The Egyptian Journal of Hospital Medicine (January 2025) Vol. 98, Page 1152- 1157

Nifedipine versus Magnesium Sulphate in Management of Preterm Labour

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ABSTRACT
Background: There is limited conclusive evidence that tocolysis directly benefits the baby, many obstetricians still use it to manage preterm labor, allowing time for steroid administration or facilitating the mother's transfer to a suitable medical facility. The relaxant effect of magnesium sulphate on uterine contractility has been widely reported. As magnesium is a calcium antagonist, by reducing intracellular calcium levels, these medications hinder the contraction process. Calcium channel blockers have shown greater efficacy in delaying preterm birth and lowering the incidence of neonatal respiratory distress compared to adrenergic-receptor agonists.
Objectives: This study aimed to compare the safety and the efficacy of oral nifedipine and intravenous magnesium sulphate in management of preterm labor.
Methods: This prospective study included 64 in-patient pregnant women who were diagnosed with preterm labor. They were divided into two groups; the first group is thirty-two pregnant women with preterm labor who received intravenous magnesium sulfate (group A) and the second group is thirty two pregnant women with preterm labor who received nifedipine orally (group B).
Results*:* There was significant difference between both groups as regards cervical effacement before and after treatment, time interval between start of tocolysis and the time of delivery and maternal side effects. So nifedipine is the suitable alternative for magnesium sulphate in management of preterm labor.
Conclusion: Our study demonstrated that oral nifedipine was an effective alternative to magnesium sulfate, offering comparable efficacy and a similar side effect profile for managing preterm labor.
Keywords: Preterm labour, Nifedipine, Magnesium sulphate.

INTRODUCTION
Even after accounting for congenital abnormalities as a cause of death, preterm labour accounts for just a small percentage of all newborns (5–11%) and causes almost 70% of all perinatal deaths in affluent nations [(1)].

It is estimated that preterm birth accounts for 75% of newborn fatalities and 50% of childhood neurological morbidities. It is also linked to long-term expenses following hospital release [(2)]. Infants born before their due date are more vulnerable to acute problems including sepsis, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, and neurodevelopmental conditions such cerebral palsy, long-term lung diseases, blindness, and deafness are examples of long-term [(3)]. Uterine contractions are suppressed by a variety of tocolytics, including nifedipine and magnesium sulphate [(4)].

Because it inhibits the contraction process and lowers intracellular calcium concentration, magnesium is a calcium antagonist. Comparing infants born at identical gestational ages who were not exposed to $MgSO_4$, it was discovered that those exposed to $MgSO_4$ in late pregnancy had a lower risk of developing cerebral palsy [(5)]. With magnesium sulphate medication, maternal side effects might range in severity from mild respiratory diseases to moderate flushes and somnolence [(6)].

Nifedipine as a Calcium-channel blocker is used increasingly as a tocolytic agent. Nifedipine acts by inhibiting calcium ions influx across the cell membrane, which decreases the tone in the smooth muscle [(7)]. Loading doses of 10–30 mg immediate-release nifedipine are administered orally; during the first hour, these doses are repeated every 15-20 minutes; thereafter, 10–20 mg are administered orally every 4-6 hours. Usually minor, flushing and other side effects of peripheral vasodilation are linked to nifedipine use. This had no effect on blood pressure in normotensive women without underlying cardiac illness since it increased heart rate and stroke volume in response [(8)].
This study aimed to compare the safety and the efficacy of oral nifedipine and intravenous magnesium sulphate in management of preterm labor.

PATIENTS AND METHODS
This is prospective case-control study was conducted at the Obstetrics and Gynecology Department in EL-Sahel Teaching Hospital, Cairo from December 2023 to November 2024.

Inclusion criteria:
1. Gestational age ranges between 28-34 weeks, it could be calculated either by last menstrual period or by Ultrasound in patients who are not sure of the last menstrual period.
2. Singleton gestations.
3. Intact amniotic membranes.

Received: 13/10/2024
Accepted: 13/12/2024

4. Documented regular painful uterine contractions at least 4 in 20 minutes or 8 in 60 minutes lasting from 10-30 seconds monitored by digital examination or tocogram and cervical change does not exceed 4 cm in dilatation.

Exclusion criteria:

1. Symptoms and signs of chorioamnionitis (maternal fever, fetal tachycardia, maternal tachycardia and uterine tenderness).
2. Non-reassuring of the heart rate tracings of the fetus.
3. Contra-indication to tocolysis such as placental abruption, acute fetal distress, and some medical disorder such as severe preeclampsia.
4. Contraindication to the specific used tocolytics, for example magnesium sulphate is contraindicated in cases with renal impairment and calcium channel blockers are contraindicated in cases suffering from heart failure.
5. Congenital fetal malformation
6. Pregnant female with previous uterine scar.

When preterm labour is diagnosed, the patient counseled about the study then the patients who agreed and consented to join the study were subjected to the following:

1. History taking for detection of inclusion and exclusion criteria such as history of previous preterm labour.
2. Complete general examination.
3. Local examination to detect cervical change as dilatation and effacement and to exclude vaginal bleeding and amniotic membrane rupture. An ultrasound examination was performed before the start of the treatment to calculate the amniotic fluid index (AFI), and to exclude contraindication for tocolysis such as congenital malformation.

Patients were divided into two groups:

Group A (32): Pregnant women with preterm labour who received intravenous magnesium sulfate infusion loading dose followed by a continuous infusion at rate of 1 g/h for 24 hrs.

Group B (32): Pregnant women with preterm labour who received nifedipine 10 mg oral tablet initially then repeated every 15 minutes till cessation of contraction then every 6- 8 hour.

The medications were given for a maximum of 48 hours. Uterine contractions were counted by palpation. Both groups received corticosteroid for enhancing lung maturity in the form of dexamethasone 8 mg every 12 hours for 48 hours.

Follow up: Patients who were on magnesium sulphate therapy were monitored by urine output as the amount of urine should not be less than 30 ml/hour, neurological reflexes especially deep tendon reflex and respiratory rate should be 12 or more/minute. Patients who were on nifedipine therapy were monitored by blood pressure and pulse.

Then they were discharged for follow up in outpatient clinic.

Therapy was considered unsuccessful:

1. If the medication was stopped or another agent added 48 hours before to arrest uterine contractions.
2. If tocolytics was continued after the initial 48 hours study in persistent preterm labor after 48 study period. Persistent preterm labor is defined as continued contractions of at least 8 per hour with cervical changes.
3. If pre-term labor is progressed.

Ethics approval and consent to participate: The study proposal was reviewed and approved by The General Organization for Teaching Hospitals and Institutes Research Ethics Committee no. HS000123 on 15/11/2023. Throughout the course of the investigation, the Helsinki Declaration was adhered to.

Statistical analysis

The statistical software for the social sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA) was used for coding and data entry. While quantitative variables, the mean and standard deviation were used to summarize the data. For categorical variables, the frequencies (number of cases) and relative frequencies (percentages) were used. The unpaired t test was used to compare the groups. The Chi square (χ^2) test was implemented to compare categorical data. When the anticipated frequency was below 5, the exact test was employed. To identify independent predictors of (SSI) logistic regression was done. $P \leq 0.05$ were considered statistically significant.

RESULTS

No significant difference between group A (Patients received magnesium sulfate) and group B (Patients received nifedipine) as regards demographic data, parity, gestational age and past history of preterm labor (Table 1).

Table (1): Demographic data

	(A)	**(B)**	t	p
Age (years)				
X±SD	**27.75±2.7**	27.9±2.9	0.13	0.89 NS
Range	**23-33**	23-34		
Weight (Kg)				
X±SD	71.6±6.9	71.7±8.0	0.06	0.94 NS
Range	60-85	55-87		
	(A) **N %**	**(B)** **N %**	**X2**	**P**
Parity				
PG	10 31.3	7 21.9	0.72	0.39 NS
Multi	22 68.8	25 78.1		
Gest. age				
X±SD	30.65±1.7	30.8±1.7	0.36	0.71 NS
Range	28-34	28-34		
History Of PTL				
-VE	22 68.8	24 75.0	0.31	0.57 NS
+VE	10 31.3	8 25.0		

No statistically significant difference between studied groups as regards cervical dilatation before and after admission (Table 2).

Table (2): Vaginal examination

	(A)	**(B)**	**X^2/t**	**p**
Before				
Closed	7 (21.9%)	6 (18.8%)	0.23	0.62
Effacement X±SD	50±7.6	49.6±7.2		
Range	40-60	40-60	0.18	0.85
After				
Closed	5 (15.6%)	4 (12.5%)	0.34	0.55
Effacement X±SD	57.4±17	60.7±18.4		
Range	40-90	40-90	0.69	0.49

There was statistically significant difference between studied groups as regards cervical effacement as effacement significantly increased on both groups but more in group B (Table 3).

Table (3): change of effacement before and after

Group			**Paired t**	**P**
A	**Before**	50±7.6	**2.612**	**0.018***
	After	57.4±17		
B	**Before**	49.6±7.2	**3.12**	**0.004***
	After	60.7±18.4		

No statistically significant difference between studied groups as regards cessation of uterine contractions (Table 4).

Table (4): Cessation of uterine contractions

	(A) N %	**(B)** N %	**X2**	**P**
Cessation of contraction				
No	7 21.9	6 18.7	0.09	0.75 NS
Yes	25 78.1	26 81.3		

There was a statistically significant difference between studied groups as regards time interval between start of tocolysis and the time of delivery (Table 5).

Table (5): Time (days) interval between start of tocolysis and the time of delivery

	(A) N %	**(B)** N %	**Mann Whitney**	**P**
Median	12	17.5		
Range	0.3-20	0.4-27	-2.05	0.039* Sig
X±SD	10.8±6.9	14.2±9.5		

There was a statistically significant difference between studied groups as regards treatment side effect (Table 6).

Table (6): Maternal S/E

	(A) N %		**(B)** N %		**X2**	**P**
No	25	78.1	26	81.3		
Flushing	7	21.9	0	0.0		
Hypotension	0	0.0	6	18.8	13.02	0.001* * HS

No statistically significant difference between studied groups as regards neonatal outcome (Table 7).

Table (7): Neonatal outcome

APGAR Score	**(A)**	**(B)**	**t**	**P**
1 st min				
X±SD	6.65±1.0	6.7±0.8		
Range	5-9	4-8	0.3	0.76 NS
5 min				
X±SD	9.2±0.8	9.3±0.9		
Range	6-10	6-10	0.63	0.52 NS

No significant difference between both groups as regards neonatal complication (Table 8).

Table (8): Neonatal complication

	A		**B**		**X^2**	**P**	**X^2**	**P**
	N	%	N	%				
GE	6	18.7	5	15.6	0.28	0.59		
Respiratory distress	11	34.3	12	37.5	0.14	0.71		
Hypoglycemia	4	12.5	3	9.3	0.47	0.49		
Septicemia	4	12.5	3	9.3	0.47	0.49		
Transient tachypnea	2	6.2	3	9.3	0.62	0.43		
Neurological complications	1	3.1	3	9.3	3.1	0.07		

DISCUSSION

Tocolytics come in a variety of forms and are used to stop uterine contractions. Many centers utilized nifedipine and magnesium sulphate [5].

In the present study no significant differences was noted between group A (patients received magnesium sulfate) and group B (patients received nifedipine) as regards treatment failure as uterine contractions didn't stop in 7 patients in group A & 6 patient in group B that was consistent with other study that found no significant difference between nifedipine and magnesium sulphate [9]. In a different trial, serious adverse effects such hypotension and flushing led to the discontinuation of treatment in 6% of patients receiving nifedipine and 2% receiving magnesium sulphate. Conversely, 20% and 16% of patients in the magnesium sulphate and nifedipine groups respectively, experienced a therapeutic failure due to the inability of contractions to stop, necessitating the administration of additional tocolytic drugs. There was no statistically significant difference in these traits between the two groups [10]**.** On the other hand, the results of 23 trials involving more than 2,000 pregnancies support our findings, which contradicts previous research on magnesium sulphate tocolysis for premature labour. The findings indicated that magnesium sulfate did not demonstrate a clinically meaningful tocolytic effect. It failed to significantly influence the rate of deliveries occurring within 48 hours, both overall and in subgroup analyses. Additionally, no notable improvements in neonatal outcomes were observed [11].

Our results showed that there were statistically significant differences between group A (patients received magnesium sulfate) and group B (patients received nifedipine) as regards time interval between start of tocolysis and the time of delivery. This is consistent with study that stated that the use of calcium channel blockers when compared with any other tocolytic agent resulted in a statistically significant decrease in the number of women giving birth within seven days of initiation of treatment and prior to 34 weeks gestation [12]. In other study, compared oral nifedipine with intravenous magnesium sulphate as tocolytic lines of treatment for preterm labour, 120 patients were randomly assigned (57 received nifedipine and 63 received magnesium sulfate). Delivery was delayed for 48 hours in 47 (82%) and 55 (87%) of the patients in the nifedipine and magnesium sulphate groups respectively [13].

Our results showed that there were statistically significant differences between group A (patients received magnesium sulfate) and group B (patients received nifedipine) as regards maternal side effects, as seven patients (21.9%) in group A had flushing and six patients (18.8%) in group B had hypotension. Hypotension set in two to four hours after the initiation of tocolysis, accounting for the majority of adverse medication events observed in women receiving nifedipine [14]. According to another study, one patient (2%) experienced acute flushing, and three patients (6%) experienced severe hypotension when taking nifedipine. The medicine was stopped as a result of these negative effects. The common adverse effects experienced by patients in the nifedipine group were four cases (8%) of headache and one case (2%) of flushing, respectively. Additionally, there was no statistically significant difference in any of the obstetric features [9].

In our study, there was no statistically significant difference between group A (patients received magnesium sulfate) and group B (patients received nifedipine) as regards neonatal outcome after delivery (APGAR score). A different study found that there were no statistically significant differences in neonatal weight, admissions to the neonatal intensive care unit, Apgar scores of less than seven at five minutes, neonatal sepsis, or perinatal mortality when comparing the use of calcium channel blockers with any other tocolytic agent. However, there was a statistically significant increase in gestation at birth and a decrease in neonatal respiratory distress syndrome (RDS), necrotizing enterocolitis, and intraventricular hemorrhage [15]. Also In other study, compared oral nifedipine with intravenous magnesium sulphate as tocolytic lines for treatment of preterm labour. In this study, the Apgar score was calculated for neonates at 1 minute and 5 minutes after delivery, which showed that there was no statistically significant difference between both groups [10]**.** In a different trial, the care of patients admitted with a diagnosis of premature labour was compared between magnesium sulphate and nifedipine. They came to the conclusion that in the treatment of premature labour, oral nifedipine would be a good substitute for magnesium sulphate, having similar side effects and effectiveness [9].

CONCLUSION

Our study revealed that oral nifedipine served as a viable alternative to magnesium sulfate, demonstrating equivalent effectiveness and a comparable side effect profile for treating preterm labor.

Availability of data and materials: Necessary datasets validating the findings of this research can be acquired from the relevant author upon a valid request. Data access was subject to institutional data-sharing policies and ethical guidelines.

Funding: No funds were received.

Authors' contributions: H.M.E; conceptualization, methodology, software. A.M.S, M.A.E; data curation & writing original draft preparation. S.B. & A.M.S; visualization and investigation. H.M.E; software &

validation. F.M.S; writing-reviewing and editing. S.B; supervision. All authors read and approved of the final manuscript.

Conflict of interest: There are no conflicts of interest.

Acknowledgements: The authors express gratitude to Dr. Mossad Abd El Hamyd and Mohamed Shahen for their valuable assistance and guidance throughout the study time.

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