ORIGINAL RESEARCH

Maternal and Fetal outcome in usage of magnesium sulphate for fetal neuroprotection in pregnancy less than 34 weeks of gestation

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ABSTRACT
Magnesium is an essential component in the central nervous system and is irreplaceable in several metabolic functions in the cell, therefore occupying a key place in cell death and developmental processes. Although the effects of magnesium sulfate are not well understood, its neuroprotective properties can be explained by its anti-inflammatory and anti-excitotoxic effects. This is an observational study done in the Department of Obstetrics and Gynecology, Kodagu Intitute of Medical Sciences, Madikeri from November 2020- November 2021 involving 52 pregnant women. Mode of delivery, 14(27%) had term cesarean delivery,18(35%) had preterm vaginal delivery, 13(25%) had full term vaginal delivery and 7(13%) had preterm cesarean delivery. 96.2% had no reactions, minor reactions noted were tachycardia, blurring of vision, absent knee jerk only among 2 persons. Among 23 babies had normal birth weight,27 were born with low birth weight and 5 babies were born with very low birth weight.In our study 3 perinatal deaths occurred. 2 cases developed delay in development. 1 at 3 months and another 1 case had severe gross motor dysfunction at 6 months postnatal follow up.
Key words: Magnesium sulphate, fetal neuroprotection, maternal and fetal outcome

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INTRODUCTION

With the rising trend in preterm birth in most developed and developing countries, although much of these are iatrogenic, globally, preterm birth is a major cause for perinatal morbidity and mortality [1].

Cerebral palsy is defined as a group of permanent movement and posture disorders strongly associated with fetal or perinatal brain lesions. It causes a significant reduction in health-related quality of life for patients with moderate to severe disabilities [4]. It remains one of the major long-term effects associated with preterm birth. 25% of all cerebral palsy cases occur in preterm babies born before 34 weeks of gestation [1, 2].

Magnesium is an essential component in the central nervous system and is irreplaceable in several metabolic functions in the cell, therefore occupying a key place in cell death and developmental processes. Although the effects of magnesium sulfate are not well understood, its neuroprotective properties can be explained by its anti-inflammatory and anti-excitotoxic effects [3].

In spite of Magnesium Sulphate's inexpensiveness and recommendations, very few comparative Indian studies are available on its use for neuroprotection. Reducing perinatal morbidity is the need of the hour and can be achieved not only by good neonatal care but also through timely interventions to the mother in the form of MgSO4, antenatal steroids, as well as antibiotics [5].The prevention of preterm birth represents one of the most significant challenge to the field of obstetrics. Preterm infants born before 3oth week of pregnancy are at risk peri/inter ventricular hemorrhages and periventricular leukomalacia both of

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which specifically affect the pyramidal tracts of lower extremities.[6]

Bearing in mind the cost-effectiveness of MgSO4 which is key in optimizing individual MgSO4 coverage, it would be of much use in tertiary healthcare centers like ours where preterm deliveries are on the rise. This study will also contribute to furthering the research about MgSO4 and its role in fetal neuroprotection in preterm neonates.

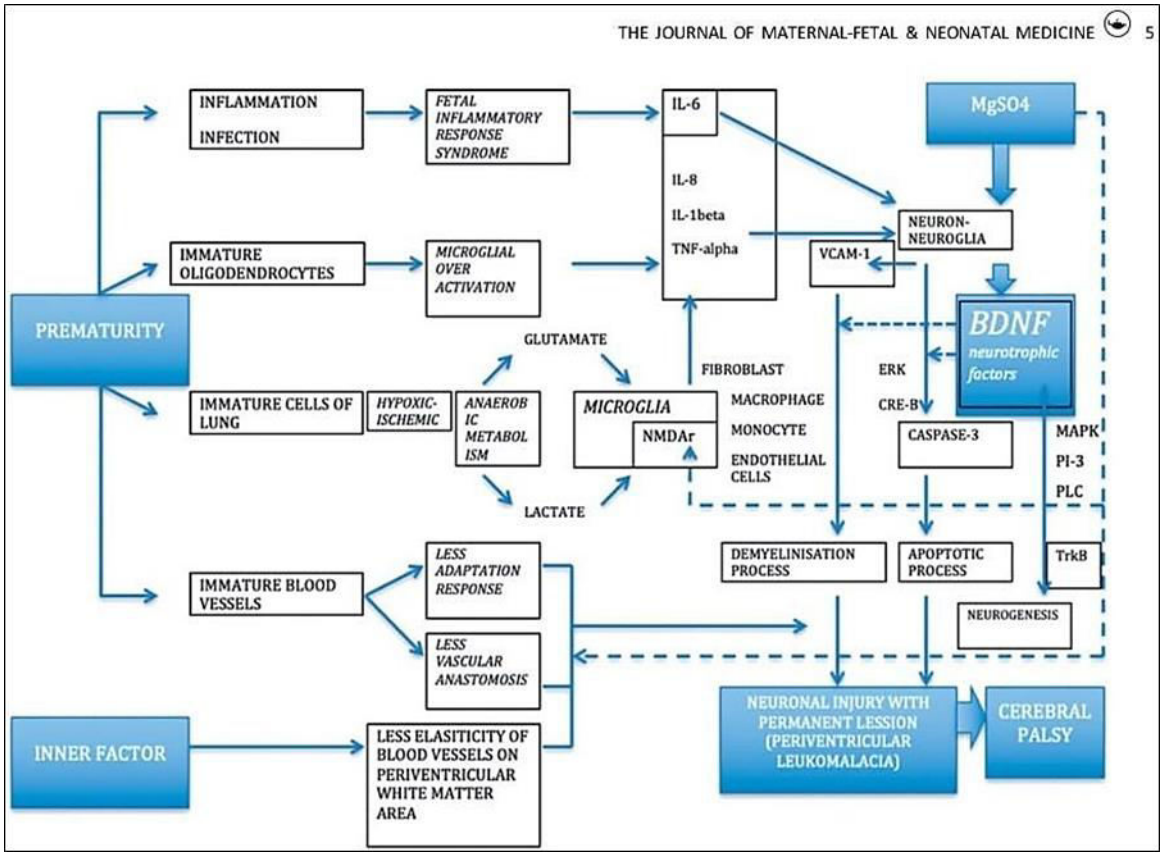

Figure 1: Pathway of antenatal magnesium sulphate in fetal neuroprotection

Muhammad AdrianesBachnas, Muhammad IlhamAldika Akbar, ErryGumilarDachlan&Gustaaf Dekker (2019): The role of magnesium sulfate (MgSO4) in fetal neuroprotection, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2019.1619688[1]

AIMS AND OBJECTIVES

1. To assess the effectiveness of magnesium sulphate for fetal neuroprotection in pregnancy less than 34 weeks of gestation.
2. To report maternal and fetal adverse events during magnesium sulphate usage.

METHODOLOGY

This is an observational study done in the Department of Obstetrics and Gynecology, Kodagu Intitute of Medical Sciences, Madikeri from November 2020-November 2021 involving 52 pregnant women. As in the management protocol of preterm pregnant women admitted to antenatal ward or the labour room in view of preterm labour, monitoring required in view of high-risk factors like fetal growth restriction, oligohydramnios, pre-eclampsia, gestational diabetes mellitus, 2 previous cesarean section, fetal doppler changes, PPROM. Pregnant women having the above-mentioned risk factors were admitted, evaluated as per institutional protocol and only steroid prophylaxis was being practiced initially before the study was undertaken, i.e.; 4 doses of Inj. Dexamethasone 6mg IM 12 hours apart for fetal lung maturation. This study implemented MgSO4 as part of the protocol for treating pregnant women with preterm gestation.

NEED FOR THE STUDY

Administration of antenatal MgSO4 prior to preterm gestation is not routinely practiced in our setup. Hence, the present study was taken up to assess the importance of MgSO4 for neuroprotection among preterm babies born at gestational age less than 34 weeks and to support the evidence of the benefits of MgSO4 for women at risk of imminent preterm birth with gestational age less than 34 weeks to reduce the likelihood of neurological abnormalities like gross developmental delay and cerebral palsy in the neonate.

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SOURCE OF DATA

INCLUSION CRITERIA

1. Pregnancy period of gestational age less than 34 weeks due to maternal and fetal indications.
2. Preterm labor and threatened preterm labor.
3. Preterm premature rupture of membranes.

EXCLUSION CRITERIA

1. Fully established preterm labor (active stage).
2. Stage 3 and 4 FGR.
3. Severe oligohydramnios.
4. Chorioamnionitis.
5. Fetal distress.
6. Abruptio placenta/bleeding placenta previa.
7. Eclampsia/DIC.
8. Severe preeclampsia with imminent symptoms.

SAMPLING METHOD: CONVENIENCE SAMPLING

After admission to ANC ward, details of the pregnant women were entered according to the proforma after obtaining informed consent from the women and the patient's bystander. Following this, investigations were carried out including NST, USG with BPP with fetal Doppler, Blood investigations including CBC, urine routine, high vaginal swab for culture and sensitivity, LFT, RFT, CRP, Blood grouping and Rh typing, serum electrolyes, S. Magnesium, S. Calcium. Initially conservative management considered, including 1. Steroid prophylaxis-Inj. Dexamethasone 6mg IM 4 doses given 12 hours apart 2. Magnesium Sulphate- loading dose 4g iv stat (8mL MgSO4 in 12mL distilled water, diluted in 20mL syringe given iv slowly over 20 minutes). Followed by this, maintenance dose of 10g MgSO4 (10 ampoules=20mL) in 500mL NS at the rate of 20mL/hr iv infusion for 24 hours. In this study, only 14 grams of MgSO4 was used.

In our institution MgSO4 loading dose was used only in imminent preeclampsia cases, but in the study it was given for women with pregnancy without imminent symptoms of preeclampsia and those who were fulfilling inclusion criteria . MgSO4 administration was done in the HDU with intense monitoring for 24 hours with a monitoring chart including pulse, BP, RR, SpO2, knee jerk, urine output, FHR monitoring. NST prior to the administration of MgSO4 and NST after administration to assess the fetal well-being was done. Any adverse events like itching, flushing, giddiness, disorientation, chills, fever, hypotension, difficulty in breathing during administration were noted. If adverse reactions occurred, MgSO4 was stopped immediately and the pregnant mother was monitored with conservative management. In indicated cases like preterm premature rupture of membranes, threatened preterm labour and in preterm labour, IV antibiotics Inj. Ceftriaxone 1g IV BD for 48 hours was given. Details regarding the delivery including gestational age at which delivery happened, mode of delivery, APGAR score, birth weight, condition of the baby, SNCU admission required or not, discharge, follow-up of the baby were done with simultaneous consultation with paediatrician, in the department of Paediatrics. Due to COVID-19 pandemic, follow-up of the babies were difficult, as the majority of the women belonged to the tribal community and hilly stations. Telephonic follow up was challenging as well and hence, only 52 cases could be followed up and presented in this study.

Neurosonogram was performed only for few cases at birth, and for missed cases it was done at the third month. Follow up was done at the 3rd and 6th postnatal months for developmental milestones. Results were calculated using Epi-info ver 7.2 statistical methods. Descriptive statistics was used and data was presented in the form of tables and pie charts.

RESULTS

In the present study 52 antenatal women with preterm gestation <34 weeks were admitted who were fulfilling the inclusion criteria. Epi-info ver 7.2 software is used to calculate the results. All 52 cases were followed up. Of this majority were from the age group 19-38 years.

Mean maternal age was 25.17+/- 5.07 years.

RANGE: 19-38 years.

MEAN MATERNAL AGE: 25.17 ± 5.07 years.

Table 1: Parity Distribution Among the Study Subjects

Parity	Frequency	Percentage
Primigravida	26	50
G2	14	26.9
G3	8	15.4
G4	4	7.7

Table 2: Distribution of High-Risk Factors among Study Subjects

Depicts the involvement of high risk factors for which preterm gestation admission was required Among that major risk factor was preeclampsia

High Risk Factors	Frequency	Percent
1 previous IUD with Gestational Hypertension	1	1.9
2 previous IUD (Male (10 week). Female (24week)) with Moderate Anaemia	1	1.9
Abruptio placenta, pre-eclampsia and moderate anaemia	1	1.9

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Anaemia and Twin pregnancy	2	3.8
FGR	2	3.8
GDM and Gestational HTN	1	1.9
GDM with polyhydraminos with Pre-eclampsia	1	1.9
Gestational hypertension	2	3.8
Grade 3 placenta previa	1	1.9
Chronic Hypertension	1	1.9
Hypothyroidism	1	1.9
Marginal Placenta previa	1	1.9
None	3	5.8
Obesity	2	3.8
Oligohydraminos	1	1.9
Oligohydraminos with FGR	1	1.9
Patent foramen ovale	1	1.9
PPROM	1	1.9
Pre-eclampsia	10	19.2
Pre-eclampsia and GDM	2	3.8
Preterm	2	3.8
Preterm with PE	1	1.9
Previous CD	2	3.8
Rh negative pregnancy	1	1.9
Rh negative pregnancy and obesity	1	1.9
Severe Oligohydraminos	1	1.9
Severe pre-eclampsia	1	1.9
Severe pre-eclampsia with impending signs	1	1.9
Short Stature	2	3.8
Threatened Pre-term	3	5.8
Vaginal Infection	1	1.9
Total	52	100.0

Incidence of high-risk factors among mothers = 94.2% (49 out of 52)

Mean gestational age at delivery was 36.17+/-2.39 weeks.

44.2% had deliveries within 37 weeks and 55.8% had deliveries >37 weeks.

Mean gestational age at delivery: 36.17 ± 2.39 weeks.

Table 3: Gestational age at delivery

Gestational age at delivery	Frequency	Percentage
< 37 weeks	23	44.2
≥ 37 weeks	29	55.8

Table 4: Gestational age at delivery

Gestational age at delivery	Frequency	Percentage
31 weeks	2	3.8
32 weeks	3	5.8
33 weeks	4	7.7
34 weeks	5	9.6
35 weeks	4	7.7
36 weeks	5	9.6
37 weeks	11	21.2
38 weeks	9	17.3
39 weeks	8	15.4
40 weeks	1	1.9

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Table 5: USG findings

The table shows the frequency distribution of USG findings in pregnant women who were given MgSO4 for neuroprotection.

USG findings	Frequency
Stage 1 FGR	8
Placenta previa	2
Oligohydramnios + FGR	3
Normal USG with no significant findings	39

Mode of delivery, 14(27%) had term cesarean delivery, 18(35%) had preterm vaginal delivery, 13(25%) had full term vaginal delivery and 7(13%) had preterm cesarean delivery.

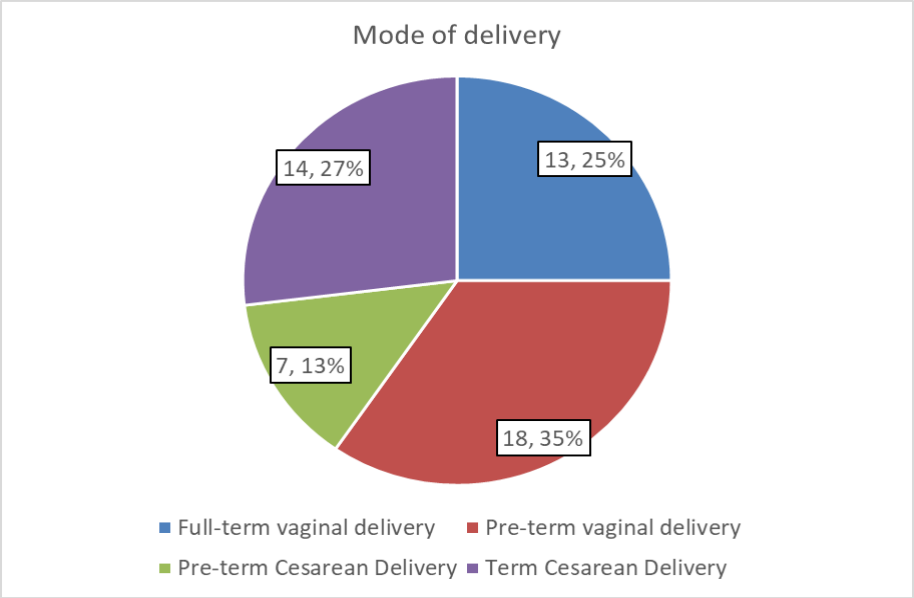

Table 6: Side effects of MgSO4 in the mother

96.2% had no reactions, minor reactions noted were tachycardia, blurring of vision, absent knee jerk only among 2 persons.

Adverse events	Frequency	Percentage
No reaction	50	96.2
Tachycardia	1	1.9
Blurring of vision, absent knee jerk	1	1.9

Table 7: Distribution of babies born to pregnant women who received MgSO4 according to Apgar Score at 1 minute and 5 minutes

Apgar score	4 to 6	7 to 10	Total
At 1 minute	09 (17%)	44 (83%)	53 (100%)
At 5 minutes	02 (3.8%)	51 (96.2%)	53 (100%)

Table 8: Incidence of Congenital anomalies: 7.27% (4 out of 55)

After birth 5 babies were identified with congenital anomalies.

Congenital anomalies	Frequency	Percentage
Cleft palate, hypospadias and B/L undescended testis	1	1.8
Omphalocoele with hypospadias	1	1.8
Club foot	1	1.8
SitusAmbigus	1	1.8
None	51	92.8
Total	55	100

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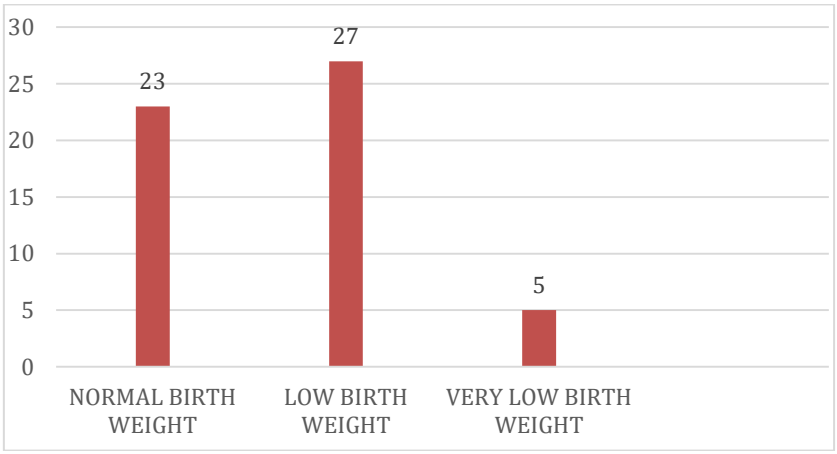
Table 9: Paediatric Mortality
3 babies died out of 55 at the particular duration due to various causes.
Paediatric mortality: 5.45% (3 out of 55).

Day 9	1	Extreme LBW, birth asphyxia, sepsis
Day 45	1	Multiple anomalies
Two months	1	Due to aspiration

Table 10: NICU admission
This table depicts the different causes for which the babies were admitted to NICU.
Of this the highest percentage of babies who were admitted to NICU were due to prematurity and low birthoutco**.**

NICU admission	Frequency	Percentage
Fetal distress	1	1.82
LBW	6	10.91
Neonatal jaundice	1	1.82
Premature LBW, Jaundice	2	3.64
Premature, LBW	8	14.55
No NICU admission	37	67.27

INCIDENCE OF LOW-BIRTH WEIGHT: 58.2% (32out of 55).
The graph shows the distribution of birth weight of babies of pregnant women who received MgSO4.Among these 23 babies had normal birth weight,27 were born with low birth weight and 5 babies were born with very low birth weight.



38 babies were followed upto 12 weeks they had normal developmental milestones,2 had delayed milestones, 1 had atypical febrile convulsions,1 baby expired. 1 had hearing defect.
At 6 months, 48 babies were followed up 1 had severe developmental delay and 1 died.

Table 11: Babies follow up

	At 12 weeks	At 6 months
Developmental milestones Normal for age	38	48
Delayed development	2	1
Atypical Febrile convulsions	1	
Death	1	1
Hearing defect	1	–

DISCUSSION
Table 12: Guidelines for Foetal Neuroprotection [1]

Guidelines	Eligibility	Dosage
RCOG	Upper limit 30 weeks (B)	Loading dose 4g IV (20-30min) Maintenance dose 1g/hr IV over 12 hours(A)
ACOG	Early preterm gestation (A)	No specific guidelinesregardingwhen and how it was started (C)
RANCOG	Early preterm imminent birth <30 weeks (B)	4g IV, 1g/hr until birth or for 24 hours (A).

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	The benefit is expected for birth occurring at least 4 hours after the initial dose. (A)	No place for magnesium as a tocolytic.
SOGC	Imminent preterm birth (</= 31 weeks + 6 days (A)	4g IV, 1g/hruntill birth(B).
SA perinatal practice guidelines	24+0 weeks - 30+0 weeks women at risk of preterm birth within 24 hours	4g IV over 20 minutes 1g/hruntill birth

Grade of recommendation: A-Strong, B-Fair-Weak

- Considerations of antenatal MgSO4 administration apart from its usage as an essential drug in severe pre-eclampsia, it has also been considered as a neuroprotective agent among preterm gestation. Considering various protocol recommendations internationally.

Table 13: Studies of magnesium sulfate for neuroprotection in prematurity[1]

Parameters	Beam (2008)	Premag (2007)	Active MgSO4 (2003)	Magnet (2002)	Present Study
Study Subject	2136	688	1047	106	52
Gestational Age in Weeks	24-31	<33	</=30	24-33	28-34
Dose and Duration	6G Bolus, 2g/h for 12 Hours	4G Bolus	4G Bolus, 1g/h for 24H	4G Bolus	4G Bolus, 0.04g/h for 24 hours (20ml/hr for 24 hours)
Total dose Recieved	30g	4g	28g	4g	14g
Outcome	Neurological disability is signficantly lower (1.9% vs 3.5%) Paediatric mortality is higher (9.5%vs 8.5%)	Neurological disability is significantly lower (10%vs11.7%) Paediatric mortality is slighlty lower (13.8% vs 17.1%)	Neurological disability is slightly lower (6.8% vs 8.2%) Paediatric mortality is slighlty lower (13.8% vs 17.1%)	This trial was prematurely stopped due to neonatal adverse event	Neurological disability is significantly lower 3.63% Paediatric mortality is slighlty lower 5.4%

In the present study 4g loading dose IV slowly for 20 minutes, followed by maintenance dose 20ml/hr [10g in 500 ml NS] for 24 hours for the preterm gestation 28-34 weeks.

FIGO RECOMMENDATION (2021)

In women at risk of early imminent preterm birth <32-34 weeks of gestation, the use of MgSO4 for neuroprotection of the fetus should be considered. IV 4g over 20-30 min slowly. 1gm/hr maintenance IV continued until birth, stop after 24 hours if undelivered.

Antenatal MgSO4 treatment has good cost effectiveness with regard to neuroprotection regardless of gestational age, cause of preterm birth and total dose.[3]

WHO (2017) recommended administration from 28-32 weeks gestational age with risk of imminent preterm birth.4g IV loading dose, 1g/hr for 12 hours regardless of the cause of preterm birth[3]

Table 14: Dose Recommendation

FIGO (2021) [2]	4g IV loading dose over 20-30 mins and 1g/hr for 24 hours	<32-34 weeks
WHO (2017) [3]	4g IV loading dose for 20 mins 1g/hr for 12 hours	23-32 weeks
Mohammed Abu Faza (2017) *et al.* [9]	4g IV for 20 mins (150ml/hr) x 20 mins **Loading dose:** 1g/hr for 4 hours (infusion rate 12.5ml/hr)	29 weeks 6 days-30 weeks
Our Study (2020-2021)	4g IV loading dose followed by 20ml/hr over 24 hours (10 grams in 500 ml).	28-34 weeks

We used low dosage of MgSO4 for the purpose of easy monitoring and to avoid the possible risk of toxicity.

Our study is similar to an Indian study (2021) Vandana Bansal *et al*., 4 grams IV loading dose in 100 ml NS over 30 mins preferably 4 hours apart prior to birth as per standard of care, Maintenance dose was not given [5].

Mathew Lecuyer*et al*., stated that their data as first mechanic evidence of double sword and dose dependant actions of MgSO4 on nervous and vascular systems. This strongly supports the clinical use for neuroprotection protocols validated for the lowest (4g) loading dose of MgSO4 [4].

In Cochrane review 2009,five prospective randomized studies were published which included a total of 6145 children. The studies found a significant reduction in the incidence of infantile cerebral palsy(relative risk 0.68; 95%confidence interval 0.54 to 0.87), as well as the incidence of gross motor skill dysfunction

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(relative risk 0.61 ; 95%confidence interval 0.44 to 0.85) among children whose mother has been treated with magnesium sulphate.[6]

Table 15: Comparing maternal age, gestational age and other risk factors involved in preterm gestation with other studies [5, 8, 12]

Studies	Age	Range	Mean Gestational Age at Which Birth Occured
Our study (2020-2021)	25.17+/- 5.07 years Nulliparous 26 years	19-38 years	36.17+/- 2 weeks [2 weeks]
Vandana Bansal *et al*. (2020)	28.2+/-4.74 years	19-41 years	31+/-1.73 weeks
Dane A De Silva (2018) Pre-Mag Mag CP	31 years 31 years 31 years	-	30-34 weeks
Pierre-Emmanuel Bouet (2015)	29.3+/- 6.2 years Nulliparous 40years	-	29.6+/-2.1 87.5% have birth in 24 hours

In the present study associated risk factors were 94.2% where as in Vandana Bansal study the risk factors for preterm labor was 83% [5],Among them, pre-eclampsia accounting to 19.2%, Pre-PROM seen in 1.9%.

In PPROM (24-33 weeks + 6 days) corticosteroids should be given, when pregnancy is complicated by PPROM after 24 weeks of gestation offer expectant management upto 37 weeks if no contraindication in continuing the pregnancy.

If planning for preterm birth within 24 hours IV MgSO4 was offered between 24 weeks to 29 weeks 6 days of gestation (A) [15].

Before 33 weeks of gestation cesarean delivery occurred in 52 subjects (n=81) (64.2%) [8].In present study (n-52) preterm CD was 7(13%) and term CD was 14(27%).

When MgSO4 is administered, subject women were monitored for clinical signs of MgSO4 toxicity every 4 hours by recording pulse, BP, deep tendon reflexes [11].

Adverse effects were seen in 4 out of 50 women who received MgSO4(8%) [5] but in present study 2 out of 52 had mild reactions (3.8%). The reactions were tachycardia, blurring of vision, absent knee jerk reflex were noted. Conde-Agudelo*et al*., study showed 50% increase in hypotension and tachycardia was observed. 70% presented with flushing, nausea, vomiting, sweating and injection site infection was present which were not clinically significant [7].

In Pierre-Emmanuel Bouet*et al*. (2015) study (n-81), flushing sweating (4), nausea and vomiting (2), hypotension [9].

Magnesium ion can be toxic to the mother based on serum Magnesium levels.

~8mEQ/L-Patellar reflex disappears.

~10-11mEQ/L-Respiratory depression.

Less clarity observed on neonatal effect like respiratory depression, hypotonia and hyporeflexia [9].

In our study low birth weight babies were 58.2% (32 out of 55). Incidence of anomalies were 7.27%.

In our study condition of the baby based on APGAR score at 1 minute <7 was seen in 17%. At 5min <7 was seen in 3.8%. 11 babies required resuscitation. NICU admission was required for 18 babies due to LBW (10.91%) and prematurity with LBW (14.55%).

Mina AbbassiGhanavati*et al*., study observed 1min and 5 min APGAR scores, admission rates, hypotonia were significantly increased as maternal serum magnesium concentration increased [13].

Pierre-Emmanuel Bouet*et al*. study in 2015 stated that in Magnesium sulphate group (n-94) mean birth weight was 1.373+/-393.9 kgs, mortality 3, severe neurological morbidity 6, APGAR score at 5 min <7 is 11, NICU admission seen in 45 [8].

Emily shepherd *et al*. (2019) systematic review includes 197 studies report showed on adverse reactions for babies whose mother were treated with MgSO4 in pregnancy. APGAR score <7 at 1 min in 2 studies, 199 participants RR 1.67 and APGAR score <7 at 5 min included 5 studies 12,729 participants RR 1.02 [17].

Magnesium sulphate administration also did not have significant effects on any less serious neonatal morbidities studied, including 5 min APGAR less than <7, respiratory distress syndrome, need for assisted ventilation or NEC [16].

NICU admission seen in 80.1% in Dane A. De silva study, pre mag study 82% and MAG CP 77.2% which were statistically significant.[12] Intensive resuscitation required only among 1630 in 5314(30.6%) [12]. In our study only 11 babies required resuscitation out of 55 babies (20%).

Out of 100, 7 deaths occurred among them 5 occurred in MgSO4 group due to low birth weight (<1 kg) < 30 weeks of maturity [5]. In our study 3 died (5.45%) out of 55 babies due to preterm birth <30 weeks of gestation cause being birth asphyxia with low birth weight.

In our study 3 deaths occurred. 2 cases developed delay in development. 1 at 3 months and another 1 case had severe gross motor dysfunction at 6 months postnatal follow up. Primary outcome in Crowther *et al*. (2013) relative risk of death 0.95(0.80 to 1.12 CI), and of gross motor dysfunction 0.84, (0.71 to 1.00 CI) [10].

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Dev Med Child Neurol 2019, 61: 25–30

Table I: Main outcomes of randomized controlled trials and meta-analyses assessing the impact of antenatal administration of magnesium sulphate

	Randomized controlled trial					Meta-analysis				
						Standard				IPD
	MAGnet: Mittendorf et al.[22]	PREMAG: Marret et al.[24,25]	ACTOMgSO$_4$: Crowther et al.[23]	BEAM: Rouse et al.[26]	Magpie: Altman et al.[27]	Doyle et al.[30]	Conde-Agudelo et al.[31]	Costantine et al.[32]	Zeng et al.[33]	Crowther et al.[34]
Paediatric mortality[a]	9.41 (1.23–71.9)	0.87 (0.61–1.07)	0.81 (0.61–1.07)	1.18 (0.89–1.55)	1.27 (0.96–1.68)	1.04 (0.92–1.17)	1.01 (0.89–1.14)	1.01 (0.89–1.14)	0.92 (0.77–1.11)	1.03 (0.91–1.17)
Intraventricular haemorrhage[a]	1.11 (0.53–2.34)	0.83 (0.62–1.09)	1.11 (0.92–1.34)	0.91 (0.78–1.08)	N/A	0.96 (0.86–1.08)	0.96 (0.86–1.08)	N/A	1.05 (0.86–1.29)	0.98 (0.87–1.09)
Periventricular leukomalacia[a]	2.83 (0.12–68.37)	0.92 (0.55–1.53)	1.04 (0.58–1.88)	0.82 (0.47–1.45)	N/A	0.93 (0.68–1.28)	0.93 (0.68–1.28)	N/A	1.30 (0.81–2.10)	0.91 (0.66–1.25)
CP[b]	0.94 (0.20–4.53)	0.70 (0.41–1.19)	0.85 (0.55–1.31)	0.59 (0.40–0.85)	0.40 (0.08–2.05)	0.68 (0.54–0.87)	0.69 (0.55–0.88)	0.7 (0.55–0.89)	0.61 (0.42–0.89) (moderate to severe CP)	0.68 (0.54–0.87)
Death or CP[b]	4.83 (0.60–38.90)	0.80 (0.58–1.10)	0.82 (0.66–1.02)	0.90 (0.73–1.10)	1.09 (0.92–1.29)	0.94 (0.78–1.12)	1.01 (0.89–1.14)	0.92 (0.83–1.03)	N/A	0.86 (0.75–0.99)
Number needed to treat to avoid one case of CP						63 (43–155)	74 (41–373)	Before 30wks' gestation: 46 (26–187) Between 32–34wks' gestation: 56 (34–164)	N/A	46 (CI not shown)

Values are odds ratio (95% confidence interval [CI]). [a]Neonatal outcomes. [b]CP at 2 years. The randomized controlled trials MAGnet, PREMAG, ACTOMgSO$_4$, and BEAM were fetal neuroprotective trials. The Magpie trial aimed for neuroprotection of the mother with pre-eclampsia. Children's neurological outcomes were available from the centre where follow-up was feasible. Meta-analyses concerned the five randomized controlled trials quoted in the first part of the table. IPD, individual participant data; N/A, not available; CP, cerebral palsy.

Muhammad AdrianesBachnas, Muhammad IlhamAldika Akbar, ErryGumilarDachlan&Gustaaf Dekker (2019): The role of magnesium sulfate (MgSO4) in fetal neuroprotection, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2019.1619688(1)

LIMITATIONS OF THE STUDY

1. Sample size was small and followed upto 6 months postnatally.
2. Lack of health education in follow up cases.

CONCLUSION

In present study, MgSO4 introduction in the protocol of management of preterm gestation for admitted antenatal cases for prevention of neurological abnormalities is very much effective and it is feasible in a tertiary obstetric healthcare. Administration of MgSO4 in preterm management protocol is safety and cost effective with less side effects to the mother and neuroprotective effects to the newborn.

It is listed as "high alert medication" strict monitoring is required.

Magnesium sulphate is qualified to use as definitive intervention to prevent or to treat preterm birth related disabilities mainly neurological abnormalities.

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