

Original Research Article

# COMPARATIVE STUDY ON EFFICACY OF ORAL NIFEDIPINE VS ISOXYPRINE HYDROCHLORIDE AS TOCOLYTICS IN THE PREVENTION OF PRETERM LABOUR IN A TERTIARY CARE HOSPITAL

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## ABSTRACT

**Background:** The occurrence of preterm labor is a substantial clinical challenge for obstetricians worldwide due to its potential to endanger the health and survival of both the mother and the fetus. The purpose of this study was to conduct a comparative analysis of isoxpurine hydrochloride and nifedipine as tocolytic agents for the management of premature labor.

**Materials and Methods:** The Department of Obstetrics & Gynecology conducted a prospective cohort study with 400 pregnant women who experienced preterm labor. This study was done between September 2022 to July 2023. Among a cohort of 200 women who met the criteria for tocolysis, a group of 100 participants received isoxpurine hydrochloride, while the remaining 100 participants were randomly assigned to receive nifedipine. The data collected was subjected to statistical analysis using SPSS 10.0 for Windows 2003.

**Results:** The prevalence of preterm labor was found to be 22%, whilst the prevalence of premature delivery was seen to be 20.9%. Nifedipine demonstrated a twofold greater efficacy compared to isoxpurine hydrochloride as a tocolytic drug, with comparable adverse effects. In the context of premature labor, it has been observed that nifedipine demonstrates greater effectiveness compared to isoxpurine in cases of early diagnosis, as well as in cases of late diagnosis if nifedipine itself is employed.

**Conclusion:** India has a significantly elevated prevalence of premature labor. Nifedipine demonstrates superior efficacy as a tocolytic agent compared to isoxpurine hydrochloride, particularly when initiated promptly at the emergence of initial indications of preterm labor.

**Keywords:** Preterm birth, uterine tocolytics, prematurity nifedipine, Isoxpurine hydrochloride.

## INTRODUCTION

Preterm labor is a substantial clinical problem for obstetricians worldwide due to its potential to jeopardize the health and survival of both the mother and the fetus. The global prevalence of preterm labor is between 8% and 10%, contributing to approximately 80% of infant morbidity. India exhibits a significantly elevated prevalence of preterm labor and preterm delivery.<sup>[1,2]</sup>

The occurrence of premature labor and delivery poses a significant issue for obstetricians, as does the care of preterm infants for pediatricians. The prevalence of preterm delivery in the United States is approximately 11%, whereas in poorer countries, it may be substantially higher. Furthermore, preterm delivery is responsible for a significant proportion, ranging from 40% to 75%, of neonatal mortality. The prevalence of preterm labor and delivery exhibits a rising trajectory in nations where data is accessible.<sup>[3-5]</sup>

Potential factors contributing to this phenomenon may include assisted reproductive procedures, psychosocial stress, or medically induced preterm. Despite substantial research on the subject, it is currently not feasible to accurately predict and avoid premature labor. It is imperative to address the occurrence of preterm labor and effectively administer care to patients based on their specific gestational age.<sup>[6]</sup> The management of preterm labor occurring prior to 34 weeks gestation necessitates the administration of betamethasone to delay delivery for a minimum of 48 hours, so allowing for the attainment of fetal lung maturity. The act of delivering a baby between the gestational ages of 34 and 37 weeks has been found to decrease the likelihood of respiratory distress syndrome. However, it is important to note that this timing does not eliminate the possibility of other issues associated with premature birth.<sup>[7,8]</sup> One of the medications that has been found to have the ability to relax uterine smooth muscles and halt preterm labor is isoxsuprine. Prior research has indicated that the intravenous administration of isoxsuprine, in conjunction with oral maintenance medication, is efficacious in extending pregnancy duration among women who are at risk of delivering prematurely. Research has demonstrated that the administration of nifedipine effectively inhibits preterm labor while minimizing adverse effects on both the fetus and the mother. The administration of this substance has been linked to a reduction in uterine blood flow, resulting in fetal hypoxia and acidosis, as well as maternal palpitations and headaches. However, the available safety data for this substance is limited and further research is needed to confirm its safety profile.<sup>[9,10]</sup>

Therefore, tocolytic drugs are commonly employed in the field of obstetrics. In India, two frequently employed tocolytic medicines include isoxsuprine hydrochloride, a B-adrenergic receptor blocking drug, and nifedipine, a calcium channel blocker. The purpose of this study was to assess the effectiveness and evaluate the overall results of tocolytics in managing preterm labor at a tertiary care center in India.<sup>[11,12]</sup>

## MATERIAL AND METHODS

The study consisted of a cohort of 400 prenatal women and was done within the Department of Obstetrics & Gynecology. This study was done between September 2022 to July 2023. The study obtained written informed permission from the participants who were recruited. The study population consists of antenatal women who are currently between 22 and 37 weeks of gestation and have been diagnosed with preterm labor based on the criteria. The individuals underwent a comprehensive evaluation, which included a complete analysis of their medical history, a detailed clinical examination, and, if not previously conducted, an assessment using ultrasonography. The condition of the amniotic

membrane was observed during a vaginal examination.

## RESULTS

Among the entirety of antenatal admissions observed throughout the designated study period, a total of 600 cases were recorded specifically for the purpose of addressing premature labor. This accounts for approximately 24% of the overall antenatal admissions, which amounted to 2,500 in total. During the specified time period, there were a total of 1824 live births, with 356 of them being classified as preterm deliveries. This indicates an incidence rate of preterm delivery of 20.9%. Among the total of 832 cases of preterm labor (PTL), a subset of 400 patients received tocolysis treatment. The distribution of patients and their final outcome, categorized by gestational age, is presented in Table 1.

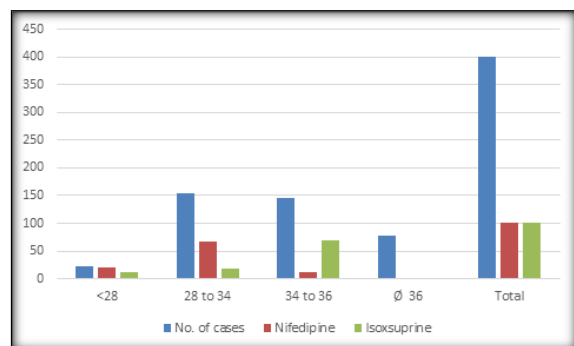


Figure 1: Gestational age distribution of premature labor cases

Table 2 illustrates that there was an absence of substantial disparities in the main confounding factors between the two groups.

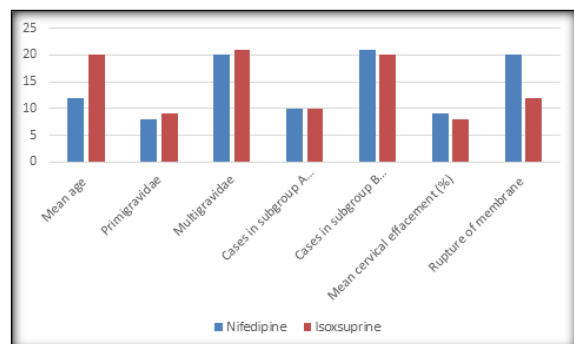


Figure 2: Pregnancy-related variables in both study groups

The collective impact of the two distinct forms of tocolytic therapy. The overall success percentage of tocolysis was found to be 74%. The nifedipine group demonstrated successful tocolysis in 80% of cases, whereas the isoxsuprine group obtained successful tocolysis in 68% of cases. This difference between the two groups was found to be statistically significant, indicating a clear advantage for the nifedipine group. Among the 400 cases of preterm

labor (PTL) examined, subgroup A accounted for 244 cases, while subgroup B accounted for 156 cases. The analysis of the tocolytic effect in the two subgroups revealed that subgroup A exhibited a higher success rate in comparison to subgroup B. The efficacy of nifedipine demonstrated a statistically significant superiority over isoxsuprine in subgroup A.

The comparable effectiveness of the two medications was found to be similar within subgroup B. A total of 356 instances of preterm rupture of membranes were seen, with 156 cases being managed through spontaneous labor based on previously outlined reasons, while tocolysis was administered in 62 cases. The reported failure rate was significantly higher in instances with ruptured membranes (45.2%) compared to situations with intact membranes (22.5%). There was no observed significant difference in result between the groups administered with nifedipine and isoxsuprine.

In 24 out of the 34 cases where successful tocolysis was achieved, labor induction was performed, whereas the remaining ten individuals experienced spontaneous labor after one week. Maternal side effects were observed in 17% of cases in the nifedipine group and 23% in the isoxsuprine group, with no statistically significant difference between the two groups. The predominant adverse effects

observed in both cohorts were nausea, vomiting, headache, and palpitation. The occurrence of flushing was frequently observed in patients administered with nifedipine, while a single instance indicated the presence of tachypnea following the administration of isoxsuprine. There were no instances of pulmonary edema observed within any of the experimental groups. During the designated research duration, a total of 44 infants born prematurely were identified among a cohort of 356 preterm deliveries. The neonatal death rate was seen to be 30% for infants born before 34 weeks of gestation, however it decreased significantly to 3.4% for infants born after 34 weeks of gestation. The observed levels were notably elevated, even among infants who were administered betamethasone.

Instances of neonatal morbidity were observed in the form of septicemia, encephalitis, and respiratory distress syndrome (RDS). The individuals who received betamethasone exhibited a notably decreased RDS, while there was no statistically significant difference in total morbidity between those who received betamethasone and those who did not (P value 0.043). There were two instances of fetal demise occurring before 34 weeks of gestation, one in the group receiving nifedipine and another in the group receiving isoxsuprine.

**Table 1: Preterm labor cases by gestational age distribution (n = 400)**

Gestation age (weeks)	No. of cases	Nifedipine	Isoxsuprine	Total	No. of preterm deliveries
<28	22	20	12	22	80
28 to 34	155	68	18	155	110
34 to 36	145	12	70	145	90
> 36	78	-	-	78	76
Total	400	100	100	400	356

**Table 2: Differences in maternal variables between treatments**

Sr. No.	Factors	Nifedipine	Isoxsuprine
1.	Mean age	12	20
2.	Primigravidae	08	09
3.	Multigravidae	20	21
4.	Cases in subgroup A (Uterine count)	10	10
5.	Cases in subgroup B (Uterine count)	21	20
6.	Mean cervical effacement (%)	9	8
7.	Rupture of membrane	20	12

## DISCUSSION

The prevalence of preterm labor in our country is significantly higher when compared to developed nations. The study revealed a prevalence rate of 22%. Obstetricians encounter the task of effectively managing a diagnosed preterm labor with pharmaceutical interventions. These interventions vary in terms of their uterine specificity, efficacy, and the potential negative effects they may have on both the mother and the fetus. The aforementioned tocolytic medications function by impeding uterine contractions and inducing relaxation of the uterine myometrium through various mechanisms, ultimately resulting in the cessation of premature labor.<sup>[13,14]</sup>

Beta-sympathomimetics exert their effects by modulating cyclic guanosine monophosphate (cGMP) to impede uterine contractions, whereas calcium channel blockers directly impede the influx of calcium ions across the cell membrane, hence reducing smooth muscle tone. In this research investigation, a comparison was conducted between two commonly utilized tocolytic medications in India, namely isoxsuprine hydrochloride and nifedipine. The Cochrane analysis conducted in 2004 about preterm labor establishes that tocolysis is unequivocally recommended prior to reaching 34 weeks of gestational age.<sup>[15,16]</sup> This phenomenon can be attributed to the decline in the proportion of women giving birth during the subsequent seven days, leading to a subsequent drop in the occurrence of neonatal morbidity associated with respiratory distress

syndrome (RDS), necrotizing enterocolitis, intraventricular hemorrhage, and neonatal jaundice. The study revealed that tocolysis resulted in a delay in birth for 39% of all cases, with the highest delay observed in the gestational age range of 28-34 weeks, which is considered the most susceptible population.<sup>[17,18]</sup>

The postponement in the transportation process provides an opportunity for the steroids to expedite the development of the lungs and enhance the chances of survival for newborns. In contrast to the circumstances observed in affluent nations, there exists a notable disparity in newborn morbidity and mortality rates between poor countries, even when the administration of betamethasone is implemented as a regular practice.<sup>[19,20]</sup> The findings of the current study demonstrate that delaying delivery until the gestational age of 36 weeks provides advantageous outcomes for the newborn in terms of mitigating additional challenges associated with prematurity. The current study demonstrates that nifedipine has much superior efficacy in prolonging the time until delivery by 48 hours, in comparison to Isoxsuprine, which only achieves a 68% success rate. Nifedipine was found to extend pregnancies up to 36 completed weeks in 36% of cases, whilst isoxsuprine achieved this in 29% of cases. In their study, Smith and Woodland conducted a comparative analysis of the tocolytic impact of nifedipine and terbutaline, revealing comparable efficacy between the two pharmaceutical agents.<sup>[20-22]</sup>

In a study conducted by Jannet et al., the authors examined the effects of salbutamol and nicardipine on a total of 45 cases of preterm labor in each treatment group. The results indicated that the mean gestational age at delivery and the proportion of deliveries occurring after 37 weeks were both higher in the nicardipine group compared to the salbutamol group. Several studies have conducted comparisons between ritodrine and nifedipine, revealing that both medications exhibit equivalent efficacy in suppressing preterm labor.<sup>[21-23]</sup> However, it has been observed that nifedipine is associated with much fewer negative effects in comparison to ritodrine. In our investigation, we observed no statistically significant difference in maternal and newborn adverse effects. However, a lower incidence of side effects was observed in the group treated with nifedipine. Headache and palpitation were among the side effects that were documented in association with the administration of nifedipine. The occurrence of preterm premature rupture of membranes is a prevalent factor contributing to the onset of preterm labor.<sup>[24,25]</sup>

The effectiveness of tocolysis is reduced in circumstances when the membranes are not intact. In situations of preterm premature rupture of membranes (PPROM), there is a 55% likelihood of experiencing a 48-hour delay in delivery, compared to a 78% likelihood in the group with intact membranes. There was no observed substantial disparity in the effectiveness of the two tocolytic medications in this

regard. According to the Royal College of Obstetricians and Gynaecologists (RCOG), ritodrine is no longer the preferred initial option for tocolytic medication administration. Atosiban and nifedipine exhibit a higher degree of desirability due to their reduced incidence of undesirable effects and apparent similarity in efficacy. The selection of a tocolytic medication, which has the potential to enhance neonatal outcomes without causing adverse effects in the mother or newborn, remains undetermined.<sup>[24-26]</sup>

## CONCLUSION

In this extensive investigation, it has been determined that Nifedipine exhibits greater efficacy compared to isoxsuprine. Within subgroup A, there exists a notable disparity in success rates between the two tocolytic drugs. This observation suggests that the prompt beginning of tocolysis using nifedipine is undeniably advantageous in instances of premature labor.

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