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Original Research Article

Comparison of safety, efficacy and perinatal outcome of isoxsuprine and nifedipine in women with preterm labour

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ABSTRACT

Background: Over the last 50 years, extensive research has been conducted with the objective of preventing, predicting and optimizing the outcome of patients with preterm labour. Currently, the therapeutic foundation for treating preterm labour involves the use of tocolysis. An attempt is made to study the tocolytic effect of Isoxsuprine and nifedipine in suppression of preterm labour.

Methods: This is a prospective study, carried out in the department of Obstetrics and Gynaecology of S S institute of medical sciences and research centre, Davangere, over a period of 15 months- from October 2014 to January 2016.

Results: 60 antenatal cases with 28-36 weeks of gestation with painful intermittent uterine contractions were considered for the study. Subjects were randomly allotted into two groups - Group A (Isoxsuprine) and Group B (Nifedipine) 30 patients each. Main outcomes include prolongation of pregnancy, maternal side effects and neonatal outcome were compared. Baseline characteristics were well matched in both study groups. Mean prolongation of pregnancy was 31.68 days in Nifedipine and 27.54 days in Isoxsuprine group which was statistically significant. Success rate with Nifedipine was found to be 96% as compared to Isoxsuprine which was 75%. Maternal side effects like hypotension (13.33%) and tachycardia (6.66%) were common in Isoxsuprine group, while facial flushing was seen in 16.66% patients in Nifedipine group. Neonatal outcome was similar in the both groups.

Conclusions: Nifedipine is a safe and effective tocolytic agent than Isoxsuprine with less maternal complications.

Keywords: Nifedipine, Preterm labour, Tocolysis

INTRODUCTION

Determination of efficacy and safety of tocolytic agents has been a difficult task because of various reasons. The cause of preterm labour is generally unknown. Therefore therapy cannot be directed to a specific cause. In about 30% of the patients with apparent preterm labour, uterine contractions cease spontaneously without treatment. Clinicians can never be sure which patient will progress in labour. There is lack of uniformity in the definition of preterm labour.

The diagnosis of preterm labour may be in error as much as 80% of the time. Also the criteria for success of

tocolysis have been different by different authors. There are no accurate recent worldwide data but estimates of preterm birth range from a relative stable 5-10% in developed countries to as high as 25% in some of the worst hit developing countries.¹ This prospective study was designed to find out the safety, efficacy and perinatal outcome of Isoxsuprine and Nifedipine in women with preterm labour.

METHODS

60 antenatal cases with 28-36 weeks of gestation with painful intermittent uterine contractions are considered for the study. Sample size was based on the hospital

statistics, exclusion criteria and non-cooperation of the patients. The subject was taken up for the study after taking informed consent and after satisfying the inclusion criteria's, after which they were randomly allotted into two groups - Group A (Isoxsuprine) and Group B (Nifedipine).

Inclusion criteria

- Gestational age between 28-36 weeks.
- About 1-2 regular uterine contractions occur in 10 min, each lasting for 30 seconds.
- Cervical effacement of more than 80% and with dilatation of less than 3 cms with intact membranes.
- No previous administration of tocolytics.

Exclusion criteria

- Systemic diseases like diabetes mellitus, cardiac diseases, liver or renal diseases
- Obstetric complications like severe pregnancy induced hypertension, eclampsia, antepartum haemorrhage, hydramnios, hyperthyroidism
- Foetal complications like chorioamnionitis, IUGR, congenital anomaly, foetal distress, oligoamnios
- Multifoetal gestation

A detailed history, complete physical and obstetric examination and routine investigations were done for all the patients.

Method of study

Patients were taken up for the study after diagnosing preterm labour based on inclusion criteria. They are randomly allotted into two groups- Group A (Isoxsuprine) and Group B (Nifedipine).

Treatment protocol

Isoxsuprine group

Those patients assigned to Isoxsuprine group, started on Isoxsuprine infusion of 30- 60 mg in 500 ml of 5% dextrose at 0.02 mg/min, increasing the infusion rate up to 0.08 mg/min, dose administration did not exceed 0.5 mg/min, depending on the status of uterine contractions and occurrence of side effects. After discontinuation of i.v infusion, patients maintained on oral Isoxsuprine 10 mg 8 hourly for up to 7 days.

Nifedipine group

Those assigned to Nifedipine group, received prehydration with intravenous infusion of ringer lactate at the rate of 100 ml/hr, continued only till sublingual Nifedipine was administered. Nifedipine 10 mg was given sublingually, and the same dose was repeated every 20 mins for up to 4 doses. 4-6 hrs after the last sublingual

Nifedipine dose, tablet Nifedipine 10-20 mg was given orally every 6-8 hrs, for not more than 7 days as a maintenance dose.

Patients in both groups were given antibiotics and injection betamethasone 24 mg in 2 divided doses, 24 hrs apart.

Uterine contractions, foetal heart rate and vital signs were monitored in both the study groups. Side effects are noted from the time of administration of drug till the patient was discharged from the labour ward.

Treatment was considered successful, if there was abolition of uterine contractions, no progression of cervical dilatation, and also if contractions did not recur within 48 hrs of cessation of therapy.

Treatment was deemed failure, despite maximal dose mentioned for both groups, if uterine relaxation was not achieved or patient or foetus developed some significant side effects that necessitated discontinuation of therapy.

Data regarding efficacy of the drugs in terms of arrest of preterm labour, prolongation of pregnancy and the days gained in utero were noted. Details of mode of delivery, gestational age at the time of delivery, baby's sex, birth weight and Apgar score were noted.

RESULTS

Majority of the patients in the present study were between 28-32 weeks of gestation (n= 21 vs 19) in Isoxsuprine group and Nifedipine group respectively. The mean gestational age in Isoxsuprine group and Nifedipine group is 31.62 weeks and 31.9 weeks respectively [Table-1]. There is no statistically significant difference in both study groups with respect to gestational age. In the present study, primigravidae were more in Isoxsuprine group (n=17) as compared to Nifedipine group (n=14).

Commonest and most significant risk factor in Isoxsuprine and Nifedipine groups was anaemia (n=16 vs 19 respectively), followed by substance abuse (tobacco n= 13 vs 10), physical and psychological stress (n=11 vs 15) and infections (n=6 vs 4).

In our study, prolongation of pregnancy was more in Nifedipine group 31.68 days when compared to Isoxsuprine group 27.54 days. The prolongation is statistically significant P being ≤ 0.001 and it depended on the gestational age at the onset of tocolytic therapy and the time from the onset of therapy to delivery.

Period of gestation at the time of delivery was ≥ 37 weeks in 20 of cases in Nifedipine group when compared to Isoxsuprine group (14). 06 patients in Isoxsuprine and 05 patients in Nifedipine group have lost to follow up.

Table 1: Baseline characteristics of the study population.

	Group A No. of patients (n=30)	Group B No. of patients (n=30)
Gestational age (weeks)		
28-30	08	09
31-32	13	10
33-36	09	11
Parity		
Nulliparous	17	14
Multiparous	13	16
Risk factors for preterm delivery		
Previous preterm	01	03
Abortions	04	07
Evidence of infection	06	04
Previous D and E	04	04
Physical and psychological stress	11	15
Coitus during pregnancy	01	02
Substance abuse	13	10
Anaemia	16	19
No risk factor found	11	10
Prolongation of pregnancy (days)		
Mean	27.54	31.68
Gestational age at delivery (weeks)		
< 37	10	05
≥ 37	14	20
Lost to follow up	06	05
Perinatal outcome		
Birth weight- mean	1.94	2.06
Apgar score at 1', <7	14	4
>7	10	21
Maternal side effects		
Tachycardia ≥ 110bpm	02	01
Headache	00	00
Hypotension <90/60	04	00
Facial flushing	00	05
Treatment response		
Success	18	24
Failure	06	01

In the present study, mean birth weight of infants delivered is 2.06 kgs in Nifedipine group with apgar scores of >7 at 1' are seen 21 cases. In Isoxsuprine group, infants delivered had mean birth weight of 1.94 kgs with Apgar scores of >7 at 1' are 10 cases.

In our study, hypotension was noted in 04 patients of Isoxsuprine group as compared to Nifedipine group where none of them had hypotension, while other side effects like facial flushing noted in 5 patients of Nifedipine group and tachycardia in 2 patients of Isoxsuprine and 1 patient of Nifedipine group. No other

serious side effects noted in both groups. In our study Nifedipine group has highest success rate compared to Isoxsuprine group.

DISCUSSION

Prematurity continues to be the major contributor to the perinatal morbidity and mortality. The approaches which prevent and treat preterm labour will have great impact on society and long term public health care costs. None of the currently available tocolytic agents are ideal. Calcium channel blockers are safer and more effective than betamimetics. The measures taken to prolong pregnancy have shown to reduce neonatal morbidity and mortality.

This prospective study was designed to find out the safety, efficacy and perinatal outcome of Isoxsuprine and Nifedipine in women with preterm labour. Patients were included into the study group in which uterine contractions continued even after complete bed rest. This could reduce the number of patients in false labour being included in the study. Since the late 1970's Nifedipine has been known to relax the pregnant and non-pregnant uterus (Ulmsten, Anderson KE).²

The patients in both groups were well matched regarding age, antenatal care, gravidity, previous obstetric history and socio economic status. This is supported by well-matched randomised controlled trials conducted by Kedar MG et al, Kalita D et al, Rayamajhi R et al, Singh N.³⁻⁶

Most of the studies so far conducted have compared the efficacy and safety between Nifedipine and Ritodrine. Only few studies have been done between Nifedipine and Isoxsuprine. Kedar MG et al, Kalita D et al, Rayamajhi R et al, Singh N have conducted studies about comparison between the efficacy and safety of Nifedipine and Isoxsuprine in the suppression of preterm labour.³⁻⁶

The mean prolongation of pregnancy in the present study was 31.68 ± 8.37 days with Nifedipine and 27.54 ± 7.38 days with Isoxsuprine. These results were similar to those reported by Kalita D et al study.⁴ Kalita et al reported mean prolongation of pregnancy as 31.16 ± 10.2 days with Nifedipine and 23.06 days with Isoxsuprine.⁴ Kedar et al³ reported mean prolongation of pregnancy as 22.4 ± 15.6 days with Nifedipine and 16.5 ± 14.5 days

with Isoxsuprine. Rayamajhi et al reported mean prolongation of pregnancy as 25.71 days with Nifedipine and 19.18 days with Isoxsuprine.⁵ Tewari et al reported mean prolongation of pregnancy as 39.26 ± 25.5 days with Nifedipine and 25.5 ± 15.75 days with Isoxsuprine.⁷ Indian study conducted by Singh S and Gupta K observed that prolongation of pregnancy was more when the period of gestation was less, being 47.44 days at 22-24 weeks and only 10.18 days at 33-36 weeks of gestation.⁸ We infer that prolongation of pregnancy depends not only on

the gestational age at the time of tocolysis, duration of tocolysis but also the dose given for tocolysis.

In the present study, successful tocolysis was achieved in 96% with Nifedipine group and 75% with Isoxsuprine group. These results were similar to those reported by Kedar et al, 88% with Nifedipine and 76% with Isoxsuprine group.³ Rayamajhi et al reported 81.25% successful tocolysis with Nifedipine and 70% with Isoxsuprine group.⁵

The maternal side effects observed in our study were less as compared to Kedar et al and Rayamajhi et al study.^{3,5} No significant change in blood pressure was observed with Nifedipine group in our study that necessitated discontinuation of therapy, as Nifedipine exhibits greater selectivity for inhibition of uterine activity relative to cardiovascular effects. This may be attributed to the use of prehydration in the nifedipine regime.

CONCLUSION

Preterm labour and delivery remains a major cause of perinatal morbidity and mortality. Tocolytic agents are currently the principal preterm birth preventive measure and will remain so until the aetiology of preterm labour is better understood. Calcium channel blockers (nifedipine) are safer and more effective in suppressing preterm labour.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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