Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Obs & Gynae

Efficacy and Safety of Nifedipine as a Tocolytic Drug for the Treatment of Preterm Labour: Comparison with Levosalbutamol

Dr. Mousumee Mondal[1*], Dr. Rehana Parven[2], Dr. Mst. Marzina Khatun[2], Dr. Most. Sharifa Begum[3], Dr. Shadia Sharmin Sultana[4]

[1]Registrar, Department of (Obs & Gynae), Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[2]Junior Consultant, Department of (Obs & Gynae), Patnitala Upazila Health Complex, Naogaon, Rajshahi, Bangladesh
[3]IMO, Department of (Obs & Gynae), Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[4]Junior Consultant, Department of (Obs & Gynae), Porsha Upazila Health Complex, Naogaon, Rajshahi, Bangladesh

DOI: 10.36347/sjams.2023.v11i10.013 | **Received:** 05.09.2023 | **Accepted:** 11.10.2023 | **Published:** 27.10.2023

***Corresponding author:** Dr. Mousumee Mondal
Registrar, Department of (Obs & Gynae), Rajshahi Medical College Hospital, Rajshahi, Bangladesh

Abstract **Original Research Article**

Background: The rising prevalence of preterm birth is a significant public health concern. This study aimed to assess the efficacy and safety of the calcium channel blocker Nifedipine compared to the β2 agonist Levosalbutamol for inhibiting uterine contractions in early preterm labor, with a focus on maternal side effects and perinatal outcomes. ***Methods:*** A randomized clinical trial was conducted at Rajshahi Medical College Hospital over one year, involving pregnant women experiencing early preterm labor (24-36 weeks gestation, regular uterine contractions, cervical dilation 1-3 cm). a total N=66 patients were randomly assigned to receive either Nifedipine (Experimental group) or Levosalbutamol (Control group). Primary maternal outcomes included tocolysis, time to tocolysis, prolongation of pregnancy by ≥2 days, and delivery at term. Secondary perinatal outcomes included birth asphyxia, perinatal mortality, and the need for emergency NICU admission. Secondary maternal outcomes included side effects such as headache, hypotension, nausea/vomiting, and tachycardia. ***Results:*** Over 90% of patients in the Nifedipine group achieved tocolysis compared to 72.7% in the Levosalbutamol group ($p = 0.054$). Nifedipine achieved significantly faster tocolysis (8.7 hours vs. 29.3 hours, $p < 0.001$). The Experimental group showed higher rates of arresting preterm labor for ≥2 days and lower rates of preterm delivery. Maternal side effects were lower for headache but higher for hypotension and nausea/vomiting in the Nifedipine group. Tachycardia occurred in the Control group but not the Experimental group. Both groups had low rates of birth asphyxia. Perinatal mortality was lower in the Experimental group, and NICU admission was less frequent. ***Conclusion:*** Nifedipine demonstrated superior efficacy over Levosalbutamol in terms of tocolysis, time to tocolysis, prolongation of pregnancy, delivery at term, with fewer maternal side effects and improved perinatal outcomes in pregnant women with early preterm labor.

Keywords: Nifedipine, Levosalbutamol, preterm labor, tocolytic, maternal outcomes.

INTRODUCTION

Preterm labor, defined as the onset of labor after the gestational viability but before the completion of 37 weeks of gestation, poses a significant challenge in maternal and child healthcare worldwide. In industrialized countries, the prevalence of preterm labor ranges from 5% to 12% of all pregnancies [1]. Alarming trends have emerged, especially in the United States, where the incidence has risen from 9% to 12% over the past two decades. Beyond the immense psychosocial and emotional burden it places on families, preterm birth carries substantial economic costs. In the United States alone, managing preterm birth annually incurs a staggering cost of $26.2 billion [2].

Preterm birth stands as the foremost determinant of adverse infant outcomes, encompassing both survival and quality of life. A striking 75% of all perinatal mortality cases are attributed to preterm birth, with an accompanying 10-15% risk of childhood disabilities for births occurring before the 37th week of gestation [3]. Neonates born prematurely are at heightened risk for complications such as respiratory distress, white matter injury, intracranial hemorrhage, cerebral palsy, subnormal neuropsychological development, and school performance deficits. The severity of neonatal outcomes is intricately tied to the gestational age at delivery, often exacerbated by factors like infection. The lower the gestational age, the greater the risk of mortality and morbidity [4].

The precise mechanisms underlying preterm labor remain elusive. It may stem from either premature activation of the physiological uterine contraction process or pathological factors instigating uterine contractions, ultimately leading to preterm delivery [5]. Identified pathways contributing to preterm labor encompass uterine overdistension (as in multiple pregnancies or polyhydramnios), placental ischemia, cervical disease, immunological and allergic phenomena, decidual or retroplacental hemorrhage, fetal endocrine activation, intrauterine infections, and inflammatory processes. Elective prematurity due to maternal or fetal conditions is also emerging as a significant cause. The management of preterm labor involves the identification of high-risk women, along with prevention and treatment strategies [6].

Tocolytic drugs represent the cornerstone of primary pharmacologic management for preterm labor. They serve the crucial role of halting uterine contractions during an active episode of preterm labor (first-line therapy) or maintaining uterine quiescence after an acute episode (maintenance therapy). The primary goals are to prolong pregnancy to term, or at least to a gestational age that allows for substantial fetal maturity and increased birth weight. At minimum, tocolytics aim to extend gestation long enough for the administration of corticosteroids to enhance fetal lung maturation. However, the value of tocolytic medications must be considered in light of potential maternal and neonatal side effects, as well as uncertainty regarding whether pregnancy prolongation translates to improved infant outcomes. A diverse array of agents are advocated for suppressing uterine contractions, including beta-agonists, calcium channel blockers, prostaglandin synthetase inhibitors, nitric oxide donors, and oxytocin receptor antagonists [7].

The selection of a tocolytic agent hinges on factors such as its regulatory approval in the country, drug efficacy, safety profiles for both the mother and the fetus, and treatment costs. Selective β2 agonists, including Ritodrine and Salbutamol, have been integral to clinical practice for preterm labor management since the 1980s. These drugs act by reducing intracellular cyclic AMP concentrations and facilitating myometrial relaxation. However, their long- term tocolytic efficacy (restricted to 7 days) has not demonstrated substantial benefits in terms of perinatal mortality and morbidity rates. Furthermore, even with selective β2 adrenergic receptor agonists, significant maternal side effects, including tachycardia, dyspnea, hypokalemia, hyperglycemia, and chest pain, have been reported [8].

Another agent, Nifedipine, operates by interfering with the transfer of calcium ions across the myometrial cell membrane, thereby reducing intracellular free calcium concentration and inducing myometrial relaxation. Nifedipine has become one of the most commonly employed drugs for inhibiting preterm labor, typically administered at daily doses of 30-60 mg. Success in tocolysis is defined as the prolongation of labor for a minimum of 48 hours, enabling the enhancement of fetal lung maturity through glucocorticoid administration. A similar study that calcium antagonists significantly reduced perinatal morbidity, with fewer maternal side effects when compared to β2 sympathomimetics. Nifedipine's advantage also lies in its oral administration, as demonstrated by Hayes, who reported lower side effects with Nifedipine than with β2 sympathomimetics [9]. Additionally, a study by Naseem Junejo indicated that Nifedipine and Levosalbutamol exhibit comparable tocolytic efficacy in terms of prolonging pregnancy and neonatal outcomes, with calcium channel blockers being associated with fewer side effects [10].

Despite the critical role of tocolytic drugs in managing preterm labor, the choice of first-line agents remains a contentious issue due to inconclusive data regarding their relative safety and efficacy. Many studies in this area suffer from major design flaws or produce results that cannot be readily generalized. Consequently, this study has been designed to systematically assess the efficacy and safety of the calcium channel blocker Nifedipine in comparison to the beta 2 sympathomimetic Levosalbutamol for the treatment of preterm labor. Through a rigorous evaluation of these two commonly used tocolytics, we aim to contribute to the evidence base guiding clinical decisions in the management of preterm labor, ultimately promoting the best outcomes for both mothers and their newborns.

OBJECTIVES

General Objectives

- To evaluate the efficacy and safety of Nifedipine as a tocolytic drug for the treatment of preterm labour.

Specific Objectives

- To assess the efficacy (tocolysis, time taken to achieve tocolysis, prolongation of pregnancy for 2 or more days and delivery at term) safety (maternal and perinatal complications) of the experimental drug, Nifedipine.
- To assess the efficacy (tocolysis, time taken to achieve tocolysis, prolongation of pregnancy for 2 or more days and delivery at term) safety (maternal and perinatal complications) of the control drug Levosalbutamol.
- To assess comparative superiority between Nifedipine and Levosalbutamol in terms of efficacy and safety.

MATERIALS & METHODS

Study Design

The present study was designed as a randomized clinical trial and was conducted within the

Department of Obstetrics and Gynaecology at Rajshahi Medical College Hospital, Rajshahi, over a duration of one year, spanning from January 2020 to December 2020. The study aimed to assess the efficacy and safety of two tocolytic drugs, Nifedipine and Levosalbutamol, in the management of preterm labor. Pregnant women experiencing preterm labor and admitted to either the Outpatient Department (OPD) or the Emergency Department were considered as the study population.

Inclusion Criteria

- Age of the patient > 18 years
- Gestational age between 24-36 weeks determined by the date of 1st day of last menstrual period when known or by early ultrasonography
- Singleton pregnancy with cephalic presentation
- Palpable, regular uterine contractions at least 1 in 10 minutes
- Cervical dilatation >1 cm but < 3 cm

Exclusion Criteria

- Ruptured membranes
- Major vaginal bleeding: placenta previa or abruptio placentae
- Hypertensive diseases in pregnancy
- Urinary tract infection (UTI)
- Fetal or placental abnormalities
- Serious maternal diseases, such as- cardiac disease, diabetes mellitus, thyrotoxicosis.
- Previous exposure to any tocolytic therapy within six hours
- Evidence of fetal distress.

Randomization

Upon admission, eligible participants were randomly assigned to one of two groups: the Experimental group receiving Nifedipine or the Control group receiving Levosalbutamol. Randomization was performed using a computer-generated random number sequence to ensure equal distribution of participants between the two groups, minimizing selection bias.

Data Collection

Data was collected through a semi-structured questionnaire, finalized after field-testing. Eligible pregnant women provided written consent. A total of 66 patients, meeting strict inclusion and exclusion criteria, were randomly allocated to either the Experimental (Nifedipine) or Control (Levosatbutamol) groups using a randomized card- drawing method. Medication administration, vital sign monitoring, and uterine activity assessments were conducted per protocol. Patients were discharged if contractions ceased, and they were followed up according to antenatal schedules. Maternal and fetal outcomes were recorded to assess the drugs' efficacy and safety. Data analysis was performed using SPSS.

Data Analysis

Data collected during the study underwent rigorous assessment to ensure completeness, accuracy, and consistency before analysis. The Statistical Package for Social Sciences (SPSS), version 23, by IBM Corp., Armonk, NY, was utilized for data analysis. Descriptive statistics, chi-square ($\chi 2$) tests, and unpaired t-tests were employed as appropriate for data analysis. Categorical variables were presented as frequencies and corresponding percentages and were compared between groups using chi-square ($\chi 2$) tests. Continuous variables were expressed as means and standard deviations and were compared between groups using Student's t-tests. A significance level of 5% was set, and $p < 0.05$ was considered statistically significant.

Ethical Consideration

Ethical considerations were diligently upheld throughout the study. The research protocol gained prior approval from the Institutional Review Board (IRB) of Rajshahi Medical College. Departmental permissions were also obtained. Patients received clear, understandable explanations about the study's purpose, procedures, risks, and benefits in the local language. They were informed of their absolute right to withdraw from the study at any time for any reason. Strict confidentiality was assured for all collected information, which would solely be used for research purposes. Patients voluntarily provided written informed consent before participating in the study, ensuring their rights and well-being were upheld.

RESULTS

The present study was undertaken to determine whether Nifedipine is a better tocolytic than Levosalbutamol in prolonging the preterm delivery for at least 48 hours and safer for the mothers and neonates. Based on predefined enrollment criteria, 66 women with early preterm labour (gestational age between 24-36 weeks, palpable regular uterine contractions at least 1 in 10 minutes and cervical dilatation >1 cm but < 3 cm) were included and were randomly allocated in two treatment arms – Experimental (n = 33) and Control (n = 33) arms. Then all the outcome variables were compared between the two study groups. The findings obtained from data analyses are furnished below:

Table 1: Comparison of demographic & obstetric characteristics between study groups

Demographic & Obstetric characteristics	Group		p-value
	Experimental (n = 33)	Control (n = 33)	
Age[#] (years)	23.8 ± 5.3	23.4 ± 5.3	0.729
Gestational age[#] (weeks)	33.7 ± 1.98	33.64 ± 1.8	0.897
Parity*			
Nullipara	23(69.7)	22(66.7)	
Primipara	9(27.3)	9(27.3)	0.837
Multipara	1(3.0)	2(6.1)	
Gravida*			
Primigravida	23(69.7)	22(66.7)	
Multigravida	10(30.3)	11(33.3)	0.500
Previous history of preterm labour*	6(18.2)	9(27.3)	0.279

Comparison of demographic and obstetric characteristics between the two study groups revealed that, there was no significant difference between the groups in terms of age (p = 0.729). Gestational age was also no different between the groups (p = 0.897). Two-thirds of the patients in both groups were nullipara with no intergroup difference (0.837). Like- wise two-thirds of the in each group were primigravida (p=0.500). Previous history of preterm labour was somewhat higher in the Control group (27.3%) than that in the Experimental group (18.2%), although the difference between the groups did reach the level of significance (p = 0.279) (Table I).

Table 2: Heamodynamic state between study groups before giving tocolytics

Heamodynamic state-related variables	Group		p-value
	Experimental (n =33)	Control (n = 33)	
Systolic BP[#] (Hg mm)	109.7 ± 7.3	112.1 ± 6.9	0.172
Diastolic BP[#] (Hg mm)	73.3 ± 5.5	72.7 ± 4.5	0.628
Heart rate[#] (beats/min)	75.2 ± 3.1	74.8 ± 3.0	0.527
Fetal heart rate[#] (beats/min)	143.03 ± 3.7	142.2 ± 3.1	0.305

The mean systolic and diastolic blood pressures of the patients of Experimental and Control arms were almost similar (p = 0.172 and p = 0.628). The heart rates of the two groups were also alike (p = 0.527). The mean fetal heart rate in both groups was faster with no significant intergroup difference (p = 0.305) (Table

Table 3: Comparison of maternal outcome between study groups

Maternal Outcome	Group		p-value
	Experimental (n = 33)	Control (n = 33)	
Tocolysis achieved*	30(90.9)	24(72.7)	0.054
Time taken to achieve tocolysis[#]	8.7 ± 2.3	29.3 ± 6.9	< 0.001
Prolongation of pregnancy*			
≥ 2 days	28(93.3)	17(70.8)	0.033
< 2 days	2(6.7)	7(29.2)	
Delivery took place*			
Term	20(60.6)	6(18.2)	< 0.001
Preterm	13(39.4)	27(81.8)	

Over 90% of the pregnant women in the Experimental group achieved tocolysis as compared to 72.7% in the Control group (p = 0.054). The time taken to achieve tocolysis was significantly lower in the former group than that in the latter group (8.7 vs. 29.3 hours, p < 0.001). The incidence of prolongation of pregnancy for ≥ 2 days was also much higher in the former group (93.3%) than that in the latter group (70.8%) (p = 0.033). The incidence of preterm delivery was dramatically reduced in the Experimental group (39.4%) than that in the Control group (81.8%) (p < 0.001) (Table III).

Table 4: Comparison of maternal side-effects between study groups

Maternal side-effects	Group		p-value
	Experimental (n = 33)	Control (n = 33)	
Headache*	15(45.5)	29(87.9)	< 0.001
Hypotension*	12(36.4)	1(3.3)	< 0.001
Nausea/vomiting*	17(51.5)	5(15.2)	0.002
Tachycardia**	0(0.0)	28(84.8)	< 0.001

The incidence of headache was significantly lower in the Experimental arm (45.5%) than that in the Control arm (87.9%) ($p < 0.001$). However, hypotension and nausea/vomiting demonstrated their significant presence in the former group than those in the latter group ($p < 0.001$ and $p = 0.002$ respectively). While majority of the Contrl arm developed tachycardia, none in the Experimental arm developed it ($p < 0.001$) (Table IV).

Table 5: Comparison of perinatal outcome between study groups

Perinatal Outcome	Group		p-value
	Experimental (n = 33)	Control (n = 33)	
APGAR at 1 min*			
< 7	6(18.2)	7(21.2)	0.500
≥ 7	27(81.8)	26(78.8)	
APGAR at 5 min*			
< 7	6(18.2)	7(21.2)	0.500
≥ 7	27(81.8)	26(78.8)	
Perinatal mortality*	2(6.1)	6(18.2)	0.129
Admission to NICU*	7(21.2)	14(42.4)	0.056

The incidence of birth asphyxia (APGAR < 7) was low in both experimental and Control groups and there was no significant difference between the groups in terms of APGAR < 7 at 1 and 5 minutes ($p = 0.500$ and $p = 0.500$ respectively). The incidence of perinatal mortality was lower in the Experimental arm than that in Control arm (6.1% vs. 18.2%, $p = 0.129$). The need for NICU admission was half (21.2%) in the Experimental arm than that in the Control arm (42.4%) ($p = 0.056$) (Table V)

DISCUSSION

Preterm labor is a significant concern due to its association with preterm birth, which accounts for a substantial proportion of perinatal deaths [3]. It poses a substantial public health challenge globally, with prevalence rates varying across regions. In industrialized countries, preterm birth affects 5–12% of pregnancies [1]. In the United States, the incidence of preterm birth has risen from 9% to 12% over the past two decades. This increase not only places a heavy emotional and psychosocial burden on families but also has significant economic implications for society, with the annual cost of managing preterm birth reaching $26.2 billion in the USA alone [2].

Preterm birth is a critical determinant of adverse infant outcomes, affecting both survival and quality of life. It accounts for a staggering 75% of all perinatal deaths and carries a substantial risk of childhood disabilities, with 10– 15% of preterm infants experiencing long-term health issues. These complications include neonatal respiratory distress, white matter injury, intracranial hemorrhage, cerebral palsy, subnormal neuropsychological development, and poor school performance [3]. The risk of adverse neonatal outcomes is directly correlated with gestational age at delivery, with lower gestational ages associated with higher mortality and morbidity rates.

The mechanisms behind preterm labor are complex and not fully understood. It may involve the premature activation of the physiological uterine contracting process or the presence of pathological factors triggering uterine contractions that lead to preterm delivery. Several pathways have been identified as contributors to preterm labor, including uterine overdistension (e.g., multiple pregnancies or polyhydramnios), placental ischemia, cervical disease, immune and allergic responses, decidual or retroplacental hemorrhage, fetal endocrine activation, intrauterine infections, and inflammatory processes. Additionally, elective prematurity due to maternal or fetal conditions is becoming an increasingly significant factor contributing to preterm birth [6].

The management of preterm labor involves the identification of high-risk women, prevention, and treatment. Tocolytic drugs are the cornerstone of primary pharmacologic management for preterm labor, intended to either halt uterine contractions during an active episode (first-line therapy) or maintain uterine quiescence after an acute episode (maintenance therapy). The primary goals of tocolysis are to prolong pregnancy to term or, at the very least, extend gestation sufficiently

to facilitate fetal lung maturation with corticosteroid administration or other interventions. However, the use of tocolytics must be weighed against potential maternal and neonatal side effects, as well as uncertainty regarding whether prolonging pregnancy leads to improved infant outcomes [7]. A range of tocolytic agents are used in clinical practice to suppress uterine contractions, including beta-agonists, calcium channel blockers, prostaglandin synthetase inhibitors, nitric oxide donors, and oxytocin receptor antagonists. The choice of tocolytic agent primarily depends on factors such as regulatory approval, drug efficacy, safety profiles for both the mother and fetus, and cost considerations.

Selective beta-2 adrenergic receptor agonists, such as Ritodrine and Salbutamol, have been utilized for preterm labor management since the 1980s. These drugs work by reducing intracellular cyclic AMP concentrations, leading to myometrial relaxation [11]. However, they have demonstrated limited efficacy for long-term tocolysis (restricted to 7 days), with no significant reduction in perinatal mortality and morbidity rates. Furthermore, these agents are associated with significant maternal side effects, including tachycardia, dyspnea, hypokalemia, hyperglycemia, and chest pain [8].

Nifedipine, a calcium channel blocker, operates by inhibiting the transfer of calcium ions across myometrial cell membranes, thus decreasing intracellular free calcium concentrations and inducing myometrial relaxation. It is one of the most commonly used drugs for preterm labor inhibition, typically administered orally at doses ranging from 30 to 60 mg daily. Studies have shown that Nifedipine is effective in prolonging pregnancy and reducing perinatal morbidity while having the advantage of oral administration [9]. Furthermore, Nifedipine exhibits a better side effect profile compared to selective beta-2 agonists, with fewer instances of tachycardia and other adverse reactions.

The choice of first-line tocolytic agents for preterm labor management is a subject of ongoing debate due to inconclusive evidence regarding the relative safety and efficacy of various options [10]. This study was designed to evaluate the efficacy and safety of Nifedipine compared to Levosalbutamol for the treatment of preterm labor, addressing this critical knowledge gap.

In this randomized clinical trial, conducted at the Department of Obstetrics and Gynecology, Rajshahi Medical College Hospital, pregnant women with preterm labor between 24 and 36 weeks of gestation were included. The study aimed to assess the efficacy of Nifedipine and Levosalbutamol in prolonging pregnancy for at least 48 hours, gestational age at delivery, maternal side effects, and perinatal outcomes. After obtaining informed consent, eligible participants were randomly assigned to either the Experimental (Nifedipine) or Control (Levosalbutamol) group.

The results of the study demonstrated that over 90% of pregnant women in the Nifedipine group achieved successful tocolysis, compared to 72.7% in the Levosalbutamol group. Nifedipine also significantly reduced the time required for tocolysis, with a median time of 8.7 hours compared to 29.3 hours in the Levosalbutamol group. Moreover, the Nifedipine group experienced a higher rate of halting preterm birth for at least two days and a lower rate of preterm delivery. However, maternal side effects such as headaches, hypotension, and nausea/vomiting were more common in the Nifedipine group. Conversely, a significant proportion of the Levosalbutamol group developed tachycardia, a side effect not observed in the Nifedipine group. In terms of perinatal outcomes, both groups exhibited low rates of birth asphyxia (APGAR score < 7). However, perinatal mortality was significantly lower in the Nifedipine group, accompanied by a significantly reduced need for admission to the neonatal intensive care unit (NICU).

Comparison with related studies reinforces the findings that Nifedipine is a more effective tocolytic agent than Levosalbutamol and Salbutamol, as it prolongs gestation and improves perinatal outcomes. However, Nifedipine's advantages are counterbalanced by its maternal side effects, including hypotension and nausea/vomiting. Previous studies have also highlighted Nifedipine's advantages, including ease of administration, less rigorous maternal and fetal monitoring, and fewer side effects compared to Salbutamol, which necessitates more intensive monitoring [10].

A study from India demonstrated Nifedipine's superiority over Isoxpurine Hydrochloride as a tocolytic agent with similar side effect profiles. An Iranian study comparing Nifedipine and intravenous Magnesium Sulfate ($MgSO_4$) found no significant differences in suppressing labor pain and neonatal outcomes but reported that Nifedipine had fewer maternal side effects. However, a study by Klauser *et al*., involving three tocolytic agents, including Nifedipine, showed no significant differences in efficacy and major maternal side effects [12].

In this study provides compelling evidence supporting Nifedipine's superiority over Levosalbutamol and other tocolytic agents in terms of prolonging gestation and improving perinatal outcomes. While Nifedipine is associated with some maternal side effects, its advantages in terms of efficacy and neonatal outcomes make it a viable option for the management of preterm labor. Nevertheless, further research, including larger-scale trials, is essential to confirm these findings, address potential limitations, and establish optimal treatment protocols for preterm labor.

CONCLUSION

This study found that Nifedipine is more effective than Levosalbutamol in managing early preterm labor. It leads to quicker tocolysis and a higher rate of prolonging pregnancy for at least two days. Additionally, Nifedipine appears to result in better secondary perinatal outcomes. However, it is associated with more maternal side-effects such as hypotension and nausea/vomiting compared to Levosalbutamol.

RECOMMENDATIONS

In the light of the findings of the present study, the following recommendations are laid down:

- A large-scale multicenter study should be done to generalize the findings of the study to reference population.
- As long as there is no recommended drug for tocolysis, it is left to clinicians' discretion to use the tocolytics based on their clinical experience.

ACKNOWLEDGMENT

It is my great pleasure to express profound gratitude and indebtedness to my respected teacher, all staff, and research assistant with the Department of Obstetrics & Gynaecology at Rajshahi Medical College Hospital, Rajshahi, for valuable suggestions that make this study possible.

FUNDING: No funding sources

CONFLICT OF INTEREST: None declared

REFERENCES

1. Burke, C., & Morrison, J. J. (2000). Perinatal factors and preterm delivery in an Irish obstetric population.
2. Behrman, R. E., & Butler, A. S. (2007). Preterm birth: causes, consequences, and prevention.
3. Costeloe, K., Hennessy, E., Gibson, A. T., Marlow, N., Wilkinson, A. R., & EPICure Study Group. (2000). The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics*, *106*(4), 659-671.
4. Di Renzo, G. C., Al Saleh, E., Mattei, A., Koutras, I., & Clerici, G. (2006). Use of tocolytics: what is the benefit of gaining 48 hours for the fetus?. *BJOG: An International Journal of Obstetrics & Gynaecology*, *113*, 72-77.
5. Hubinont, C., & Debiève, F. (2011). Prevention of preterm labour: 2011 update on tocolysis. *Journal of pregnancy*, *2011*.
6. Romero, R., Espinoza, J., Gotsch, F., Kusanovic, J. P., Friel, L. A., Erez, O., ... & Tromp, G. (2006). The use of high-dimensional biology (genomics, transcriptomics, proteomics, and metabolomics) to understand the preterm parturition syndrome. *BJOG: An International Journal of Obstetrics & Gynaecology*, *113*, 118-135.
7. Lyndrup, J., & Lamont, R. F. (2007). The choice of a tocolytic for the treatment of preterm labor: a critical evaluation of nifedipine versus atosiban. *Expert opinion on investigational drugs*, *16*(6), 843-853.
8. Caritis, S. (2005). Adverse effects of tocolytic therapy. *BJOG: An International Journal of Obstetrics & Gynaecology*, *112*, 74-78.
9. Papatsonis, D. N., Timmerman, C. C., Oei, S. G., & Van Geijn, H. P. (2002). Nifedipine first choice in management of threatening preterm labor. *Nederlands Tijdschrift Voor Geneeskunde*, *146*(42), 1980-1983.
10. Junejo, N., Mumtaz, F., & Unar, B. A. (2008). Comparison of salbutamol and nifedipine as a tocolytic agent in the treatment of preterm labour. *JLUMHS*, *12*, 115-9.
11. Bernal, A. L. (2007, June). The regulation of uterine relaxation. In *Seminars in cell & developmental biology* (Vol. 18, No. 3, pp. 340-347). Academic Press.
12. Singh, N., Singh, U., & Seth, S. (2011). Comparative study of nifedipine and isoxpurine as tocolytics for preterm labor. *The journal of obstetrics and gynecology of India*, *61*, 512-515.