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A Comparative study in Suppression of Preterm Labor with Nifedipine vs Salbutamol: A Quasi-Experimental study

NAJMATUN JIKRIA[1*], NUR SAYEEDA[2], ASHIQ AHMED[3], FAHMIDA SULTANA MILI[4], UMME SALMA[5]

Abstract:

Background: *The primary cause of perinatal morbidity and mortality globally is preterm birth. Obstetricians face a significant challenge in managing preterm labor, while neonatologists face similar difficulties in caring for premature babies. Tocolytic medications are utilized to inhibit premature labor. Salbutamol and Nifedipine have demonstrated the ability to hold preterm labor for a significant and prolongation of period.*

Objective: *To assess the efficacy of nifedipine for supression of preterm labor. Materials and Methods: This comparative quasi-experimental Study was carried out at the Department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Dhaka between October 2019 to September 2021. The study was conducted on 80 patients, where half of them received Nifedipine; half of them received Salbutamol.*

Results: *The study participants were aged between 19-29 years. The mean age of the participants was 23.05 (±2.50) years, and the mean gestational age was 33.8(±1.24) weeks. 80.6% of the participants who received nifedipine can delay preterm labor for 24-48 hours ($p<0.05$), compared to 46.7% with salbutamol. Considering the complications, nifedipine had lesser complications compared to salbutamol. Palpitation (37.5%) and hypotension (5.0%) occurred with salbutamol. Among them, palpitation ($p<0.001$) was statistically significant.*

Conclusion: *Nifedipine is a superior tocolytic compared to Salbutamol, as it can prolong pregnancy for a significant period of 24-48 hours. This window provides an opportunity for administering steroids to the patient during labor, which can help reduce the likelihood of respiratory distress syndrome in neonates. Additionally, Nifedipine is associated with fewer side effects, making it one of the best tocolytic medications to be used during pregnancy.*

Keywords: *Preterm, Labor, Nifedipine, Salbutamol*

Introduction:

Preventing preterm birth remains a significant challenge in the fields of obstetrics and neonatology. Preterm labor (PTL), characterized by the onset of labor before 37 weeks of gestation, leading to preterm birth, is the most common obstetric complication associated with perinatal mortality [1]. Fetal viability, ranging from 20 to 28 weeks, varies depending on healthcare resources, with the WHO defining the lower limit at 22 weeks [2]. Preterm birth affects 5-10% of pregnancies, resulting in nearly one million newborn deaths in 2015, posing a global concern [3]. Preterm birth accounts for 35% of healthcare costs for neonates and infants, emphasizing the importance of early identification and management [4]. Delaying fetal delivery by at least 48 hours is critical to administering antepartum corticosteroids, reducing the incidence of respiratory distress syndrome (RDS), and improving

1. Indoor Medical Officer, Naogaon Sadar Hospital, Naogaon, Bangladesh
2. Ex-Professor, Dhaka Medical College Hospital, Dhaka, Bangladesh
3. Assistant Registrar, National Institute of Traumatology and Orthopaedic Rehabilitation, Dhaka, Bangladesh
4. Medical Officer, Brahmanpara Upazila Health Complex, Cumilla, Bangladesh
5. Medical Officer, Kurmitola General Hospital, Dhaka, Bangladesh

Address of Correspondence: Dr. Najmatun Jikria, Indoor Medical Officer, Naogaon Sadar Hospital, Naogaon, Bangladesh.Phone: +8801723573867, E- mail: drboney2011@gmail.com

perinatal outcomes. In-utero transfer to facilities with neonatal intensive care units is a priority [5].

Perinatal mortality linked to PTL depends on gestational age, corticosteroid use, and tertiary care quality, associated with respiratory immaturity, intracranial hemorrhage, and infections [6]. Tocolytics, antibiotics, and corticosteroids are employed to manage preterm labor, with beta-agonists and calcium channel blockers being prominent tocolytic agents [7]. Studies support oral nifedipine, subcutaneous terbutaline, and oral salbutamol as effective PTL treatments [8]. Nifedipine, a calcium channel blocker, relaxes uterine smooth muscles by inhibiting calcium influx. Salbutamol activates beta-2 adrenergic receptors, promoting uterine muscle relaxation [9]. Tocolytic treatment preserves pregnancies in over 80% of cases when administered for 24 to 48 hours. Comparative trials have shown mixed results, with some favoring nifedipine and others salbutamol. Ongoing research aims to comprehensively assess the efficacy and safety of salbutamol and nifedipine in treating preterm labor [10].

Methods:

This quasi-experimental study was conducted at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka between October 2019 and September 2021. Pregnant women between 28 – 36 weeks of gestation with regular uterine contraction, 2 or more per 10 minutes lasting for at least 30 seconds, with cervical dilatation of 3 cm or less, with cervical effacement of 50% or less, and with intact membrane were considered as eligible participants. Pregnant women with severe intrauterine growth retardation, fetal distress, multiple pregnancies, antepartum hemorrhage, hydramnios, gestational heart disease or diabetes, fetal malformation, or any condition that contraindicated the use of tocolytics were excluded from the study.

Sample size calculation:

We hypothesized that Salbutamol will be more efficacious than Nifedipine (70% vs 40%) in supressing the PTL up to the duration of 48 hours and calculated our sample size accordingly. With the level of significance set a 5% and the power of the study set at 80%, our calculation showed that we would require 40 samples in each group and hence a total number of 80 participants in the study.

Allocation to intervention groups:

Potential participants were explained about the study and invited to participate in the study. After obtaining informed consent, they were allocated to one of two groups; Salbutamol or Nifedipine sequentially.

The salbutamol group received an initial dose of oral Salbutamol 8 mg then repeated 6 hourly (if contraction persists) maximum till 24 hours, (maximum 32mg/day. The nifedipine group received oral Nifedipine 20 mg orally upon admission. If contractions persisted after 60 minutes, a similar dose was repeated. If labor was suppressed after the first or second dose, a maintenance dose of 20 mg orally every 6 hours interval was given and continued until 48 hours. All patients were followed up to the point of labor and interpreted as supression of labor for 24 hours or prolongation of pregnancy for more than 24 hours.

Data collection:

A structured questionnaire was used to collect data on age, blood pressure, gravida, gestational age, previous history of pre-term labor, uterine contraction, cervical dilatation, and effacement. The outcome variable in the form of supression of labor (24 hours/48 hours), side effects (headache, nausea, hypotension, palpitation), and method of delivery (vaginal/cesarean section) were recorded as well.

Data analysis:

Data were analyzed by using Statistical Package for the Social Sciences (SPSS) version 16 to summarize and analyze the descriptive statistics. To find out the associating factors 'the chi-square' test was performed. A p <0.05 was considered statistically significant.

Ethical considerations:

Ethical clearance was taken from the ethical review committee and concerned authority of Dhaka Medical College Hospital. Permission for the study was taken from the concerned department from where data collection was done. All study participants were thoroughly appraised about the nature, purpose and implications of the study, as well as the entire spectrum of benefits and risks of the study. Participants were only enrolled after obtaining voluntary informed written consent. Participants were assured of adequate treatment of any complications developed in relation to the study purpose. All participants were assured of their confidentiality.

Results:

A total of 80 participants were enrolled in the study, with 40 participants in each group (Nifedipine and Salbutamol). Table 1 shows the demographic and clinical features of the participants. The age of the patients ranged from 19-29 years. The majority of the patients 72(90%) belonged to the age group of 20 years or more. The mean age of the patients was 23.05(±2.50) years. The number of Primigravida (n=66; 82.5%) is higher than the number of multigravidas (n= 14; 17.5%) in this study. Similar proportions of participants across different categories (primigravida, second gravida, and third gravida) between the Nifedipine and Salbutamol groups. The mean (SD) gestational age of the participants was 33.8(1.24) with a slightly higher proportion from more than 34 weeks. the mean (SD) systolic pressure of our study participants was 118.63(15.83) mm of Hg, and the mean (SD) diastolic blood pressure was 78.51(13.34) of Hg. There was no difference in mean systolic blood pressure between the groups. Of the 14 multigravida participants, 7(50%) had a history of preterm labor. Most of the patients (61.3%) were admitted with a contraction of less than 4 per 20 minutes, whereas

Table-I

Basic demographic and clinical characteristics of the participants during admission

Variable	Overall n (%)	Nifedipine group n (%)	Salbutamol group n (%)	*p*-value
Age				
Categories				
Less than 20 years	8(10.0%)	5(62.5%)	3(37.5%)	0.712
20 years or more	72(90.0%)	35(48.6%)	37(51.4%)	
Mean (SD)	23.05(2.5)	22.78(2.54)	23.33(2.45)	0.328
Gravida				
Categories				0.906
Primigravida	66(82.5%)	32(48.5%)	34(51.5%)	
Second gravida	8(10.0%)	5(62.5%)	3(37.5%)	
Third gravida	6(7.5%)	3(50%)	3(50%)	
Gestational age				
Categories				
≤34 weeks	34(42.50%)	18(52.9%)	16(47.10%)	0.821
>34 weeks	46(57.50%)	22(47.8%)	24(52.2%)	
Mean (SD)	33.8(1.24)	33.7(1.31)	33.8(1.18)	0.722
Blood pressure				
Systole	118.63(15.83)	118.93(15.38%)	118.34(16.45%)	0.869
Diastole	78.51(13.34)	77.0(12.5%)	80.02(14.12%)	0.314
History of PTL				
Yes	7(50%)	3(42.9%)	4(57.1%)	0.592
No	7(50%)	5(71.4%)	2(28.6%)	
Contraction/20 minutes				
Categories				
≤4	49(61.3%)	28(57.1%)	21(42.9%)	0.168
>4	31(38.8%)	12(38.7%)	19(61.3%)	
Mean (SD)	4.05(1.17)	3.83(1.23)	4.28(1.08)	0.088
Cervical dilatation				
Categories				
Less than 2 cm	6(7.5)	4(66.7)	2(33.3)	0.675
More than 2 cm	74(92.5)	36(48.6)	38(51.4)	
Mean SD	2.4(0.59)	2.33(0.63)	2.47(0.54)	0.301
Cervical effacement				
Categories				
30% or less	32(40)	14(43.8)	18(56.3)	0.494
More than 30%	48(60)	26(54.2)	22(45.8)	
Mean SD	37.19(10.99)	38.25(9.84)	36.13(12.06)	0.391

Table-II

Comparison of study outcomes between the study groups

Variable	Overall n (%)	Nifedipine group n (%)	Salbutamol group n (%)	*p*-value
Supression of labor				
For 24 hours				
Yes	66 (82.50%)	36 (90.0%)	30 (75.0%)	0.139
No	14 (17.50%)	4 (10.0%)	10 (25.0%)	
For 24 - 48 hours (N=66)				
Yes	43 (65.10%)	29 (80.6%)	14 (46.7%)	0.005
No	23 (34.90%)	7 (19.4%)	16 (53.3%)	
Side effects				
Headache				
Yes	60 (75.00%)	31 (77.50%)	29 (72.50%)	0.797
No	20 (25.00%)	9 (22.50%)	11 (27.50%)	
Nausea				
Yes	22 (27.50%)	11 (27.50%)	11 (27.50%)	1.00
No	58 (72.50%)	29 (72.50%)	29 (72.50%)	
Hypotension				
Yes	2 (2.50%)	0 (0.00%)	2 (5.00%)	0.494
No	78 (97.50%)	40 (100.00%)	38 (95.00%)	
Palpitation				
Yes	15 (18.75%)	0 (0.00%)	15 (37.5%)	<0.001
No	65 (81.25%)	40 (100.00%)	25 (62.5%)	

only 38.8% were admitted with contractions of more than 4 per 20 minutes. There was no statistically significant difference between the treatment groups (57.1% vs 42.9% in the Nifedipine and Salbutamol group had 4 or fewer contractions per 20 minutes, while 38.7% vs 61.3% in the Nifedipine and Salbutamol group had more than 4 contractions per 20 minutes). The majority (92.5%) of the patients had cervical dilatation of more than 2 cm on admission. Around two third of the patients had cervical effacement of more than 30% on admission.

Table-2 shows the effect of interventions (nifedipine & salbutamol) on our primary outcome variable, the supression of labor for 24 and 48 hours. Salbutamol in prolonging of pregnancy for up to 24 hours (90% vs. 75%, p=0.139). However, among the participants with labor supressed beyond 24 hours (n=66), Nifedipine showed better efficacy in prolonging the pregnancy up to 48 hours (80.6% vs. 46.7%, p= 0.005). Table-3 shows maternal side effects associated with medication. A total of 60 (75%) participants reported headaches, while 22(27.5%), 2(2.5%) and 15(18.8%) participants reported nausea, hypotension, and palpitations respectively. There was no significant difference in the proportion of participants, who reported headache (p=0.797), nausea (p=1.0), or hypotension (p=0.494) however higher proportion of participants who received salbutamol reported palpitation (37.5 %vs. 0.0%, p< 0.001).

Discussion:

The most common cause of prenatal death and morbidity is premature delivery. This calls for the use of a uterine muscle relaxant to prolong the pregnancy for as long as feasible, preferably at least 48 hours, so that antepartum corticosteroids can be given to minimise the chance of respiratory distress syndrome (RDS) to improve perinatal outcomes. A wide range of tocolytics has been utilized for the management of preterm labor. Total 80 patients were divided into two groups of 40 each – one group received oral nifedipine as tocolytic and another group received oral salbutamol.

In our study, preterm labor was most commonly observed (90%) among younger women (aged below 30 years). Among them, 10% were very young (age less than 20 years). This was comparable to similar study majority of patients were primigravida 66 (82.5%), whereas second and third gravidae were

8(10.0%) and 6(7.5%) respectively [1,10]. The distribution of patients was not statistically significant (P= 0.906). Ashraf [11] also shows in her study that the majority of patients belonged to primigravida (81.52%). This is contradictory to findings [12,13] probably due to the increased rate of home delivery with increasing parity.

We found that nifedipine had better efficacy than salbutamol in prolonging the labor. In our study, pregnancy was prolonged for 24 hours in both of the treatment groups (90% and 75% for nifedipine and salbutamol respectively), but nifedipine prolonged the labor significantly for 24 - 48 hours (80.6%) in compared to salbutamol (46.7%) which was statistically significant (P=0.005). None of the drugs can prolong pregnancy for more than 48 hours in our study. A similar study Moramezi et al. and Weerakul et al. also showed their study that nifedipine can prolong pregnancy for 24-48 hours or more in preterm labor patients so that dosage of maternal corticosteroid can be completed [14,15].

In this study, around 77.50% of patients had headaches with nifedipine as compared to 72.50% with salbutamol. Nausea was found to be equally distributed among both groups. Hypotension (5.00%) and palpitation (37.5%) were only found to occur with the use of salbutamol (statistically significant, P<0.001). Over all this study showed less serious maternal side effects with nifedipine, which is similar to studies done by Malik,[16] and Sangkomkamhang et al,[17].

Nifedipine has emerged as an effective and rather safe alternative tocolytic agent for the management of preterm labor in comparison to salbutamol as it prolongs pregnancy by 24-48 hours. There was also a better maternal safety profile i.e. fewer side effects with nifedipine in comparability to salbutamol.

Conclusion:

This study concludes that, Nifedipine is a better tocolytic agent than salbutamol as it significantly prolongs the pregnancy for 24 to 48 hours, in which periods steroids could be administered to patients in labor to reduce perinatal mortality and morbidity. There were no significant maternal side effects with the use of nifedipine, which makes it effective tocolytic to be used in pregnancy as compared to salbutamol. As the sample size in our study was small, large randomized controlled trials are required to be conducted to determine the significance of this breakthrough in the management of preterm labor. Since prediction and prevention of preterm labor are not possible despite extensive research on the subject, appropriate management can reduce neonatal death due to PTL.

References:

1. Giacoia G, Mattison D. Obstetric and fetal pharmacology. Glob libr women's med (ISSN: 1756–2228). 2009 Jan.
2. Leonard SA, Crespi CM, Gee DC, Zhu Y, Whaley SE. Prepregnancy risk factors for preterm birth and the role of maternal nativity in a low-income, Hispanic population. Maternal and child health journal. 2015 Oct;19:2295-302.
3. Bhutta ZA, Cabral S, Chan CW, Keenan WJ. Reducing maternal, newborn, and infant mortality globally: an integrated action agenda. International Journal of Gynecology & Obstetrics. 2012 Oct;119:S13-7.
4. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. The Lancet. 2015 Jan;385(9966):430–40.
5. Haas DM, Golichowski AM, Imperiale TF, Kirkpatrick PR, Zollinger TW, Klein RW. Tocolytic therapy: a meta-analysis and decision analysis. Obstetrics & Gynecology. 2009 Jul 1;114(1):171.
6. Almeida AC, Jesus AC, Lima PF, Araújo TM. Maternal risk factors for premature births in a public maternity hospital in Imperatriz-MA. Revista Gaúcha de Enfermagem. 2012;33:86-94.
7. Junejo N, Mumtaz F, Unar BA. Comparison of salbutamol and nifedipine as a tocolytic agent in the treatment of preterm labour. JLUMHS. 2008 May;12:115-9.
8. Niaz A, Naz M, Khanum S. Role of Nifedipine as Tocolytic Agent in Preterm Labour. Annals of Punjab Medical College (APMC). 2014;8(1):1-5.
9. Rezk M, Sayyed T, Masood A, Dawood R. Nicorandil vs nifedipine for the treatment of preterm labour: a randomized clinical trial. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2015 Oct 3;195:27-30.

10. Kashanian M, Bahasadri S, Zolali B. Comparison of the efficacy and adverse effects of nifedipine and indomethacin for the treatment of preterm labor. International Journal of Gynecology & Obstetrics. 2011 Jun 1;113(3):192-5.

11. Phupong V, Charakorn C, Charoenvidhya D. Oral salbutamol for treatment of preterm labor. Journal of the Medical Association of Thailand. 2004 Sep 1;87(9):1012–6.

12. Ashraf B. Efficacy and safety of oral nifedipine with or without vaginal progesterone in the management of threatened preterm labor. International Journal of Reproductive BioMedicine. 2019 Sep;17(9):629.

13. Copper RL, Goldenberg RL, Creasy RK, DuBard MB, Davis RO, Entman SS, Iams JD, Cliver SP. A multicenter study of preterm birth weight and gestational age—specific neonatal mortality. American journal of obstetrics and gynecology. 1993 Jan 1;168(1):78-84.

14. Moramezi F, Barati M, Saadati N, Masihi S, Hemadi M. A Comparative Study between the Efficacy of 17-alpha-Hydroxy Progesterone Caproate Plus Salbutamol with Magnesium Sulfate in Treatment of Preterm Labor. International Journal of Pharmacology. 2011;7(1):130-4.

15. Weerakul W, Chittacharoen A, Suthutvoravut S. Nifedipine versus terbutaline in management of preterm labor. International journal of gynecology & obstetrics. 2002 Mar;76(3):311-3.

16. Malik KK. Comparison of nifedipine with salbutamol as tocolytic agents in preterm labour.Biomedica. 2007 Jul;23(July-December):111-5.

17. Sangkomkamhang U, Pattanittum P, Laopaiboon M, Lumbiganon P. Mode of delivery and outcomes in preterm births. Journal of the Medical Association of Thailand. 2011 Aug 6;94(4):415.