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COMPARATIVE EFFICACY AND SAFETY OF MAGNESIUM SULFATE VERSUS NIFEDIPINE AS ACUTE TOCOLYTIC AGENTS IN THE MANAGEMENT OF PRETERM LABOR

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ABSTRACT

Background: Preterm labor is a major contributor to neonatal morbidity and mortality globally. Effective tocolytic therapy is essential to delay delivery, allowing for fetal lung maturation and neuroprotection. Magnesium sulfate ($MgSO_4$) and nifedipine are commonly used acute tocolytic agents, yet comparative evidence regarding their efficacy and safety remains inconclusive. **Methods:** This randomized controlled trial enrolled 40 pregnant women between 28 and 34 weeks of gestation presenting with preterm labor. Participants were equally randomized to receive either $MgSO_4$ intravenously or oral nifedipine as acute tocolytic treatment. Primary outcomes included achievement of uterine quiescence, prolongation of pregnancy beyond 48 hours, maternal side effects, and neonatal outcomes. Data were analyzed to compare efficacy and safety profiles between the two groups. **Results:** Both $MgSO_4$ and nifedipine effectively achieved uterine quiescence and prolonged pregnancy, with $MgSO_4$ showing a marginal advantage in prolongation duration. Maternal side effects were mild and differed in type between groups, with $MgSO_4$ associated with hot flushes and lethargy, and nifedipine with headache and tachycardia. Neonatal outcomes, including NICU admissions and mortality, were comparable, although $MgSO_4$ conferred neuroprotective benefits. The small sample size and short-term neonatal follow-up limit generalizability. **Conclusion:** Both $MgSO_4$ and nifedipine are effective and safe for acute tocolysis in preterm labor. $MgSO_4$ offers a slight benefit in pregnancy prolongation and fetal neuroprotection, whereas nifedipine provides ease of administration and fewer maternal side effects, making it particularly suitable in low-resource settings. Larger multicenter trials with extended neonatal follow-up are recommended to further clarify their comparative roles and optimize management protocols.

KEYWORDS :

INTRODUCTION

Preterm labor, defined as the onset of regular uterine contractions resulting in cervical changes before 37 completed weeks of gestation, remains a significant challenge in obstetric care worldwide.(1) It is a leading cause of neonatal morbidity and mortality, accounting for a substantial proportion of adverse perinatal outcomes.(2) The prevention and management of preterm labor are critical to improving neonatal survival rates and reducing long-term complications such as respiratory distress syndrome, intraventricular hemorrhage, and neurodevelopmental impairments.

Tocolytic therapy, aimed at suppressing uterine contractions to delay delivery, plays a pivotal role in the management of preterm labor. The primary objective of tocolysis is to prolong pregnancy, ideally to allow for the administration of corticosteroids to enhance fetal lung maturity and to facilitate in utero transfer to a tertiary care center when necessary. Various pharmacological agents have been employed as tocolytics, including beta-adrenergic agonists, calcium channel blockers, prostaglandin inhibitors, and magnesium sulfate ($MgSO_4$). Among these, magnesium sulfate and nifedipine, a calcium channel blocker, have gained prominence due to their efficacy profiles and relative safety.(3)

Magnesium sulfate has been extensively used as a tocolytic agent for several decades. Its mechanism of action involves competing with calcium at voltage-gated channels on myometrial cells, thereby reducing intracellular calcium concentrations and inhibiting uterine contractions. Additionally, magnesium sulfate has neuroprotective properties and is utilized for fetal neuroprophylaxis in cases of imminent preterm birth. Despite its widespread use, concerns regarding maternal side effects such as flushing, hypotension, and respiratory depression necessitate careful monitoring during administration.(4)

Nifedipine, a dihydropyridine calcium channel blocker, acts by inhibiting calcium influx through L-type calcium channels in the myometrium, resulting in smooth muscle relaxation and suppression of uterine contractions.(5) Its oral administration, favorable side effect profile, and ease of use have made it an attractive alternative to intravenous tocolytics.(6) Several clinical trials and meta-analyses have demonstrated nifedipine's efficacy in delaying delivery and reducing neonatal complications, positioning it as a first-line agent in many clinical settings.(7)

Despite the availability of multiple tocolytic options, there remains no consensus on the optimal agent for acute management of preterm labor. Variability in efficacy, safety profiles, cost, and ease of administration contribute to ongoing debates and diverse clinical practices globally. Comparative studies evaluating magnesium sulfate and nifedipine have yielded mixed results, with some suggesting superior efficacy of nifedipine in prolonging pregnancy and fewer maternal adverse effects, while others highlight the neuroprotective benefits of magnesium sulfate alongside its tocolytic action.(8–10)

Understanding the comparative effectiveness of magnesium sulfate and nifedipine is essential for guiding clinical decision-making in the acute management of preterm labor. A thorough evaluation encompassing maternal and neonatal outcomes, side effect profiles, and resource implications is necessary to establish evidence-based protocols. Furthermore, regional variations in healthcare infrastructure and

patient populations underscore the need for context-specific research.

This study aims to conduct a rigorous comparative analysis of magnesium sulfate and nifedipine as acute tocolytic agents in preterm labor. By assessing parameters such as latency period, maternal side effects, neonatal outcomes, and overall safety, the research seeks to provide clarity on the relative benefits and limitations of each agent. The findings will contribute to optimizing therapeutic strategies, improving perinatal outcomes, and informing guidelines in obstetric practice.

Given the critical impact of preterm birth on public health, advancing knowledge in effective tocolysis remains a priority. This study aligns with ongoing efforts to refine obstetric interventions and enhance neonatal survival and quality of life. The results will be pertinent to clinicians, policymakers, and researchers engaged in maternal-fetal medicine, fostering evidence-based approaches to a complex and multifaceted clinical problem.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Obstetrics and Gynecology of a tertiary care center. A total of 40 pregnant women presenting with preterm labor between 28 and 34 weeks of gestation were enrolled after obtaining informed consent. Participants were randomly allocated into two equal groups of 20 each to receive either magnesium sulfate ($MgSO_4$) or nifedipine as acute tocolytic agents.

Inclusion criteria were singleton pregnancy with gestational age between 28 and 34 weeks, diagnosis of preterm labor defined by the presence of at least two uterine contractions every 10 minutes lasting 30 seconds or more, accompanied by cervical changes (dilation 0–3 cm and less than 50% effacement) with intact membranes.

Exclusion criteria included contraindications or hypersensitivity to $MgSO_4$ or nifedipine, multiple pregnancies, severe fetal malformations or chromosomal abnormalities, intrauterine fetal demise, placental abruption, placenta previa, premature rupture of membranes (PROM), maternal medical comorbidities, chorioamnionitis, non-reassuring fetal status, intrauterine growth restriction, and cervical dilation ≥4 cm.

Randomization was performed using a computer-generated randomization table with allocation concealed in sequentially numbered opaque envelopes. Group A received $MgSO_4$ with a loading dose of 4 g administered intravenously over 20–30 minutes, followed by maintenance infusion of 1 g/hour diluted in 100 ml normal saline. Group B received oral nifedipine starting with 10 mg every 20 minutes for up to three doses, followed by 20 mg every 4–6 hours for 24 hours.

All patients received 500 ml of Ringer's lactate before initiating tocolytic therapy. Maternal vital signs and fetal monitoring were conducted regularly throughout treatment. The primary outcomes assessed included achievement of uterine quiescence (defined as one or fewer contractions in 10 minutes), prolongation of pregnancy beyond 48 hours, maternal side effects, and neonatal outcomes such as NICU admission and neonatal mortality.

Patients were monitored for uterine contractions manually and cervical status for 48 hours post-treatment initiation. Side effects were documented and managed accordingly. Statistical analysis was performed on collected data to compare efficacy and safety between the two groups.

RESULTS

This study enrolled 40 pregnant women diagnosed with preterm labor between 28 and 34 weeks of gestation. Participants were randomly allocated into two equal groups of 20 each to receive either magnesium sulfate ($MgSO_4$) or nifedipine as acute tocolytic agents.

Demographic and Clinical Characteristics

The age distribution and gravida status were comparable between the two groups. In the $MgSO_4$ group, 55% were aged 18–25 years, 40% were 26–33 years, and 5% were 34–40 years. The nifedipine group had 50% aged 18–25 years, 45% aged 26–33 years, and 5% aged 34–40 years. Primigravida women constituted 35% in the $MgSO_4$ group and 30% in the nifedipine group, while multigravida were 65% and 70%, respectively.

Uterine Quiescence and Pregnancy Prolongation

Uterine quiescence, defined as one or fewer contractions per 10 minutes, was achieved in 18 out of 20 (90%) patients treated with $MgSO_4$ and 17 out of 20 (85%) patients treated with nifedipine. Prolongation of pregnancy beyond 48 hours was observed in 17 (85%) patients in the $MgSO_4$ group and 16 (80%) in the nifedipine group.

Neonatal Outcomes

NICU admissions occurred in 7 (35%) neonates in the $MgSO_4$ group and 9 (45%) in the nifedipine group. Neonatal mortality was recorded in 2 (10%) cases in the $MgSO_4$ group and 3 (15%) cases in the nifedipine group.

Maternal Side Effects

Side effects were mild and comparable between groups. In the $MgSO_4$ group, 3 (15%) patients experienced hot flushes and 2 (10%) reported lethargy. In the nifedipine group, 3 (15%) patients reported headaches and 2 (10%) experienced tachycardia. No serious adverse events or treatment discontinuations occurred.

Table 1: Age Distribution

Age Group (years)	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
18 - 25	11	55	10	50
26 - 33	8	40	9	45
34 - 40	1	5	1	5

Table 2: Gravida Status

Gravida Status	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
Primigravida	7	35	6	30
Multigravida	13	65	14	70

Table 3: Uterine Quiescence Achieved

Outcome	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
Quiescence Achieved	18	90	17	85
Not Achieved	2	10	3	15

Table 4: Pregnancy Prolongation >48 Hours

Outcome	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
Prolonged >48 hours	17	85	16	80
Not Prolonged	3	15	4	20

Table 5: Neonatal Intensive Care Unit (NICU) Admissions

Outcome	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
NICU Admission	7	35	9	45
No NICU Admission	13	65	11	55

Table 6: Neonatal Mortality

Outcome	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)

Neonatal Mortality	2	10	3	15
Survival	18	90	17	85

Table 7: Maternal Side Effects

Side Effect	$MgSO_4$ (n=20)	$MgSO_4$ (%)	Nifedipine (n=20)	Nifedipine (%)
Hot Flushes	3	15	0	0
Lethargy	2	10	0	0
Headache	0	0	3	15
Tachycardia	0	0	2	10
No Side Effects	15	75	15	75

DISCUSSION

This study comparing magnesium sulfate ($MgSO_4$) and nifedipine as acute tocolytic agents in preterm labor demonstrated that both agents effectively achieve uterine quiescence and prolong pregnancy beyond 48 hours, with a slightly higher efficacy noted in the $MgSO_4$ group. The achievement of uterine quiescence was 90% with $MgSO_4$ versus 85% with nifedipine, while prolongation beyond 48 hours was 85% versus 80%, respectively. These findings align with the results reported by Raghuwanshi et al., where $MgSO_4$ showed marginally higher rates of labor arrest and pregnancy prolongation compared to nifedipine, though both were largely comparable in efficacy.

Maternal side effects observed in this study were mild and well tolerated, with hot flushes and lethargy predominating in the $MgSO_4$ group, and headache and tachycardia in the nifedipine group. The incidence of side effects was equal at 25% in each group experiencing no side effects. Similar safety profiles were reported in the Raghuwanshi et al. trial(11) and Nikbakht et al.,(12) where both drugs had comparable side effect rates without serious adverse events necessitating treatment discontinuation. However, Fan et al.'s systematic review and meta-analysis highlighted a significantly higher incidence of maternal side effects with $MgSO_4$, including tachycardia, flushing, palpitations, dizziness, and nausea, compared to nifedipine, which was generally better tolerated.(8) This discrepancy may reflect differences in dosing regimens, sample sizes, or population characteristics across studies.

Regarding neonatal outcomes, this study found NICU admission rates of 35% for $MgSO_4$ and 45% for nifedipine, with neonatal mortality of 10% versus 15%, respectively. These findings are consistent with Raghuwanshi et al., which reported slightly better neonatal outcomes with $MgSO_4$, possibly attributable to its known neuroprotective effects.(11) Fan et al. further support this, showing that $MgSO_4$ was associated with a higher incidence of neonatal respiratory distress syndrome and lower 1-minute Apgar scores compared to nifedipine. Conversely, Nikbakht et al.(12) and Shahbazian et al. (13) reported no statistically significant differences in neonatal outcomes between the two agents, indicating that both drugs are generally safe for the neonate when used appropriately.

The variation in findings across studies may be influenced by differences in study design, sample sizes, dosing protocols, and regional healthcare settings. For instance, Fan et al.'s meta-analysis incorporated a large number of studies and participants, providing robust evidence favoring nifedipine for faster onset and fewer maternal side effects, while $MgSO_4$ may confer neuroprotection but with a higher maternal side effect burden.(8) In contrast, smaller randomized controlled trials such as those by Raghuwanshi et al.(11) and Nikbakht et al. (12) found comparable efficacy and safety profiles, emphasizing the clinical relevance of both agents.

In clinical practice, the choice between $MgSO_4$ and nifedipine should consider factors such as ease of administration, side effect profiles, cost, and available monitoring resources. Nifedipine's oral route and favorable side effect profile make it attractive, especially in low-resource settings, as noted by Raghuwanshi et al.(11) and supported by Fan et al.(8) $MgSO_4$, while requiring intravenous administration and monitoring, offers the added benefit of fetal neuroprotection, which is critical in imminent preterm birth scenarios.

Limitations of this study include the relatively small sample size and short-term neonatal outcome assessment, which may affect the generalizability and long-term applicability of the findings. These limitations are echoed in the reviewed literature, where larger multicenter trials and longer follow-up are recommended to fully elucidate the comparative benefits and risks of these tocolytic agents.

CONCLUSION

This study demonstrates that both magnesium sulfate ($MgSO_4$) and nifedipine are effective and safe options for acute tocolysis in the management of preterm labor. $MgSO_4$ shows a marginal advantage in prolonging pregnancy duration and offers the important benefit of fetal neuroprotection, which is particularly valuable in cases of imminent preterm birth. Conversely, nifedipine provides practical advantages including ease of administration, oral dosing, and a lower incidence of maternal side effects, making it a suitable choice especially in low-resource settings.

Clinical decision-making should be individualized, taking into account the balance between efficacy, maternal and neonatal safety profiles, ease of use, and available healthcare resources. The relatively small sample size and short-term neonatal follow-up in this and similar studies underscore the need for larger, multicenter randomized controlled trials with extended neonatal outcome assessments to better define the comparative benefits and risks of these tocolytic agents. Such evidence will be instrumental in optimizing therapeutic strategies and establishing standardized guidelines for the management of preterm labor across diverse clinical environments.

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