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# Role of Magnesium Sulphate as a Neuroprotective Agent on Neonatal Outcome in Preterm Deliveries

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**Abstract:** ***Background: Preterm birth is an important cause of neonatal morbidity and mortality, mainly due to complications such as respiratory distress syndrome, intraventricular haemorrhage, periventricular leukomalacia, sepsis, feeding difficulty and long-term neurodevelopmental impairment. Magnesium sulphate (MgSO4) has been suggested as a low-cost and effective fetal neuroprotective agent in women at risk of preterm delivery. Aim: To assess the role of magnesium sulphate as a neuroprotective agent on neonatal outcome in preterm deliveries. Methods: This hospital-based comparative study was conducted in the Department of Obstetrics and Gynaecology, PBM Hospital, Bikaner, Rajasthan. A total of 92 pregnant women with preterm labour between 28 and 36 weeks of gestation were included and divided into two groups: MgSO4 group and non-MgSO4 group, with 46 women in each group. Women in the MgSO4 group received 4 g intravenous loading dose followed by 1 g/hour infusion for 24 hours or until delivery. Neonatal outcomes were assessed in terms of APGAR score, rooting and suckling reflex, Moro's reflex, fetal outcome, neonatal morbidity, NICU admission, oxygen requirement and cranial ultrasound findings. Maternal side effects were also recorded. Results: Both groups were comparable with respect to age, residence, booking status, education, gravidity, socioeconomic status, previous preterm birth, gestational age, mode of delivery and birth weight. Mean APGAR score was significantly higher in the MgSO4 group at 1 minute (7.1±1.8 vs 5.1±1.1) and 5 minutes (8.2±1.5 vs 5.9±1.8). Complete rooting and suckling reflex was higher in the MgSO4 group (69.57% vs 43.48%), and complete Moro's reflex was also better (47.83% vs 26.09%). NICU admission was lower in the MgSO4 group (34.78% vs 56.52%). Cranial USG showed no IVH or PVL in the MgSO4 group, while controls showed IVH in 4.35% and PVL in 6.52%. Conclusion: Antenatal magnesium sulphate appears to improve early neonatal neurological outcome and reduce NICU admission in preterm deliveries, with minimal maternal side effects.***

**Keywords:** Preterm delivery, Magnesium sulphate, Neuroprotection, Neonatal outcome, APGAR score, NICU admission, Intraventricular haemorrhage, Periventricular leukomalacia, Preterm neonate.

## 1. Introduction

Preterm birth is one of the major causes of neonatal morbidity and mortality worldwide. It is defined as delivery occurring before 37 completed weeks of gestation. Preterm neonates are physiologically immature and are more prone to respiratory distress syndrome, intraventricular haemorrhage, periventricular leukomalacia, feeding difficulty, sepsis, hypothermia and long-term neurodevelopmental impairment [1,2]. Neurological morbidity is an important concern in preterm babies because immature cerebral vasculature and poor autoregulation make them vulnerable to hypoxic, ischemic and inflammatory brain injury [3].

Magnesium sulphate (MgSO4) has been widely used in obstetric practice for seizure prophylaxis in preeclampsia and eclampsia. In recent years, it has also been used as a fetal neuroprotective agent in women at risk of preterm delivery. Magnesium acts by stabilizing neuronal membranes, blocking N-methyl-D-aspartate receptors, reducing calcium influx, decreasing excitotoxicity and suppressing inflammatory injury to the developing fetal brain [4,5]. Several clinical trials and meta-analyses have shown that antenatal MgSO4 reduces the risk of cerebral palsy and severe neurological impairment in preterm infants without causing major maternal or neonatal adverse effects [6, 7].

In low-resource settings, prevention of neurological morbidity in preterm babies is very important because long-term disability creates a high burden on families and healthcare systems. MgSO4 is inexpensive, easily available and can be administered in labour room settings with proper monitoring. Therefore, this study was undertaken to assess the effect of antenatal MgSO4 on neonatal outcome in preterm deliveries.

## 2. Aim and Objectives

**Aim:**
To assess the role of magnesium sulphate as a neuroprotective agent on neonatal outcome in preterm deliveries.

**Objectives:**
1) To compare neonatal outcomes between women receiving MgSO4 and those not receiving MgSO4.
2) To compare neonatal morbidity and NICU admission between both groups.
3) To assess maternal side effects associated with MgSO4 administration.

## 3. Material and Methods

This hospital-based comparative study was conducted in the Department of Obstetrics and Gynaecology, PBM Hospital, Bikaner, Rajasthan. A total of 92 pregnant women with preterm labour between 28 and 36 weeks of gestation were included in the study. They were divided into two equal groups. Group A included 46 women who received magnesium sulphate for fetal neuroprotection, and Group B included 46 age- and gestational-age-matched women who did not receive magnesium sulphate.

All women above 18 years of age, willing to participate, and admitted with preterm labour pains between 28 and 36 weeks of gestation were included. Women in second stage of labour, those already receiving MgSO4 for preeclampsia or eclampsia, women with allergy to MgSO4, renal failure, hypocalcemia, absent patellar reflex, respiratory rate less than 16/minute, urine output less than 100 mL in previous 4 hours, or neuromuscular disorders were excluded.

After taking written informed consent, detailed history, general examination, obstetric examination and necessary investigations were performed. All women received corticosteroid coverage for fetal lung maturity as per hospital protocol. In Group A, MgSO4 was given as 4 g intravenous loading dose slowly over 20 minutes, followed by 1 g/hour infusion for 24 hours or until delivery, whichever occurred earlier. Maternal pulse, blood pressure, respiratory rate, patellar reflex and urine output were monitored regularly. Neonatal outcome was assessed by APGAR score, birth weight, neonatal reflexes, morbidity, NICU admission, oxygen requirement and cranial ultrasonography. Data were analysed using appropriate statistical tests, and p value <0.05 was considered significant.

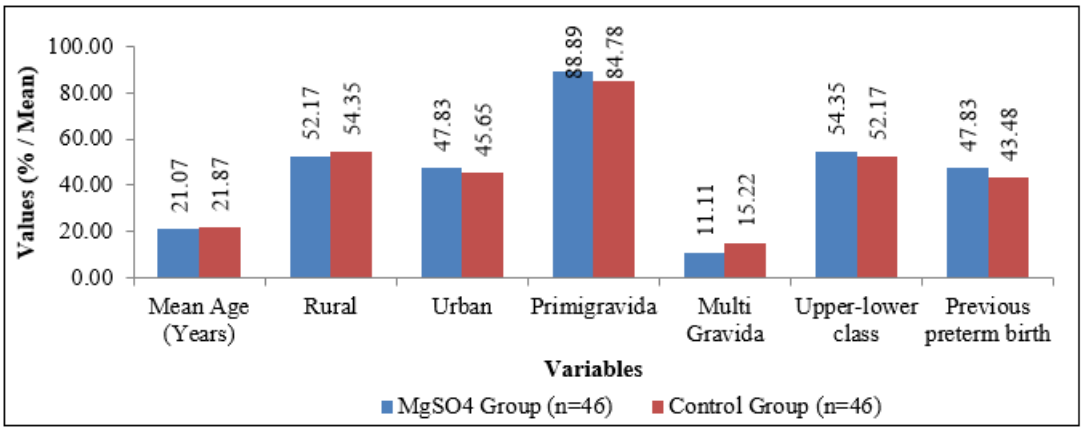
## 4. Results

A total of 92 pregnant women were included, with 46 in the MgSO4 group and 46 in the control group. Both groups were comparable with respect to age, residence, socioeconomic status, parity, gestational age and mode of delivery. The mean age was 21.07±3.31 years in the MgSO4 group and 21.87±3.15 years in controls. Most women belonged to rural areas and upper-lower socioeconomic class. The mean gestational age was 32.2±1.6 weeks in the MgSO4 group and 32.8±1.5 weeks in controls.

The mean APGAR score was significantly better in the MgSO4 group at both 1 minute and 5 minutes. Complete rooting and suckling reflex was present in 69.57% neonates in the MgSO4 group compared to 43.48% controls. Complete Moro's reflex at one month was also better in the MgSO4 group. Healthy neonatal outcome was higher in the MgSO4 group, while neonatal morbidity and NICU admission were higher in controls. NICU admission was required in 34.78% neonates in the MgSO4 group and 56.52% in controls. Cranial USG showed no intraventricular haemorrhage or periventricular leukomalacia in the MgSO4 group, whereas controls showed IVH in 4.35% and PVL in 6.52%. Maternal side effects were mild and statistically insignificant between the groups.

**Table 1:** Baseline Characteristics of Study Population

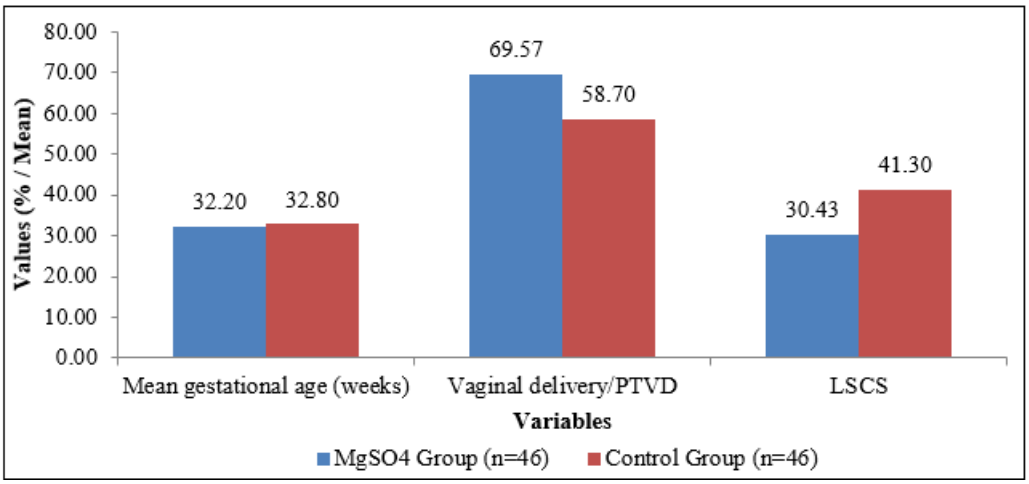
| Variable | | MgSO4 Group (n=46) | Control Group (n=46) | p value |
|---|---|---|---|---|
| Mean Age (Years) | Mean ± SD | 21.07±3.31 | 21.87±3.15 | 0.238 |
| Residence | Rural | 24 (52.17%) | 25 (54.35%) | 0.835 |
| | Urban | 22 (47.83%) | 21 (55.65%) | |
| Gravidity | Primigravida | 41 (88.89%) | 39 (84.78%) | 0.557 |
| | Multi Gravida | 5 (11.11%) | 7 (15.22%) | |
| Socioeconomic Status | Upper-lower class | 25 (54.35%) | 24 (52.17%) | 0.885 |
| History of Previous Preterm | Previous preterm birth | 22 (47.83%) | 20 (43.48%) | 0.874 |




**Graph 1:** Baseline Characteristics of Study Population

**Table 2:** Obstetric and Delivery Profile

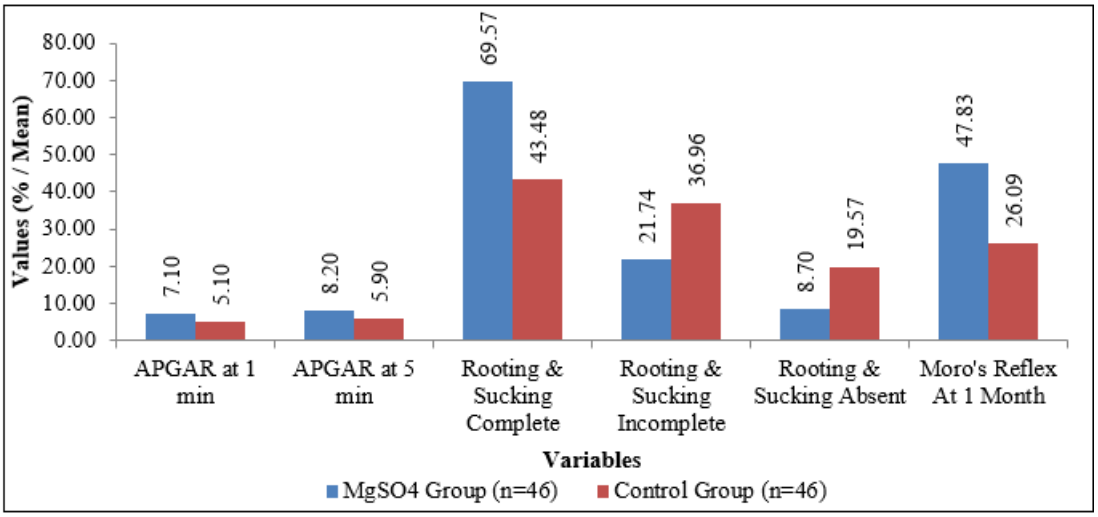
| Variable | MgSO4 Group (n=46) | Control Group (n=46) | p value |
|---|---|---|---|
| Mean gestational age (weeks) | 32.2±1.6 | 32.8±1.5 | 0.797 |
| Vaginal delivery/PTVD | 32 (69.57%) | 27 (58.70%) | 0.385 |
| LSCS | 14 (30.43%) | 19 (41.30%) | |




**Graph 2:** Obstetric and Delivery Profile

**Table 3:** Neonatal outcome

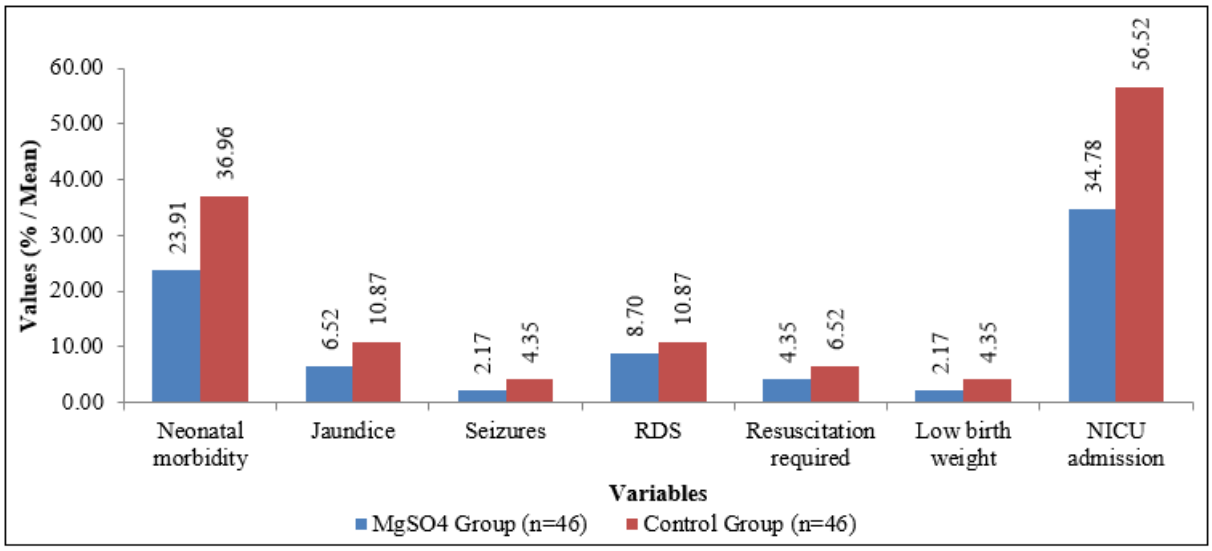
| | Variable | MgSO4 Group (n=46) | Control Group (n=46) | p value |
|---|---|---|---|---|
| APGAR Score | At 1 min | 7.1±1.8 | 5.1±1.1 | 0.0001 |
| | At 5 min | 8.2±1.5 | 5.9±1.8 | 0.0001 |
| Rooting and Sucking Reflex | Complete | 32 (69.57%) | 20 (43.48%) | 0.039* |
| | Incomplete | 10 (21.74%) | 17 (36.96%) | |
| | Absent | 4 (8.70%) | 9 (19.57%) | |
| Moro's Reflex | At 1 Month | 22 (47.83%) | 12 (26.09%) | 0.033* |




**Graph 3:** Neonatal outcome

**Table 4:** Neonatal Morbidity

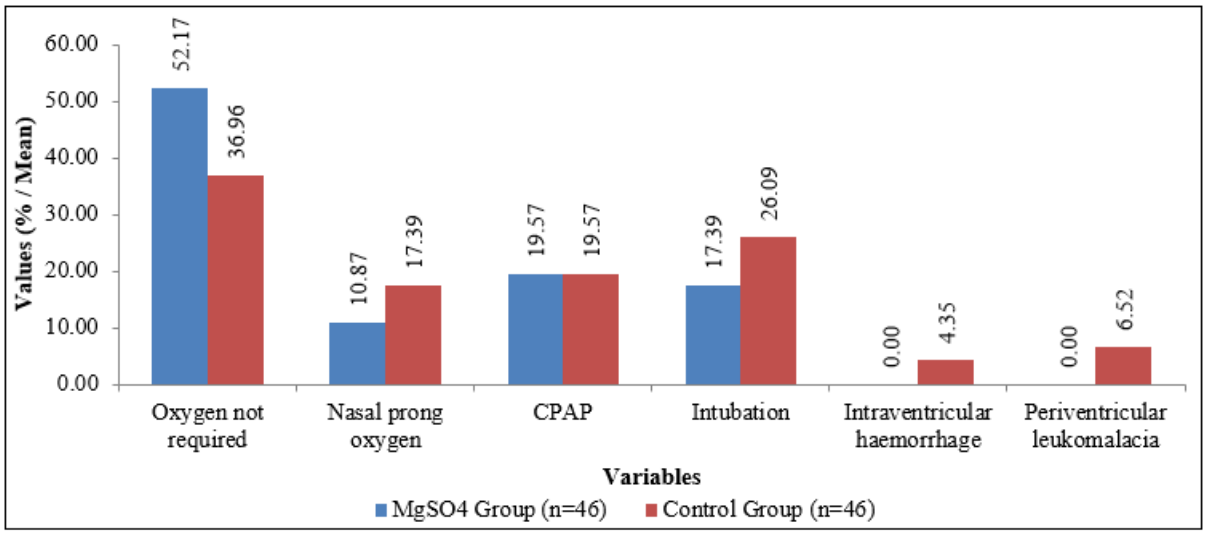
| Variable | MgSO4 Group (n=46) | Control Group (n=46) | p value |
|---|---|---|---|
| Neonatal morbidity | 11 (23.91%) | 17 (36.96%) | 0.173 |
| Jaundice | 3 (6.52%) | 5 (10.87%) | 0.713 |
| Seizures | 1 (2.17%) | 2 (4.35%) | 1.000 |
| RDS | 4 (8.70%) | 5 (10.87%) | 1.000 |
| Resuscitation required | 2 (4.35%) | 3 (6.52%) | 1.000 |
| Low birth weight | 1 (2.17%) | 2 (4.35%) | 1.000 |
| NICU admission | 16 (34.78%) | 26 (56.52%) | 0.049* |




**Graph 4:** Neonatal Morbidity

**Table 5:** Need of Oxygen Requirement and Cranial USG

| Variable | MgSO4 Group (n=46) | Control Group (n=46) | p value |
|---|---|---|---|
| Oxygen not required | 24 (52.17%) | 17 (36.96%) | 0.602 |
| Nasal prong oxygen | 5 (10.87%) | 8 (17.39%) | |
| CPAP | 9 (19.57%) | 9 (19.57%) | |
| Intubation | 8 (17.39%) | 12 (26.09%) | |
| Intraventricular haemorrhage | 0 (0.00%) | 2 (4.35%) | - |
| Periventricular leukomalacia | 0 (0.00%) | 3 (6.52%) | - |




**Graph 5:** Need of Oxygen Requirement and Cranial USG

## 5. Discussion

In the present hospital-based comparative study, antenatal magnesium sulphate was associated with better early neonatal outcome in preterm deliveries. Both groups were comparable with regard to baseline demographic and obstetric factors, suggesting that the difference in neonatal outcome may be related to MgSO4 exposure. The mean gestational age was 32.2±1.6 weeks in the MgSO4 group and 32.8±1.5 weeks in controls, which is the period where fetal neuroprotection is clinically important.

In this study, APGAR score at 1 minute and 5 minutes was significantly higher in the MgSO4 group. This finding is comparable to Gupta et al., who also observed better APGAR scores among neonates exposed to antenatal MgSO4 [8]. Better APGAR score may reflect improved immediate neonatal adaptation and better neurological responsiveness at birth. Rooting and suckling reflex and Moro's reflex were also significantly better in the MgSO4 group, supporting its possible protective effect on neonatal neurological function.

Fetal brain injury originates from inflammatory insult or mild hypoxic ischemic injury that triggers inflammation. Toll-like receptors on inflammatory cells of the placental membranes and decidua act as the inflammatory mediator leading to the induction and release of pro-inflammatory cytokines. The pro-inflammatory cytokines increase permeability of the developing fetal blood-brain-barrier (BBB), allowing recruitment of immune cells and increasing pro-inflammatory cytokines in the fetal brain. Fetal microglias are activated by

the pro-inflammatory cytokines, and these activated microglia lead to the excessive release of glutamate. Over activation of N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), and kainate receptors expressed on neurons and oligodendrocyte precursor cells (OPCs) leads to the accumulation of glutamate in the synaptic gap. Calcium ($Ca^{2+}$) and reactive oxygen species (ROS) also accumulate within the synaptic gap. Furthermore, NMDA receptors on microglia increase and exacerbate microglial activation. The over accumulation of glutamate, $Ca^{2+}$, and ROS leads to excitotoxic injury of neurons and OPCs culminating in fetal BBB damage, neural injury, and fetal brain damage.

Magnesium sulfate is a clinical fetal neuroprotective agent utilized in cases of imminent preterm birth. By blocking N-methyl-D-aspartate receptors, magnesium sulfate reduces glutamatergic signaling, which alters calcium influx, leading to a decrease in excitotoxicity.

NICU admission was significantly lower in the $MgSO_4$ group compared to controls. Similar findings were reported by Bansal and Desai, who observed reduced need for respiratory support, mechanical ventilation and shorter NICU stay among $MgSO_4$-exposed neonates [9]. In the present study, cranial USG showed no case of intraventricular haemorrhage or periventricular leukomalacia in the $MgSO_4$ group, while these complications were seen in controls. This finding supports the neuroprotective role of $MgSO_4$, as also reported by Ayed et al., who found lower risk of grade 3-4 IVH and white matter injury among $MgSO_4$-exposed preterm neonates [10]. Maternal side effects in the present study were mild, and no serious maternal complication was observed.

## 6. Conclusion

The present study shows that antenatal magnesium sulphate has a beneficial role as a neuroprotective agent in preterm deliveries. Neonates born to mothers who received $MgSO_4$ had significantly better APGAR scores, better rooting and suckling reflex, better Moro's reflex and lower NICU admission compared to controls. Neonatal morbidity, need for oxygen support, intraventricular haemorrhage and periventricular leukomalacia were also lower in the $MgSO_4$ group, although some differences were not statistically significant.

Maternal side effects were mild and manageable, and no serious adverse effect was observed. Therefore, $MgSO_4$ can be considered a safe, inexpensive and effective intervention for fetal neuroprotection in women at risk of preterm delivery. Its use should be encouraged in eligible women with proper monitoring of pulse, blood pressure, respiratory rate, urine output and deep tendon reflexes. Further studies with larger sample size and long-term neurodevelopmental follow-up are recommended to confirm its role in reducing cerebral palsy and long-term neurological disability.

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