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EFFICACY AND SAFETY OF NIFEDIPINE IN SUPPRESSION OF PRETERM LABOR

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Abstract

Objective: *To determine efficacy and complications of nifedipine in suppression of preterm labor*

Place of study: *The study was conducted at Department of Obstetrics & Gynecology, Allama Iqbal Memorial Teaching Hospital, Sialkot.*

Duration of study: *July 13, 2024 January 12, 2025*

Study design: *Descriptive case series*

Methods: *A total of 157 eligible patients received a first dose of 20mg tablet nifedipine orally. Their uterine contractions were monitored, and nifedipine-related complications like transient hypotension, cesarean delivery, and fetal distress were assessed. Data analysis, stratified by maternal age, gestational age, onset of contractions duration, and cervical length, was conducted using SPSS v22 and Chi-square test post-stratification. A p-value of ≤0.05 indicated significance.*

Results: *157 women with preterm labor participated. Mean maternal age: 28.29±6.306 years. Mean gestational age: 31.24±2.285 weeks. Mean cervical length: 2.6±0.75 cm. Mean onset of contractions: 25.3±5.3 minutes. 81.5% achieved successful tocolysis, 3.8% had transient hypotension, and 46.5% underwent c-sections.*

Conclusion: *Nifedipine is a safe and effective tocolytic for suppressing uterine contractions, with rare side effects. Delaying delivery by over 2 days helps in prescribing corticosteroids, transferring the mother to a tertiary care center, thus reducing perinatal complications and mortality.*

INTRODUCTION

Obstetricians and other medical professionals encounter a major challenge with preterm birth, a leading cause of infant mortality globally, leading to high long-term medical costs and disability rates in all nations.[1-2] In Pakistan, a study found preterm delivery at 21%, while another study reported 5-10% for deliveries after 37 weeks and 1-2% before 32 weeks.[3-4] Various health issues, such as broncho-pulmonary dysplasia, necrotizing enterocolitis, intra-ventricular hemorrhage, retinopathy of prematurity, and congenital malformations, are linked to preterm birth. Additionally, pre-discharge infant mortality, expected in up to fifty percent of cases, is a tragic consequence of premature delivery.[5]

Managing preterm labor aims to reduce perinatal risks by using medications such as beta-2 agonists, calcium

channel blockers, and others to delay premature delivery; however, their restricted use is commonly due to cost and side effects.[6-7] An ideal tocolytic agent should be effective, affordable, have minimal side effects, be easy to administer, and require less monitoring.[7-9] Nifedipine, a calcium channel blocker, is a safer and effective choice for suppressing preterm labor. Recent studies found success rates of 73.3% and 76.7% in patients treated with nifedipine for tocolysis.[10-11]

In a comparison study, nifedipine showed higher successful tocolysis rates than placebo (88.3% vs. 69.9%). However, nifedipine group had more complications like hypotension, tachycardia, cesarean delivery (53.5%), and fetal distress (8.08%), making it relatively unsafe. Failed tocolysis rate was 9.7%.[12]

Previous literature shows promising results regarding the efficacy of nifedipine for suppression of preterm labor. There is no clear cut choice for first line tocolytic medication as per American College of Obstetrics and Gynecology (ACOG).[13] For this reason every institution uses different agent for tocolysis in preterm labor. At our center, terbutaline is most frequently used tocolytic agent. Therefore, this study was conducted to determine efficacy and complications of nifedipine in suppression of preterm labor so that the decision of using nifedipine as a tocolytic drug of first choice can be made based on evidence.

METHODS

The study at the Department of Obstetrics & Gynecology, Allama Iqbal Memorial Teaching Hospital, Sialkot, took place from July 13, 2024, to January 12, 2025, after obtaining ethical approval and informed consent. It included women ages 15-45 with singleton pregnancies and preterm labor, following specific criteria. Patients were excluded for history of nifedipine use, hypersensitivity to nifedipine, fetal distress, hypotension, cervical dilation ≥3 cm, or intrauterine fetal death confirmed by an obstetrician. Preterm labor was defined as onset between gestational weeks 28 and 34, with regular painful contractions lasting over one hour, occurring at least every 10 minutes, with effacement, intact membranes, and cervical dilation less than 3 cm as confirmed by a consultant obstetrician. A sample size of 157 was calculated using the WHO sample size calculator based on a 95% confidence level, an absolute precision of 3%, and an expected frequency of transient hypotension at 3.8%.[12]

After obtaining consent, baseline characteristics, including maternal age, gestational age, cervical length, and duration of uterine contractions onset (in minutes), were documented. Patients were educated about nifedipine therapy risks and benefits. Each patient received a 20 mg oral dose initially, continuously monitored by a consultant obstetrician using external fetal monitoring. A second dose was given if contractions persisted after 30 minutes and a third dose after 60 minutes. Blood pressure was monitored at intervals. Complications from nifedipine therapy were assessed and monitored for 48 hours, including transient hypotension, cesarean delivery for fetal distress defined as specific fetal heart rate thresholds on CTG readings.

In cases of tocolysis failure leading to preterm delivery, infants received NICU care supervised by a consultant pediatrician. Comprehensive data were methodically recorded. Patients unresponsive to nifedipine were given terbutaline. Antenatal steroids were administered. SPSS v.22 analyzed variables such as maternal age and gestational age. Categorical data like successful tocolysis and complications were presented in frequency percentages. Stratification was based on various factors. Post-stratification analysis used the Chi-square test with significance at ≤0.05.

RESULTS

One hundred fifty-seven women with preterm labor were studied. Mean age was 28.29±6.306 years. Most patients (61.8%) were 18-30 years old. The average gestational age was 31.24±2.285 weeks, with 41.4% at 28-30 weeks and 58.6% at 31-34 weeks. Mean cervical length was 2.6±0.75 cm, with 44.6% having ≤2 cm and 55.4% >2 cm. The average onset of uterine contractions was 25.3±5.3 minutes. Majority (59.9%) had onset ≤20 minutes, with 81.5% achieving successful tocolysis and 18.5% not. Complications included transient hypotension (3.8%), c-sections (46.5%), and fetal distress (7.6%) **(Table-1)**. Stratification of efficacy and complications with respect to different variables has been shown in tables below **(Table-2 to 5)**.

Table-1: Frequency distribution of different variables

Category	Frequency	Percent
Maternal Age (18-30 years)	97	61.80%
Maternal Age (31-40 years)	60	38.20%
Total	157	100.00%
Gestational Age (28-30 weeks)	65	41.40%
Gestational Age (31-34 weeks)	92	58.60%
Total	157	100.00%
Cervical Length (≤2 cm)	70	44.60%
Cervical Length (>2 cm)	87	55.40%
Total	157	100.00%
Onset of Uterine Contractions (≤20 min)	53	32.30%
Onset of Uterine Contractions (>20 min)	111	67.70%
Total	164	100.00%
Successful Tocolysis (Yes)	128	81.50%
Successful Tocolysis (No)	29	18.50%
Total	157	100.00%
Transient Hypotension (Yes)	6	3.80%
Transient Hypotension (No)	151	96.20%
Total	157	100.00%
C-Section Delivery (Yes)	73	46.50%
C-Section Delivery (No)	84	53.50%
Total	157	100.00%
Fetal Distress (Yes)	12	7.60%
Fetal Distress (No)	145	92.40%
Total	157	100.00%

Table-2: Stratification of efficacy and complications with respect to maternal age groups

Variables		Maternal age groups		p-value
		18-30 years	31-40 years	
Efficacy	Yes	78(80.4%)	50(83.3%)	0.647
	No	19(19.6%)	10(16.7%)	
Transient hypotension	Yes	2(2.1%)	4(6.7%)	0.144
	No	95(97.9%)	56(93.3%)	
C-section	Yes	43(44.3%)	30(50.0%)	0.489
	No	54(55.7%)	30(50.0%)	
Fetal distress	Yes	6(6.2%)	6(10.0%)	0.382
	No	91(93.8%)	54(90.0%)	

Table-3: Stratification of efficacy and complications with respect to maternal gestational age groups

Variables		Maternal gestational age groups		p-value
		28-30 years	31-34 years	
Efficacy	Yes	50(76.9%)	78(84.8%)	0.211
	No	15(23.1%)	14(15.2%)	

Transient hypotension	Yes	4(6.2%)	2(2.2%)	0.200
	No	61(93.8%)	90(97.8%)	
C-section	Yes	34(52.3%)	39(42.4%)	0.220
	No	31(47.7%)	53(57.6%)	
Fetal distress	Yes	9(13.8%)	3(3.3%)	0.014
	No	56(56.2%)	89(96.7%)	

Table-4: Stratification of efficacy and complications with respect to cervical length

Variables		Cervical length		p-value
		≤2 cm	>2 cm	
Efficacy	Yes	61(87.1%)	67(77.0%)	0.104
	No	9(12.9%)	20(23.0%)	
Transient hypotension	Yes	2(2.9%)	4(4.6%)	0.572
	No	68(97.1%)	83(95.4%)	
C-section	Yes	31(44.3%)	42(48.3%)	0.618
	No	39(55.7%)	45(51.7%)	
Fetal distress	Yes	6(8.6%)	6(6.9%)	0.695
	No	64(91.4%)	81(93.1%)	

Table-5: Stratification of efficacy and complications with respect to duration of onset of uterine contractions

Variables		Duration of onset of uterine contractions		p-value
		≤20 minutes	>20 minutes	
Efficacy	Yes	76(80.9%)	52(82.5%)	0.789
	No	18(19.1%)	11(17.5%)	
Transient hypotension	Yes	5(5.3%)	1(1.6%)	0.232
	No	89(94.7%)	62(98.4%)	
C-section	Yes	45(47.9%)	28(44.4%)	0.673
	No	49(52.1%)	35(55.6%)	
Fetal distress	Yes	9(9.6%)	3(4.8%)	0.266
	No	85(90.4%)	60(95.2%)	

DISCUSSION

Premature birth is a significant challenge for expectant mothers and medical professionals due to its associated risks and complications. It occurs in 7 to 9 percent of live births, with a troubling increase noted in recent years. Preterm labor is linked to higher rates of infant mortality and morbidity, as well as an increased risk of birth defects that can impact newborn health significantly.[14]

The prevalence of neurological and sensory disorders is notably higher among gestationally immature neonates born before 31 to 32 weeks, a critical period for heightened risk factors. It is essential in the medical field to promptly identify and acknowledge high-risk female patients for preterm birth, implementing timely prevention strategies to address vulnerabilities effectively.[15]

Nifedipine, a calcium channel blocker used in clinical practice, shows promise as a more effective and better-tolerated tocolytic agent than other options. Research indicates that nifedipine effectively reduces uterine contractions with fewer side effects, allowing for a delay in delivery of over 48 hours in affected individuals. The tocolysis failure rate in the study was around 18.5%.

Maitra N's research compared the effects of nifedipine and retrodine, finding that 91.5% of women administered nifedipine experienced significantly delayed delivery beyond two weeks, in contrast to 62.9% with retrodine, showing noteworthy statistical significance.[16] The adverse effects of nifedipine

observed in the study included transient hypotension (3.8% of patients) and fetal distress (7.6% of cases). Compared to prior research, these rates were significantly lower than the concerning 17.3% incidence of cardiovascular complications associated with nifedipine noted previously.[17]

It is highly advisable to closely monitor the mother's vital signs continuously during treatment with nifedipine to ensure maternal and fetal well-being and promptly identify any adverse effects. A recent study focusing on tocolytic agents found that nifedipine successfully stopped preterm labor in 73.3% of cases, highlighting its potential effectiveness.[10]

In a similar vein, another study that aimed to evaluate the same therapeutic outcomes reported a marginally higher frequency of successful tocolysis in patients treated with nifedipine, which was documented at 76.7%, fostering a growing body of evidence supporting the use of this calcium channel blocker in obstetric practice.[11]

In a detailed comparison between nifedipine and a placebo, nifedipine showed a higher success rate of 88.3% in preventing preterm childbirth compared to 69.9% for the placebo but also resulted in more complications such as low blood pressure (3.8%), fast heart rate (1.9%), high cesarean delivery rate (53.5%), and fetal distress (8.08%), indicating potential safety concerns. Additionally, 9.7% of cases experienced failed intervention with nifedipine.[12]

CONCLUSION

Nifedipine is a safe and effective tocolytic agent that can inhibit uterine contractions with rare side effects. Prolonging delivery duration beyond two days is crucial for administering corticosteroids for fetal lung maturation and facilitating the transfer of the mother to a tertiary care center, reducing perinatal complications and mortality rates linked to preterm birth.

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