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ORIGINAL ARTICLE

Role of Nifedipine, Magnesium Sulphate and Nitroglycerine Dermal Patch in Preterm Labour

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Abstract

Background: ***The combination of oral nifedipine and transdermal nitroglycerine is an effective method for managing premature labor. Tocolysis plays a critical function in preterm labor cessation.***

Aim: ***To assess the efficiency of dermal patches containing nifedipine, magnesium sulfate, and nitroglycerine in the management of premature labor.***

Patients and methods: ***This is a randomized controlled research performed on 150 preterm labor women receiving nifedipine, magnesium sulfate and nitroglycerine who attended the Department of Gynecology and Obstetrics at El Hussein University Hospital during the period from January 2022 to February 2023.***

Results: ***In terms of birth weight and gestational age at delivery, group II significantly increased more than groups III and I.Furthermore, group I experienced a significantly longer NICU stay than groups II and III. In contrast to groups II and III, inpatient admissions to the NICU and respiratory distress in infants were more prevalent in group I. Although there was no significant distinction identified among the groups analyzed with regard to infant fatalities, hemorrhage, bleeding, or modes of delivery, group II exhibited a higher incidence of CS in contrast to groups I and III, and group III had a higher incidence of NVD than groups I and II. In comparison to groups I and II, group III exhibited the highest frequency of PROM.***

Conclusions: ***For the treatment of preterm labor, oral nifedipine is a good substitute for magnesium sulfate, having the same effectiveness and adverse effects.***

Keywords: Dermal patch; Magnesium sulphate; Nifedipine; Nitroglycerine; Preterm labour

1. Introduction

One of the biggest problems facing obstetricians globally is preterm birth. An estimated thirteen million infants are born prematurely each year before the full 37 weeks of gestation have passed. It is the main factor contributing to newborn mortality and morbidity. Two-thirds of cases of preterm birth include preterm labor that develops after spontaneous labor begins.[1]

The cause of preterm labor is still unknown in 45–50% of instances. Therefore, efforts at prevention have not yielded much hope, yet it is still imperative that preterm labor be stopped. The survival of a premature newborn and the therapeutic options for managing preterm labor provide challenges for obstetricians.[2]

Preterm labor causes long-term morbidities in infants, such as non-neurological conditions like retinopathy of prematurity and bronchopulmonary dysplasia, as well as neurodevelopmental disabilities, cerebral palsy, seizure disorders, blindness, and deafness.[3] By stopping preterm labor, we can lessen the financial cost of preterm delivery, the worry and shame that mothers feel about the reason behind their baby's premature arrival, and the care that preterm birth brings to families and communities.[4]

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Nifedipine, a calcium channel blocker, is one of the most successful treatments for preterm labor and has been linked to better neonatal outcomes. It works much better at extending pregnancy than 48 hours and effectively postponing delivery for up to 7 days.[5] Because of its safety profile and few adverse effects on mothers and fetuses, nitroglycerine patches have also been claimed to be an effective tocolytic medication.[6]

The goal is to identify substitutes that are more effective at extending pregnancy, safer, and better tolerated. It has been demonstrated that nifedipine and 2 nitroglycerine are both beneficial in premature labor. Few studies, however, have directly contrasted the effectiveness and safety of transdermal nitroglycerine patches vs. oral nifedipine as tocolytic drugs in premature labor.[7]

For almost 25 years, obstetricians have utilized magnesium sulfate to treat premature labor. At greater dosages, magnesium sulfate effectively delays birth for at least 48 hours in patients with premature labor. This medication was first used to treat premature labor since it was found to reduce the frequency and severity of contractions in preeclamptic women going into labor.[8]

Although there have been notable improvements in the last ten years in the care of preterm infants, a considerable portion of perinatal morbidity and death is still attributable to the aftereffects of preterm labor. Preterm labor should be suppressed, especially in units lacking easy access to facilities for neonatal intensive care.[9]

This study compares the effectiveness of nifedipine, magnesium sulfate, and nitroglycerine dermal patch in treating premature labor.

2. Patients and methods

This is a randomized controlled experiment that was conducted from January 2022 to February 2023 on 150 preterm labor women who were given nitroglycerine, magnesium sulfate, and nifedipine at El Hussein University Hospital's Department of Gynecology and Obstetrics.

2.1.Ethical consideration: The Al-Azhar Faculty of Medicine in Cairo, Egypt's Ethical Scientific Committee, accepted the study. Every participant requested written informed consent in line with the 2013 revisions to the Helsinki guidelines.

Inclusion criteria: We involved individuals who had a singleton pregnancy (confirmed on ultrasonography), uterine contractions due to PLT, and cervical softening or effacement of a maximum of four centimeters of dilatation (determined by per abdominal examination and pelvic examination). Individuals' gestational ages were determined by the first day of their last menstrual period. A pregnant woman in preterm labor with gravity to gravida 5 was also included in the group.

Exclusion criteria: We excluded all patients who had intrauterine death (IDD) confirmed by USG, vaginal bleeding from placenta previa or placental abruption (defined by per speculum examination), known fetal abnormalities (confirmed by USG), hypertension (BP >130/90mmHg at least 2 readings taken 6 hours apart), and premature rupture of membrane (PPROM).

The participants were separated randomly by utilizing the lottery method in 3 groups:

Group I (Nifedipine): comprised 50 preterm women who received 10 mg of nifedipine orally every 15 minutes, up to a maximum of 10 doses; after 10 doses, 20 mg of nifedipine orally every 8 hours for 48 hours was administered.

Group II (Nitroglycerine): comprised 50 preterm women who received a 10 mg nitroderm patch and were watched to see if their palpable contractions stopped. Tocolysis was deemed effective when it came to extending pregnancy for at least 48 hours.

Group III (Magnesium Sulfate): included 50 preterm women who received a loading dose of 4 grams of magnesium sulfate intravenously over 20 minutes and then a 2-gram per hour infusion until uterine quiescence was reached.

All patients were subjected to: The chosen groups' initial parameters comprised body mass index, parity, weight, height, gestational age, and mother's age. Vital indicators include pulse, systolic, and diastolic blood pressure—risk factors for the present pregnancy's preterm birth. Delivery is delayed by 48 hours, 7 days, or longer. The duration of the uterine contractions until they stop. Medication side effects include lightheadedness, nausea, vomiting, heat flashes, impaired vision, and muscle weakness.

Maternal and Neonatal outcomes are represented by Time of delivery, average gestational age extension, drug withdrawal due to adverse effects, Baby birth weight, respiratory distress in neonates, morbidity and mortality in neonates.

2.2.Sample size estimation:

Based on the previous study by Zulfiqar et al.,[10], They concluded that nitroglycerine patches work just as well as nifedipine to prolong pregnancy and suppress premature labor. In order to achieve 80% power, detect a difference of -9.0 between the alternative hypothesis with a mean of 49.5 and the null hypothesis with a mean of 40.5, with estimated group standard deviations of 10.3 and 14.9, and with a significance level (alpha) of 0.05, a minimum sample size of 150 patients (50 for each group) was needed.

2.3.Statistical analysis

MICROSOFT EXCEL 2019 and the SPSS V.25 application for MICROSOFT WINDOWS 10 were the standard computer programs used to tabulate and statistically evaluate the results. The following test was included in the descriptive statistic: For

quantitative data, the data was described using mean () SD; for qualitative data, frequency and proportion were used, and the mean was calculated by dividing the total number o observations by the sum of all the observations On the other hand, the standard deviation gauges how widely different kinds of things are differen from one another. One test used in analytica statistics was this one: Mann-Whitney test (U) Chi-Squared (x2), and one-way ANOVA (F). I value ≤0.05 is regarded as a significant threshold.

3. Results

El Hussein University Hospital received 211 inquiries concerning the use of nifedipine magnesium sulfate, and nitroglycerine derma patches in preterm labor. One hundred fifty participants were willing to participate in the research and were split into 3 groups; 17 people were eliminated from the trial (29 patients denied consent, and 32 patients did not match the inclusion requirements). Groups I and II go nifedipine (n = 50), magnesium sulfate (n = 50), and nitroglycerine dermal patch (n = 50), respectively, figure 1.

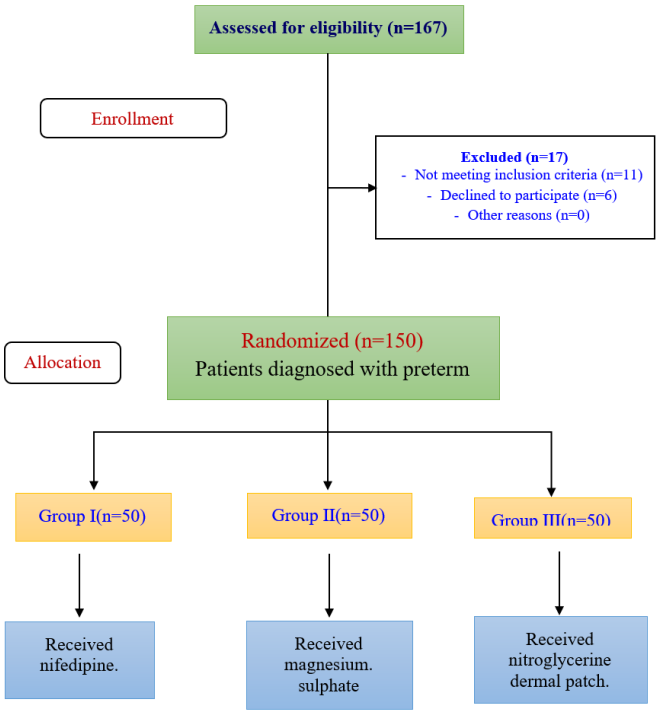

Figure 1. Flowchart of patients with preterm labour.

Table 1. Demographic data and history among the studied groups (N=150).

VARIABLES	GROUP I (N=50)		GROUP II (N=50)		GROUP III (N=50)		F	*P-VALUE*
AGE/YEAR							2.79	0.350
MEAN± SD	28.62±6.36		37.56±4.77		29.34±4.82			
RANGE	19-39		29-45		22.00-40			
POST HOC: P_1<0.001, P_2=0.067, P_3<0.001								
WEIGHT/KG								
MEAN± SD	82.64±9.03		93.22±11.11		84.42±8.01		17.87	<0.001
RANGE	93.22-11.11		70-120		70-100			
POST HOC: P_1<0.001, P_2=0.504, P_3<0.001								
HEIGHT/M								
MEAN± SD	165.90±6.41		159.42±5.10		163.66±3.11		21.15	<0.001
RANGE	160-185		150-168		159-168			
POST HOC: P_1 <0.001, P_2<0.001, P_3=0.028								
GESTATIONAL AGE/WEEK								<0.001
MEAN± SD	32.92±2.55		34.82±1.49		33.26±2.42		10.53	
RANGE	28-36		30-36		28-36			
POST HOC: P_1 <0.001, P_2=0.443, P_3=0.001								
GRAVIDITY								<0.001
MEAN± SD	3.22±1.22		4.28±1.14		3.62±0.96		16.69	
RANGE	1-5		3-6		1-5			
POST HOC: P_1<0.001, P_2=0.654, P_3<0.001								
PARITY								<0.001
MEAN± SD	1.92±0.94		3.00±0.97		2.06±0.93		19.13	
RANGE	0-3		2-5		0-4			
POST HOC: P_1<0.001, P_2=0.462, P_3<0.001								
MODE OF DELIVERY	N	%	N	%	N	%	X^2	
CS	34	68	39	78	22	4	13.148	0.001
NVD	16	32	11	22	28	56		

PREVIOUS DELIVERY	30	60	40	80	19	38	20.49	<0.001
CS	16	32	10	20	28	56		
NVD	4	8	0	0	3	6		
PRIME								
PREVIOUS PRETERM DELIVERY							1.363	0.506
NO	38	76	40	80	35	70		
YES	12	24	10	20	15	30		

CS: Cesarean, NVD: Normal vaginal delivery F: One way ANOVA X2: Chi square

P1: group 1 compared to group II, P2: group I compared to group III, P3: group II contrasted with group III

In terms of weight, height, gravidity, and parity, group II significantly increased more than groups III and I. However, group II and III saw a much lower rate than group I. In terms of delivery modality and prior delivery, group II had more common CS than groups I and III, group III had more common NVD than groups I and II, and group I had more common prime than groups III and II. However, age and prior preterm delivery did not significantly differ between the groups under study.

Table 2. Vital signs and risk factors among the studied groups (N=150).

VARIABLES	GROUP I (N=50)	GROUP II (N=50)	GROUP III (N=50)	U	P-VALUE
SBP MEAN± SD RANGE	119.80±15.05 100-150	135.00±9.95 120-150	123.60±6.15 110-130	25.84	<0.001
		POST HOC: P_1<0.001, P_2=0.082, P_3<0.001			
DBP MEAN± SD RANGE	79.20±12.43 60-100	93.00±6.23 80-100	82.70±3.07 80-90	38.10	<0.001
		POST HOC: P_1<0.001, P_2<0.001, P_3=0.035			
PULSE MEAN± SD RANGE	87.44±3.00 80-90	88.50±2.50 80-92	88.80±1.48 85-90	4.39	0.014
		POST HOC: P_1=0.03, P_2<0.001, P_3=0.535			

RISK FACTORS	19	38	18	36	41	82	$X^{2=}$	<0.001
NO	31	62	32	64	9	18	70.598	
YES	7	22.6	8	25	3	33.3		
DIABETIC	5	16.1	8	25	6	66.7		
PREECLAMPSIA	7	22.6	16	5	0	0		
PROM	12	38.7	0	0	0	0		
HYPERTENSION								

SBP: Systolic blood pressure DBP: Diastolic blood pressure

Regarding SBP and DBP, group II significantly increased more than groups III and I. Regarding pulse, there was a significant increase in group III in contrast to groups II and I. In terms of risk factors, however, group III had a higher prevalence of diabetes and preeclampsia than groups I and II, while group I had a higher frequency of PROM than groups II and III.

Table 3. Completion of antenatal steroid cover and Side effect of drugs among the studied groups (N=150).

VARIABLES	GROUP I (N=50)		GROUP II (N=50)		GROUP III (N=50)		X^2	P-VALUE
COMPLETION OF ANTENATAL STEROID COVER	2	4	8	16	7	14	4.113	0.128
NO	48	96	42	84	43	86		
YES								
SIDE EFFECT OF DRUGS	43	86	42	84			41.251	<0.001
NO	7	14	8	16	38	76		
YES	5	71.43	2	25.0	12	24		
TACHYCARDIA	2	28.57	6	75.0	5	41.67		
HYPOTENSION					7	58.33		

X2: Chi square test

Regarding the examined groups, there was no significant variation in the completion of antenatal steroid cover (P>0.05). However, when it came to the drug side effect profile, group II had more tachycardia than groups III and I, and group I had more hypotension than groups III & II.

Table 4 Maternal and neonatal outcome among the studied groups (N=150).

VARIABLES	GROUP I (N=50)		GROUP II (N=50)		GROUP III (N=50)		F	P-VALUE
GESTATIONAL AGE AT DELIVERY/WEEKS	33.92±2.42		34.88±1.48		33.12±2.34		4.46	0.013
MEAN± SD	29 -36		30-36		28-36			
RANGE								
POST HOC: P_1=0.025, P_2=0.15, P_3=0.005								
HEMORRHAGE	2.00±0.00		2.00±0.00		2.00±0.00		---	---
MEAN± SD	2-2		2-2		2-2			
RANGE								
BLEEDING	2.00±0.00		2.00±0.00		2.00±0.00		---	---
MEAN± SD	2-2		2-2		2-2			
RANGE								
MODE OF DELIVERY	34	68	43	86	19	38	25.52	<0.001
CS	16	32	7	14	31	62		
NVD								
PROM	37	74	26	52	19	38	13.28	0.001
NO	13	26	24	48	31	62		
YES								
BIRTH WEIGHT (KG)	2.95±0.41		2.47±0.50		2.50±0.48		15.54	<0.001
MEAN± SD	2-3.6		1.5-3		1.4-3			
RANGE								
POST HOC: P_1 <0.001, P_2=1.00, P_3<0.001								
DURATION OF NICU STAY /DAYS	2.00±3.08		11.62±11.08		1.88±3.77		32.008	<0.001
MEAN± SD	0-7		0-28		0-14			
RANGE								
POST HOC: P_1 <0.001, P_2<0.001, P_3=0.932								
NICU ADMISSION	N	%	N	%	N	%	X^2	<0.001
NO	31	62	15	30	34	68	16.768	
YES	19	38	35	70	16	32		
NEONATAL RESPIRATORY DISTRESS	47	94	34	68	43	86	12.376	0.002
NO	3	6	16	32	7	14		
YES								
NEONATAL DEATHS	47	94	42	84	43	86	2.652	0.266
NO	3	6	8	16	7	14		
YES								

As regard birth weight and gestational age at delivery, group II significantly increased more than groups III and I. Furthermore, group I experienced a significantly longer NICU stay than groups II and III. Compared to groups I and III, group II had a higher frequency of NICU admissions and newborn respiratory distress. While there was no significant variation amongst the groups under study in terms of hemorrhage, bleeding, or infant fatalities, in terms of mode of delivery, group II had more cases of CS than groups I and III, and group III had more cases of NVD than groups I and II. Compared to groups I and II, group III had the most common PROM.

Table 5 Means and medians for survival time using Kaplan-Meier survival analysis among the studied groups.

Means and Medians for Survival Time								
Groups	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
Group I	4.122	0.276	2.860	5.623	6.000	1.088	3.868	8.132
Group II	1.997	0.570	0.880	3.115	1.000	0.120	0.764	1.236
Group III	3.400	0.766	2.620	3.940	4.000	0.207	3.594	4.406
Overall	3.150	0.274	2.613	3.687	3.000	0.732	1.566	4.434

According to Kaplan-Meier survival curves, the estimated mean survival times were 4.122±0.766 for the group III, followed by 3.40±0.276 months for the group I, then 1.97±0.570 for group II. Cases in group II and III start higher survival rate than cases in group I but the difference between them did not reach to significant level (log-rank test, P=0.863).

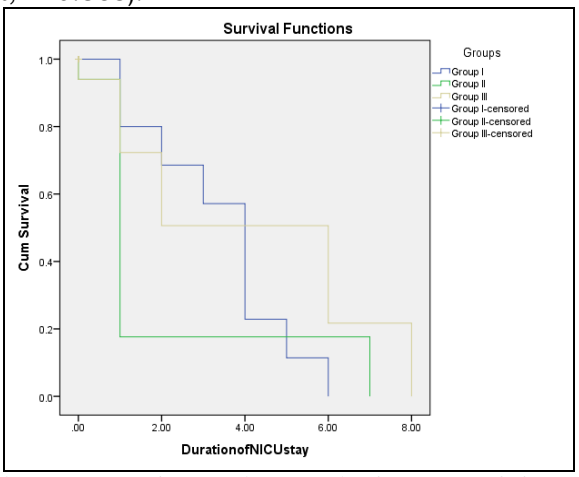

Figure 2. Kaplan-Meier survival curves of the studied groups.

Although the survival rates of cases in groups II and III begin greater than those in group I, the variance among the two did not become statistically significant (log-rank test, P=0.863).

4. Discussion

According to the current study, group II had significantly higher levels of age, weight, height, gravidity, and parity than groups III and I. However, in contrast to Group I, there was a considerable decline in Groups III and II. In terms of delivery mechanism and prior delivery, Group II had more common CS than Groups I and III, Group III had more common NVD than Groups I and II, and Group I had more common prime than Groups III and II. However, there was no discernible difference amongst the groups under study in terms of prior preterm deliveries.

According to a review of the literature, a study found that the gestational age at admission was between 24 & 34 weeks in a study by Amorim et al.[11] The entrance gestational age of each research group varied significantly.

In the trial by Taherian and Dehdar,[12], the gestational age varied from twenty-six to thirty-six weeks. In the Kashanian et al.[13] study, the gestational age varied from twenty-six to thirty-four weeks. According to the results of the current investigation, Group II had significantly higher SBP and DBP than Groups III and I. However, group III's pulse was significantly higher than those of groups II and I.

In a previous study by Kaur et al.,[14] discovered that headache was observed in the NTG group (42%), compared to the nifedipine group (6%). Palpitations occurred in 6% of women, tachycardia in 20% of Group A, and hypotension in 2% of women; in Group B (nifedipine), these symptoms were seen in 28%, 4% and 10% of women, respectively.

In the research by Amorim et al.,[11] There was no statistically significant disparity in the overall frequency of indicated adverse effects among the two treatment groups; however, over 30% of patients taking nitroglycerine and 8.3% of individuals on nifedipine reported experiencing headaches.

Based on risk factors, group III had a higher prevalence of diabetes and preeclampsia than groups I and II did. In contrast, Group I had a higher prevalence of PROM than Groups II and III, with Group II having the highest prevalence of PROM. In terms of the medication's adverse effect

profile, Group II experienced more tachycardia than Groups III and I, whereas Group I experienced more hypotension than Groups III and II. However, when it came to the investigated groups' completion of antenatal steroid cover, there was no discernible difference.

In this research, Group II had a significantly higher gestational age at delivery than Groups I and III. In terms of delivery mechanism, Group II had more common CS than Groups I and III, whereas Group III had more common NVD than Groups I and II. Compared to Groups I and II, Group III had the most prevalent PROM. However, when it came to hemorrhage and bleeding, there was no discernible variation among the groups under study.

Concerning birth weight, Group II significantly increased more than groups III and I did in the current study. Furthermore, Group I experienced a significantly longer NICU stay than groups II and III. Contrasted with groups II and III, group I had a higher frequency of NICU admissions and infant respiratory distress ($P<0.05$). However, there was no discernible variation in neonatal fatalities between the groups under study ($P>0.05$).

5. *Conclusion*

For the treatment of preterm labor, oral nifedipine is a good substitute for magnesium sulfate, having the same effectiveness and adverse effects.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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