



COMPARATIVE STUDY OF ISOXSUPRINE AND NIFEDIPINE IN THE MANAGEMENT OF PRETERM LABOR.

Gynaecology

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ABSTRACT

Background: The purpose of the study was to compare the efficacy of Isoxsuprine and Nifedipine as a tocolytic agent on pre-term labor and to compare the obstetrical outcome.

Material And Methods: This was a prospective study of all patients with preterm labor who attended the obstetrics labor room of Nalanda medical college and hospital, Patna, and underwent Isoxsuprine and Nifedipine therapy from September 2019 to September 2020.

The patient who fulfilled the inclusion criteria for the study were divided into two groups

Group A consisted of 50 patients treated with nifedipine for tocolysis and group B consisted of 50 patients treated with Isoxsuprine for tocolysis and were monitored throughout treatment.

Results: Successful tocolysis was achieved by nifedipine in 71.1% of cases as compared to 68.2% with Isoxsuprine treated cases

Conclusion: Nifedipine is a more effective tocolytic agent as compared to Isoxsuprine. The neonatal outcome concerning birth weight, Apgar score, and Perinatal death was better in the cases treated with nifedipine as compared to Isoxsuprine.

KEYWORDS

Isoxsuprine, nifedipine, preterm labor

INTRODUCTION

Preterm labor is defined as the initiation of regular contraction at least 1 in every 10 min lasting for 30 sec or more associated with cervical changes, progressive cervical dilatation, and effacement after 28 weeks and before completion of 37 weeks of gestation (unless inhibited by tocolysis) culminating in the delivery of preterm birth.

Pre-term delivery affects 11% in the US or even greater in developing countries (23% in India) and it accounts for 75 -80% of perinatal morbidity and mortality.

The incidence of preterm labor and preterm delivery may vary widely based on populations and shows increasing trends, it could be due to assisted reproductive techniques, psychosocial stress, or medically induced maturity.

Prematurity is the leading cause of perinatal morbidity and mortality also contributes to mental retardation, visual- hearing impairment, and cerebral palsy. Throughout the years a wide variety of drugs with different pharmacologic principles have been used to manage preterm labor

This study was done to compare their efficacy and analyze the overall outcome of preterm labor using tocolytics.

MATERIALS AND METHODS

This prospective cohort study was carried in the Department of obstetrics and gynecology at Nalanda medical college and hospital. Patna from September 2019 to September 2020. All patients with pre term labor reported in the labor room during this duration were taken into study. After written informed consent was obtained, a well-designated questionnaire was used to collect data of recruited patients which included socio-demographic characteristics such as maternal age, parity, socioeconomic status, previous abortion, previous preterm delivery, gestational age on admission.

Study Design: A single- Centre, prospective cohort study

Study Duration: September 2019 to September 2020

Study Location: This was tertiary care teaching hospital-based study done in the labor room of department obstetrics and gynecology, Nalanda medical college, and hospital, Patna. A total of 100 cases of preterm labor who fulfilled the inclusion and exclusion criteria were selected. These 100 cases had been randomly allocated into Group A and Group B of 50 cases each and were matched approximately. The study was approved by the institutional ethical committee.

Inclusion Criteria:

1. Antenatal women with singleton pregnancies between 28 to 37

weeks of gestation

2. Regular uterine contractions with or without pain (at least 1 in every 10 minutes)

3. The presence of cervical changes in the form of effacement (80% or greater) and dilatation (not exceeding 3 cm) even minimal cervical dilatation (1-3cm) were taken into considerations

Exclusion Criteria:

1. Patients suffering from uncontrolled diabetes, thyrotoxicosis, severe hypertension, chorioamnionitis, hydramnios, PROM, hypothyroidism, cardiovascular disease, placenta previa or abruption, severe mental illness, bronchial asthma, and anemia.

2. Fetal factors such as severe IUGR, fetal anomalies, fetal death.

3. Pregnancy beyond 36 weeks.

4. Patients in the advanced stage of labor

A complete history was taken regarding age, occupation, socioeconomic status, and any h/o infections, obstetrics history, and h/o previous preterm deliveries, abortions, h/o diabetes mellitus, heart disease, chronic renal failure, hypertension, and asthma.

The period of gestation was calculated from Naegele's rule, otherwise assessed by clinical examination and ultrasound.

The patient's general physical examination was done.

Vitals were recorded.

The cardiovascular system and respiratory system were examined.

Abdominal Examination-

uterine heights, presentations, position, a lie of the fetus, liquor volume, fetal heart rate were recorded.

Uterine contractions were evaluated concerning frequency and duration.

Per vaginal examination-the consistency, position, dilatation and effacement of the cervix, the status of membranes, and status of presenting parts to be noted.

Routine investigations like Hb %, total count, differential count, ESR, urine for albumin, sugar and microscopy, blood grouping & Rh typing, HIV, HBsAg, HCV, USG, non-stress test, cervical swab or high vaginal swab for culture and sensitivity, urine for culture and sensitivity were done.

METHOD OF TOCOLYSIS:

Patients were allocated into the study group A and B. Written informed

consent was taken from the participants.

GROUP(A) Nifedipine:

Patients were preloaded with 500 ml of crystalloid solution infused over 30-45 mins and then maintained at 100 ml/ hour to prevent the hypotension caused by Nifedipine.

Loading dose: 20 mg oral nifedipine were given, maximum up to 4 doses over 20 min till uterine relaxation.

Maintenance dose: 10-20 mg of oral nifedipine, every 6-8 hourly is started for not more than 7 days, however, if uterine contraction persists for 60 mins after the second dose the treatment is considered a failure.

GROUP(B) : Isoxsuprine

Loading dose: 10 mg i.m and repeated 6 hourly intervals for 48 hrs. once responded were switched to-

Maintenance dose: 20 mg oral every 2 hourly for 1 week

MONITORING:

Blood pressure, pulse rate, FHS, uterine contractions were monitored till the patients were admitted and later on the patients were discharged on maintenance dose.

Apart from tocolysis, antibiotics and betamethasone were given.

Injection Betamethasone 12 mg 2 doses 24 apart to be given for lung maturity.

After the delivery placenta was examined and neonates were evaluated for GA, BIRTH WEIGHT, APGAR SCORE at 1 & 5 min, and congenital anomalies.

As per requirement, the baby is shifted to NICU. Follow up of these babies is done for perinatal complications during a hospital stay.

The goal of the tocolysis is to delay the delivery for 48hrs in patients with rupture of membrane and through 36 completed weeks of gestation in patients with intact membranes.

Treatment is considered failed if the uterine quiescence was not achieved despite maximum doses and delivery occur within 48 hrs. Patients in whom delivery was delayed for 48hrs were taken as cases of primary success. Patients were followed till deliveries and data were recorded about side effects that patients developed during the treatment, time interval between admission and delivery, and neonatal outcome.

Statistical Analysis:

Of 100 cases was done using chi-square. P-value <.05 was considered significant.

RESULTS:

We take 100 patients but 3 patients were excluded because they left the city in the middle of the study. so only 97 participated and data collected and analyzed. Gestational age-wise distribution and clinical profile of the subjects are presented in table 1. homogeneity of the two groups in age, parity, Gestational age, socio-economic status, and obstetrical history was found significant.

Table 1:- Clinical Profile Of The Subjects

Parameters	Nifedipine (N=46)	Isoxsuprine (N=51)	
1.Age (Mean) Years	24.75±4.57	25.20±5.35	P=0.531
2.Parity	P0	22 (47.82%)	X ² =2.4664 P=0.48
	P1	12 (26.09%)	
	P2	8 (17.39%)	
	P3	4 (8.70%)	
3. SES	Upper Class	1 (2.17%)	X ² =1.9236 P=0.75
	Upper Middle Class	3 (6.52%)	
	Middle Class	7 (15.22%)	
	Lower Middle	25 (54.35%)	
	Lower	10 (21.74%)	

4. Residual Area	Urban	16 (34.78%)	11 (21.57%)	X ² =2.1024 P=0.15
	Rural	30 (65.23%)	40 (78.43%)	
5.Previous abortion History		7 (15.22%)	8 (15.69%)	X ² =1.8764 P=0.39
6.Previous Preterm Delivery		6 (13.04%)	12 (23.53%)	
7.Gestational age on Admission (Weeks)		33±1.5	31±2	

[Table 2] shows the tocolysis in two groups, Nifedipine tocolysis was successful at 75.1% and delivery was delayed for 7 days at 30.4 % and up to 28 days at 26.08 %. The mean prolongation of pregnancy was 23.02 days while Isoxsuprine tocolysis was successful at 68.2% and delivery delayed for 7 days at 21.56% and up to 28 days at 15.68 %. The mean prolongation of pregnancy was 19.9 days in the Isoxsuprine group.

Table 2:- Comparison Of Tocolysis In Group A And B

Admission Delivery Interval	Nifedipine N(46)	Isoxsuprine N(51)	P-value
<48 hours	10(21.7%)	18(35.29%)	X ² =3.870 P=0.424
48 hours—7 Days	14(30.4%)	11(21.56%)	
7 Days—14 Days	7(15.2%)	10(19.60%)	
14 Days---28 Days	12(26.08%)	8(15.68%)	
>28 Days	3(6.52%)	4(7.84%)	

[Table 3] shows maternal side effects of the drugs like Tachycardia, Hypotension, Headache, Nausea, Vomiting, and Hot flashes were seen more in Isoxsuprine groups.

Table 3: Side Effects Of The Drugs

Side Effects	Nifedipine N(46)	Isoxsuprine N(51)	P-value
Hypotension	12(26.08%)	15(29.41%)	X ² =12.6 p=0.0275
Tachycardia	11(23.91%)	25(49.01%)	
Headache	15(32.60%)	4(7.84%)	
Nausea	4(8.69%)	3(5.8%)	
Vomiting	2(4.34%)	3(5.88%)	
Hot flashes	2(4.34%)	1(1.96%)	

[Table4] shows the Apgar score in the Nifedipine and Isoxsuprine group.

Table 4:- APGAR score

Variable	Distribution	Nifedipine N=46	Isoxsuprine N=51
Apgar Score	0	2(4.34%)	3(5.88%)
	<4	3(6.52%)	4(7.84%)
	4—6	8(17.39%)	9(17.64%)
	>7	33(71.73%)	35(68.62%)

[Table 5] shows birth weight and APGAR scores in the Nifedipine and Isoxsuprine group.

Table 5:- Birth Weight

Variable	Weight (kg)	Nifedipine N=46	Isoxsuprine N=51
Birth weight	>2.5	9(19.56%)	10(19.60%)
	2-2.5	19(41.30%)	11(21.56%)
	1.6-2	8(17.39%)	16(31.37%)
	1.1---1.5	9(19.56%)	12(23.52%)
	<1	1(2.17%)	2(3.92%)

DISCUSSION

Preterm labor resulting in prematurity and neonatal complications is still a major obstetrical problem, no definite cause or preventive measure have been found, over the last 2 decades, several drugs have been used to suppress uterine activity.

Gulati A et al found Nifedipine prolong pregnancy for 21.1±17.4 days,^[2] Kalita D et al found it as 31.68±10.02 days,^[3] Sachan A et al 39.26±15.5 days.[4] In our study, Nifedipine was found to prolong pregnancy for 15.50±12.79 days. In the isoxsuprine treated group. Gulati A et al found pregnancy was prolonged for 13.10±18.40 days,^[2] Kalita D et al 23.08±9.30 days,^[3] Sachan A et al 39.26±25.5 days,^[4] and 13.44±13.53 days in our study.

In Nifedipine treated group, Smith CS et al found Successful tocolysis in 75% of the patients,^[5] Gulati A et al 80% of the patients,^[2] Kalita D et al 84% of the patients,^[3] and Nagpal P et al 85.3% of the patients.^[6] Nisha S et al reported successful tocolysis in 80% of the patient.^[7]

Bankatlal JP et al reported 90% with nifedipine.^[8] In the present study, successful tocolysis was seen in 71.1% of the patients with preterm labor treated with nifedipine. Gulati A et al found successful tocolysis in 52% of the patients treated with isoxsuprine,^[2] Kalita D et al 64% of the cases,^[3] Sachan A et al 50%.^[4] And in the present study successful tocolysis was achieved in 68.2% of the patient treated with isoxsuprine. Nisha S et al reported successful tocolysis with isoxsuprine in 68% of the patient.^[7] Bankatlal JP et al found 68.3% with ritodrine.^[8] Our findings are comparable to Smith CS et al (1993) and Gulati A et al (1993).

The mean birth weight of the babies in the nifedipine treated group was 1989.3±519.88 gm in this study which was similar to the mean birth weight of the babies found in the studies of Patki A et al (1993), Gulati A et al (1993), and Kalita D et al (1996) In the Isoxsuprine treated group the mean birth weight of the babies was 1882.54±498.59 gm in the present study which was comparable to Gulati A et al (1993) and Patki A et al (1993).

Regarding the Apgar score of babies, there was no significant difference between the two groups. 71.73% of the babies in the Nifedipine group and 68.62% of the babies in the Isoxsuprine treated group had Apgar scores of >7 at 5 min after delivery, which is comparable to the findings of Gulati A et al (1993) and Kalita D et al (1996) in their studies.

Regarding the side effects of the drugs, Ganla KM et al observed tachycardia in 46% of the Nifedipine group as compared to 56% of the Isoxsuprine treated group. Hypotension was seen in 36% and 20% of the patients on Isoxsuprine and Nifedipine treated groups respectively. Nausea and vomiting were seen in Isoxsuprine 34% and Nifedipine 10%. Hot flashes and headache were seen in 40%, 30%. 17% and 12% of the patients on Isoxsuprine and Nifedipine respectively.^[10] Palenik SR et al observed flushing in 96%, headache in 38% of the patients treated with nifedipine. He reported a transient fall of blood pressure following the second dose of nifedipine which was not significant. He also reported that isoxsuprine caused nausea in 22 – 30% of the patients and palpitation and tachycardia in 50% of the patients.^[11] In this study, transient hypotension was seen in 26.08% of the patients treated with nifedipine as compared to 29.41% of the patients treated with isoxsuprine. Tachycardia was seen in 23.91% and 49.01% of the patients on nifedipine and isoxsuprine respectively. Headache was seen more commonly with nifedipine (32.60%) as compared to isoxsuprine (7.84%). 32% of the patients on isoxsuprine had more than one side effects while only 10% of the patients on nifedipine had more than one side effects.

CONCLUSION:

Lowering the incidence of preterm delivery is a better way of reducing neonatal morbidity and mortality especially in India, where sophisticated neonatal intensive care units are not available everywhere. Thus, various drugs have been tried for tocolysis, to prolong intrauterine existence. This study shows that Nifedipine, a dihydropyridine derivative calcium channel blocker is an effective tocolytic agent, comparable to Isoxsuprine in efficacy, with fewer side effects and lesser hemodynamic compromise. The neonatal outcome concerning birth weight, Apgar score, and perinatal death was better in the cases treated with nifedipine though the difference was not significant statistically. The mortality of the infant was not related to nifedipine or isoxsuprine, but due to prematurity and respiratory distress syndrome.

Limitations of the study: Keeping in view the relatively small number of patients and a short period of study in the present study, further controlled study involving a large number of patients, preferably coordinated multicenter trial with special attention to hemodynamic changes due to the drugs will be necessary to throw more lights on the subject.

REFERENCES

1. Main DM, Main EK. Management of preterm labor and delivery, Obstetrics – Normal and Problem Pregnancy. 1st ed. Churchill Livingstone Inc. Broadway, New York; 1986.
2. Gulati A, Rai U. Suppression of preterm labor with Nifedipine. Journal of Obstetrics and Gynaecology of India. 1993; 43:196-201.
3. Kalita D, Goswami A, Majumdar KL. A comparative study of Isoxsuprine and Nifedipine in the Management of preterm labor. Journal of Obstetrics and Gynaecology of India. 1996; 48:47-50.
4. Sachan A, Tiwari S, Gulati N. Nifedipine a safe alternative tocolytic in preterm labor. The Indian Practitioner. 1997; 4:307-310.
5. Smith CS, Woodland MB. Clinical comparison of oral Nifedipine and subcutaneous terbutaline for tocolysis. American Journal of Perinatology. 1993; 10:281-283.

6. Nagpal P, Maheswari M, Sunder K. The role of nifedipine in the suppression of preterm labor. Journal of Obstetrics and Gynecology of India. 1998; 48:35-37.
7. Nisha S, Uma S, Shikha S. Comparative study of nifedipine and isoxsuprine as tocolytics for preterm labor. Journal of Obstetrics and Gynaecology of India. 2011; 61:512-515.
8. Bankatlal JP, Dhabadi VB. Nifedipine versus ritodrine for suppression of preterm labor and analysis of side effects. Journal of Obstetrics and Gynaecology of India. 2011; 61:534-537.
9. Patki A, Mane S, Lenka S, Ganla K, Desai S, Daftary. Suppression of preterm labor, Comparison between nifedipine and isoxsuprine. Journal of Obstetrics and Gynaecology of India. 1993; 43:683-686.
10. Ganla KM, Shroff SA, Desai S, Bhide AG. A prospective comparison of nifedipine and isoxsuprine for tocolysis. Bombay Hospital Journal. 1998; 48:47-50.
11. Palenik SR, Morisson JC. Tocolysis an update for the practitioner. Obstetrical and Gynaecological Survey. 2002; 57:9-15