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Original Research Article

Comparative study of nifedipine and isoxsuprine in suppression of preterm labour

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ABSTRACT

Background: A prospective study was conducted to compare the efficacy of nifedipine against isoxsuprine in preventing preterm labour and also to evaluate maternal side effects and neonatal outcome.

Methods: This was a randomized prospective comparative study done at MGM hospital and research center, Patna, Bihar between 15/03/2014 to 15/02/2016. 75 antenatal women with gestational age between 28 to 36 weeks were selected who fulfilled the inclusion criteria for the study, were given nifedipine and were monitored throughout the course of treatment.

Results: Groups were compared with mean prolongation of delivery, side effects, neonatal outcome, parity, cervical effacements. Nifedipine was twice more effective than isoxsuprine hydrochloride as a uterine tocolytic agent while side effects were comparable with fewer side effects in nifedipine group. Neonatal outcome was better with nifedipine in comparison to isoxsuprine.

Conclusions: There is a high incidence of preterm labour in India. The present study found that nifedipine has better tocolytic efficacy, less side effects and better tolerability as compared to isoxsuprine.

Keywords: Preterm labor, Tocolytics, Nifedipine, Isoxsuprine hydrochloride, Ritodrine

INTRODUCTION

Preterm labor remains one of the unconquered frontiers in the present era of obstetrics. Its incidence is about 7-9% of pregnancies accounting for three quarters of the mortality and morbidity among newborns without congenital anomalies.¹ Preterm delivery affects 11% in United States or even greater in developing countries (23.3% in India) and it accounts for 40-75% of neonatal deaths.^{2,3}

Throughout the years a variety of drugs with different pharmacologic principles are used to suppress preterm labour. The choice is limited by their efficacy, safety and side effects. Ritodrine, beta sympathomimetic is one such

agent which is commonly used tocolytic. It has serious maternal and fetal side effects limiting its use.⁴ Beta adrenergic receptor blocking agent isoxsuprine and nifedipine, a calcium channel blocking agent is the most widely used tocolytic agent in India.⁵ Several nonrandomized and randomized trials suggest that nifedipine is effective in suppressing preterm labor with minimal side effects on the mother and fetus.^{1,6-8} Nifedipine is an effective smooth muscle relaxant with low toxicity and low teratogenicity.⁹ There is a growing body of nifedipine, that it is an effective, potentially safer and better tolerated tocolytic agent with no known fetal side effects. This study compares in a prospective design, the efficacy and safety results of nifedipine with that of isoxsuprine in the expression of preterm labour and also

to compare maternal and perinatal outcome in these patients.

METHODS

This was a prospective study of 75 antenatal women conducted at MGM hospital and research center Patna, Bihar in the department of obstetrics and Gynecology. Written informed consent was taken from the subjects recruited in the study from 15/03/2014 to 15/02/2016. Patient included in the study were between 28-36 weeks of gestational age and four uterine contractions in 20min with or without cervical dilatation more than 1cm or effacement 80% or greater were recruited in the study as per the ACOG criteria.

Female patients with more than 36 completed weeks, those in active labour (>4cm dilatation), those with severe pregnancy induced hypertension, eclampsia, gestational Diabetes mellitus, cardiac disease, Abruptio placenta, chorio-amnionitis, fetal distress, fetal anomaly, hyperthyroidism were excluded from the study. For group 1, who received nifedipine were given 20mg oral nifedipine initially followed by 10mg at four hour interval for 48 hour. If contractions persisted at 90min, the first 10mg dose was started at the same time. For group 2, patient were started on infusion of injection isoxsuprine 40mg in 500ml ringer lactate at 0.08mg/min, increasing the infusion rate up to 0.24mg/min depending on the status of uterine contractions and occurrence of side effects. After discontinuation of intravenous infusion, patient's were maintained on oral isoxsuprine 10mg eight hourly for upto 7 days. Either of the treatment was discontinued if no uterine contraction occurred within 48 hours.

Vital signs, uterine contractions and fetal heart sound were monitored half hourly and side effects were noted until the patient was discharged from labour ward and started on maintenance doses. All patients received injection Betamethasone 12mg intramuscularly for two doses 24hours apart, to enhance fetal lung maturation. All the patients were followed up weekly for cervical dilatation. Goal of tocolysis was to delay delivery for 24hours, in patient with ruptured membranes and through 36 completed weeks of gestation in patients with intact membranes. Tocolysis was considered failed if uterine quiescence was not achieved despite maximum dose and delivery occurred within 48hours. Data regarding mean prolongation of pregnancy (at 48hour, 1 week, 37 weeks), side effects, failure of treatment, gestational age at delivery and neonatal death were recorded. In this hospital, incidence was 24% during the study period.

RESULTS

During the prospective study of 75 women who received oral nifedipine following results were found.

Table 1: Mean prolongation of delivery.

	Nifedipine	Isoxsuprine
Age (years)	22.2±5.5	23.4±4.6
Parity		
Primigravida	67 (90%)	60 (80%)
Multigravida	8 (10%)	15 (20%)
Gestation at treatment (in Weeks)	30.5±3.5	31.4±2.8
Mean prolongation of delivery (in days)	22.4±15.6	16.5±4.5

In group I, 90% of patient was primigravida with mean age of 22.2±5.5 Yrs and with mean gestation at treatment was 30.5±3.5 Weeks and mean prolongation of delivery was 22.4±15.6 days where as with the isoxsuprine in group II patient mean prolongation of delivery was 16.5±14.5 days.

Table 2: Pregnancy outcome.

	Nifedipine n (%)	Isoxsuprine n (%)
Success	67 (90%)	57 (76%)
Failure	8 (10%)	18 (24%)
Total	75 (100%)	75 (100%)

n= no. of patient

From Table 2, we conclude that 90% success rate was seen in group I while the success rate in group II was only 76%.

Table 3: Side effects.

	Nifedipine n (%)	Isoxsuprine n (%)
Tachycardia	35 (76%)	42 (50%)
Hypotension	15 (20%)	27 (36%)
Nausea/Vomiting	7 (10%)	25 (34%)
Chest pain	3 (4%)	7 (10%)
Pulmonary edema	0	7 (2%)
Hot flushes (transient)	30 (40%)	26 (39%)
Headache	27 (30%)	9 (12%)

Nausea, vomiting, headache and palpitation were main side effects in both the group. More Incidences of 40% transient hot flushes was seen in group A than in group B. Pulmonary edema was reported in 1 case with isoxsuprine, following which therapy was discontinued. Hypotension and tachycardia were commonest maternal side effects (Table 3).

DISCUSSION

Incidence of preterm labor is quite high in our country compared to developed countries (11% USA).^{2,3} It has been found to be 24% in our study.

Cochrane review 2004 on preterm labor concludes that tocolysis is definitely indicated before 34 weeks gestational age, this is because of the reduction in number of women delivering within next 7 days and resultant decrease in neonatal morbidity.¹⁶ In our study, it was found that tocolysis delayed delivery in 90% of total cases and maximum in 28-34 gestation age. This delay in delivery allows times for the steroids to accelerate pulmonary maturity and neonatal survival.

Isoxsuprine was the first beta sympathomimetic drug used to inhibit preterm labor in 1961. Many studies have shown it to have limited therapeutic value in light of unpleasant side effects and efficacy.¹⁰⁻¹³ Nifedipine, a calcium channel blocker was first used clinically as a tocolytic by Ulmsten et al in 1980. Since then it has emerged as a safe and effective tocolytic.^{6,14,15} In the present study, nifedipine shows significantly better efficacy (90%) in delaying delivery for 24 hrs as compared to isoxsuprine (76%). Kalita et al reported a success rate of 84% with nifedipine and 64% with isoxsuprine.¹² Read et al reported a success rate of 83% with nifedipine.¹⁵ Kupfermine et al reported 83% success with nifedipine and 77% with ritodrine.¹

The mean prolongation of pregnancy in the present study was 22.4 days with nifedipine and 16.5 days with isoxsuprine. Kalita et al reported mean prolongation of pregnancy as 31.16 days with nifedipine and 23.06 days with isoxsuprine.¹²

In our study, no significant difference was noted in maternal and neonatal side effects but lesser side effects was seen with nifedipine. Ferguson, Meyer, Kupfermine and Papatsonis all found nifedipine to be associated with significantly fewer maternal side effects as compared to isoxsuprine. Kalita et al have reported a significantly higher incidence of side effects with isoxsuprine than with nifedipine.^{1,4,9,12,17} Tewari et al have reported a much higher incidence of tachycardia in both groups.¹¹ In the present study, transient hypotension, nausea, vomiting, tachycardia, chest pain, headache in 20%, 10%, 46%, 4%, 30% in nifedipine group. Headache was more in nifedipine group as seen in present study and that of Rayamajhi et al.¹⁸ In our study, cardiovascular side effects were more seen in isoxsuprine group. This is comparable to the study of Read and Wellby who observed more cardiovascular side effects with isoxsuprine compared to nifedipine.¹⁵

The RCOG recommends that if a tocolytic drug is to be used, ritodrine is no longer the first choice.¹⁹ Atosiban and nifedipine appear to be preferable as they have fewer adverse effects and seem to have comparable effectiveness. The reported experience with nifedipine as a tocolytic has been found to be reassuring in view of the increasing evidence of its efficacy and safety combined with its ease of administration; it appears likely that nifedipine will play an expanded role in suppression of preterm labor.

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

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