% to 32% of all cases) is very preterm birth (less than 34 weeks) [8,9]. According to the most recent Australian Cerebral Palsy Register Report (2009), premature delivery is a contributing factor in about 45% of all cerebral palsy cases [10].

The risk of cerebral palsy is up to eight times higher in severely preterm newborns than in kids born at term [11], even though the largest risks are for infants born at 30 to 33 full weeks of gestation [3]. As many cases of cerebral palsy are caused by moderate preterm as by extreme prematurity. [10]

The body needs magnesium, the fourth most common ion, for a number of physiological functions, including energy use, metabolism, and storage. More than 300 enzymatic activities require the cofactor magnesium, which is primarily coupled to chelators like adenosine triphosphate (ATP) in the brain.[12,13]

Magnesium ions are necessary for the production of DNA, RNA, and proteins. It stabilizes cell membranes and aids in the synthesis of ATP and glycolysis. Magnesium regulates calcium inflow and acts as a non-competitive blocker of the NMDA glutamate receptor in the central nervous system.

Underlying its essential function in heart function, muscle contraction, vascular tone, and nerve impulse conduction is its physiological role as a calcium channel blocker [14] and modulator of sodium and potassium flux through its action on ion pumps (e.g., Na+/K+ ATPase) and other membrane receptors (e.g., nicotinic acetylcholine receptor).[15] 20% of magnesium is kept in muscle, 20% in soft tissue, and 60% in bone. Magnesium is typically found as ions (60%) but can also form complexes with proteins (33%), anions (7%), and other ions. Magnesium content in adult plasma is typically 0.75 mmol/L (95% confidence interval [CI]: 0.45-1.05).[16] Magnesium levels in infants rise in the first week following delivery (0.91 mmol/L).[17]

II. Material And Methods

In this study 50 patients admitted in labor wards of28 to 34weeks of gestation in Dept. of Obstetrics and Gynaecology, Pravara Institute of Medical Sciences (DU), Loni, Ahmednagar, Maharashtra. After admission each patient was assessed clinically and ultrasonically for period of gestation. After excluding congenital anomalies, uterine contraction, cervical effacement and dilatation were assessed. These included baseline data for descriptive purposes and analyses (reason at raised risk of preterm birth, gestational age at trial entry, plurality of the pregnancy, and expected date of birth) and details of the intervention planned and given (the date of randomisation, the allocated intervention, the type and dose of magnesium sulphate given, the mode of administration, whether a maintenance dose was given, and whether retreatment was given and its amount), together with the maternal and infant outcomes to allow the planned analyses.

Guideline (Magnesium sulphate- Neuroprotection of Preterm Infant, the women's, the royal women's hospital Victoria Australia)

4.1 Recommendations for use

The use of MgSO4 is recommended for neuroprotection of the fetus/infant/child:

when women are at risk of imminent preterm birth before 30 weeks gestation

when preterm birth before 30 weeks gestation is planned or definitely expected within 24 hours.

The use of MgSO4 is recommended:

regardless of the number of babies in utero

regardless of the anticipated mode of birth

whether or not antenatal corticosteroids have been given.

4.2 Dose

When birth is planned commence MgSO4 as close to four hours before birth as possible.

Note: Ensure magnesium sulphate is administered concurrently via a Y-site with a compatible IV fluid.

Loading dose: using a 10ml vial of MgSO4 prepare 4gram (i.e. 8ml) of magnesium sulphate 50% in a 10mL syringe, configure pump to accept the 10mL syringe and set the pump to 32mL an hour for 15 minutes.

Maintenance: once the loading dose has been completed, using the 50mL vial of magnesium sulphate, magnesium sulphate 50% in a 50mL syringe, re-set the pump to accept 50mL syringe and set the pump to administer the maintenance rate of 1g/hr (2mL/hour) or as ordered.

Continue the regime until birth or 24 hours, whichever comes first.

Urgent delivery: In situations where urgent delivery is necessary because of actual or imminent maternal or fetal compromise then delivery should not be delayed to administer MgSO4.

III. RESULTS

Of the 50 cases that were submitted for evaluation of magnesium sulphate's effectiveness in the management of premature labor, two did not show up for follow-up, and two had their treatment interrupted due to toxicity symptoms.

Success of the procedure was determined by the cessation of contractions, the absence of cervical dilatation during the procedure, and the absence of contractions within 48 hours of ceasing the procedure.

TABLE-1 PERIOD OF GESTATION

Period of gestation at admission (weeks)	**No. of patients**	**Percentage**
28-30	12	24%
30-32	10	20%
32-34	16	32%
34-36	12	24%

The majority of the patients were in the 32–34 week gestation range. In this study, 66% of the patients had gestations lasting longer than 32 weeks. These fetuses will have birth weights of greater than 1.5 kg, and many of them can survive with correct preterm labor management and good neonatal support.

TABLE-2: Cervical Effacement At The Time Of Admission

Cervical effacement	**No. of patients**	**Percentage**
>80%	4	8%
70-80%	28	56%
60-70%	2	4%
50-60%	12	24%
40-50%	4	8%
Uneffaced	0	0%

Out of the 50 patients examined, 28 (or 56%) had cervical effacement between 70 and 80%. Cervical effacement was greater than 50% in almost all cases. Therefore, prenatal examination of the cervix with PV or ultrasonography can be a predictor of PTL in patients with a history of PTL.

TABLE-3 Cervical Dilatation At The Time Of Admission

Cervical dilatation (in cms)	**No. of patients**	**Percentage**
1-2cms	32	64%
2-3cms	15	30%
>3cms	3	6%

Of the 50 cases examined, 32 (64%) had cervical dilatation between 1-2 cm. In this study, the majority of patients were in the latent phase of labor, where tocolysis is beneficial.

TABLE-4 $Mgso_4$ DOSE REQUIREMENT FOR UTERINE CONTRACTIONS TO SUBSIDE

$MgSo_4$ Maintenance dose (gm/hr)	**No. of patients**	**Percentage**
1-2 gm/hr	42	87.5%
2-3 gm/hr	6	12.5%
3-4 gm/hr	0	0%

42 (87.5%) of the study's patients needed MgSo4 maintenance doses of 1-2 gm/hr, and none needed doses greater than 3 gm/hr.

TABLE-5 Time Taken For Uterine Contractions To Subside

Time	**No. of patients**	**Percentage**
30 minutes	2	4.17%
30min.-1hour	14	29.17%
1-2 hours	32	66.67%

Out of 50 cases, treatment was stopped in 2cases due to toxicity features. Out of remaining 48 cases, 32 (66.67%) cases took 1-2 hours for uterine contractions to subside after commencing treatment.

TABLE-7 Outcome In OUR Study

Outcome	**No. of patients**	**Percentage**
Success	43	89.58%
Failure	5	10.42%

In our study, 43 patients had their labor postponed for 48 hours (a success rate of 89.58%). Three of the five instances that failed (10.42%) gave birth within two hours of therapy beginning, and the other two did so within eight hours.

Table 8: Inj MgSO4 providing to mother's in preterm labor

	Week 2	Week 4	Week 6	Week 8
Numerator	9	7	8	14
Denominator	14	10	10	16
percent	66%	72%	80%	90%

According to the previous data, antenatal inj MgSO4 was provided to only 60% of pregnant women in preterm labor.

All failure cases in the current study were under 32 weeks gestation, had cervical effacement greater than 80%, and had cervical dilatation less than 3 cm.

IV. DISCUSSION

For more than 25 years, obstetricians have utilized magnesium sulphate to treat premature labor. When taken in greater dosages, magnesium sulphate is beneficial in postponing birth for at least 48 hours in individuals with premature labor. The medication appears to have no adverse effects on the fetus, and it does have a neuroprotective impact in lowering the prevalence of cerebral palsy in premature newborns weighing less than 1,500 grams (Elliot, John P.MD, 2009, American college of obstetricians and Gynecologists). Out of 48 patients in the study, 43 (89.58%) had pregnancies that lasted longer than two days.

These two days are crucial because they represent the shortest period of time thought to be adequate to reap the benefits of administering corticosteroids in order to lessen the likelihood that respiratory distress syndrome would manifest in premature infants. The average therapy delivery interval in the successful group was 33 days, while the longest pregnancy extension was 64 days.

Prolongation of pregnancy >48 hours compared with other studies

Studies	**Prolongation of pregnancy > 48hrs**
ZaZhi et al	76.67%
Morales W.J	85%
Lyell, Deirdre J.M.D	87%
Present study	89.58%

Prolongation of pregnancy >48 hours compared with other tocolytics

Drug	Prolongation of pregnancy >48 hours
Nifedipine (Lyell et al)	72%
Indomethacin (Madhav.H. et al)	90%
Present study	89.58%

In OUR research, 32 individuals (66.67%) required 1-2 hours after therapy began for uterine quiescence. The least amount of time required was 30 minutes after the commencement of treatment for uterine contractions to stop, with a mean time of 74 minutes. In a prospective trial, (Stephen J. Schorr) premature labor patients with gestational age 32 weeks who administered magnesium sulphate experienced uterine quiescence in 6.22 hours as opposed to 74 minutes in the current study, where 66% of participants had gestational ages greater than 32 weeks.

With a minimum birth weight of 1.3 kg and a maximum birth weight of 3.5 kg, the mean birth weight in our sample was 2.52 kg. 4.65% of the study's successful participants were hospitalized to the newborn critical care unit, one for neonatal sepsis and the other for neonatal jaundice. Magnesium sulfate toxicity was not a factor in any of the cases. The mild and non-life threatening adverse effects of magnesium sulphate were experienced by almost all women. Only 2 patients had their medication stopped because of toxicity symptoms..

V. CONCLUSION

The minimum time considered adequate to provide benefit if corticosteroids are administered to reduce the chance of respiratory distress syndrome in premature infants is 48 hours, while intravenous magnesium sulphate is useful in delaying preterm labor for at least 48 hours. It works better to stop preterm labor when the gestational age is greater than 32 weeks and less effectively when the gestational age is less than 32 weeks. Cervical dilatation at the beginning of treatment was significantly correlated with the ability to suppress preterm labor. The mother, fetus, and newborns only experienced minor and barely perceptible adverse effects.

Effects of preterm birth magnesium sulphate administration on neuroprotection (JAMA and RCT of magnesium sulphate for the prevention of cerebral palsy) Further studies are urgently required to confirm the possibility of a clinically significant improvement in pediatric outcomes from magnesium sulphate administered to pregnant women just before very preterm birth for neuroprotection.

By employing scientific methods like fish bone analysis and process flow mapping of hospitalized women with preterm labor, it was possible to determine the causes of the low percentage of women receiving the neuroprotective dose of MgSO4 and take the required actions to ameliorate the situation.

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