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Comparative Study between Nifedipine and Isoxsuprine for Suppression Preterm Labour

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Abstract

Objectives: To compare the efficacy and safety of oral nifedipine and parenteral isoxsuprine in suppression of preterm labour. *Methods:* This is a prospective trial. 100 antenatal cases with 28- 36 weeks of gestation with threatened or early preterm labour were selected and divided in 2 groups. Group A received oral nifedipine, while group B received parenteral isoxsuprine. Outcome was analyzed with respect to prolongation of pregnancy, maternal and fetal side effects. *Conclusion:* Nifedipine is preferred tocolytic agent than isoxsuprine in arrest of early preterm labour with lesser maternal side effects.

Keywords: Preterm Labour; Nifedipine; Isoxsuprine.

Introduction

Preterm birth is the most important single determinant of adverse neonatal outcome, in terms of both survival and quality of life. Preterm birth is defined as birth before 37 weeks of gestation, although major complications occur when born before 34 weeks of gestation.

WHO has estimated that 15 million babies are born preterm every year that is more than 1 in 10. Over 1 million die annually from preterm birth complications making it the leading cause of death in newborn and second leading cause in children less than 5 yrs of age. India has maximum number of preterm births with 3,519,000 of them followed by china with 1,172,300. Thus alone India holds the burden of 24% of total preterm births. In may 2012 WHO published a report- *born to soon: the global action report on preterm birth* with aim to save 16 million lives by 2015 [1].

Antenatal steroid, tocolysis and antibiotics are the main stay in treatment of preterm labour. Tocolytic agents inhibit the uterine contractions and prolong the duration of pregnancy or at least in some cases give time for steroids to act. In both ways it plays important role in management of patients with preterm labour.

Various types of tocolytic agents are used with varied success rates and side effects, but it is still not clear what the first line tocolytic agent should be [2]. Those in the current use are beta agonists, calcium channel blockers, prostaglandin synthatase inhibitors, nitric oxide donors and oxytocin receptor antagonist. Isoxsuprine is most commonly used tocolytic agent in our institute.

This study was conducted to compare the efficacy and adverse effects of nifedipine and isoxsuprine as tocolytic agents.

Material and Methods

This was a randomized, prospective study conducted in Department of obstetrics and gynaecology in PDVVPF's medical college and hospital, during July 2013 to November 2014. 100 pregnant women with gestational age between 28 to 36 weeks with preterm labour were included in present study. Diagnosis of preterm labour was done following ACOG criteria i.e. 4 uterine contractions in 20 min with or without cervical dilatation > 1 cm or cervical effacement more than 80%. Detailed history and through examination of patients was done to rule out presence of any exclusion criteria.

Exclusion criteria were Advanced preterm labour (cervical dilatation more than 4 cm), Chorioamnionitis, Antepatrum haemorrhage, Fetal distress, Intrauterine fetal death, Fetal anomaly, Medical disorders in mother like hypertension , diabetes, heart disease, Pre-eclampsia.

Written and informed consent was taken and patients were randomized in 2 groups. Group A (nifedipine) and group B (isoxsuprine).

Patients in group A were given tablet nifedipine 20 mg stat orally, followed by 10 mg every 6 hourly for 48 hours. Patients were then shifted to tablet nifedipine 20 mg twice a day for next 5 days.

Patients in group B received injection isoxsuprine 10 mg intramuscularly 6 hourly for 48 hours. Those who had cessation of uterine activity were shifted to oral isoxsuprine table 10 mg TDS for next 5 days.

Antibiotics and steroids were given in both groups. The primary aim of tocolysis was to delay the delivery for at least 48 hours and further till 37 completed weeks if possible. Treatment was labeled as failure if uterine contractions fail to cease in 48 hours. Those who responded were then shifted to the wards with oral tocolysis and observed for next 24 hours for uterine activity and discharged to be followed up to delivery. Data regarding primary success of tocolysis, mean prolongation of pregnancy and side effects were recorded.

Results

100 patients were enrolled in present study. They were divided in two groups as group A (nifedipine) and group B (isoxsuprine).

Table 1: Distribution of patients according to gestational age

Gestational age (weeks)	Group A Nifedipine n=50	Group B Isoxsuprine n=50
28-30	7(14%)	5(10%)
30-32	21(42%)	20(40%)
32-34	15(30%)	16(32%)
34-36	7(14%)	9(18%)

Table 2: Distribution of age & parity

	Group A Nifedipine n=50	Group B Isoxsuprine n=50
Mean age (years)	27.1	25.4
Parity		
Primigravida	19 (38%)	21(42%)
Multigravida	31(62%)	29(58%)

Table 3: Results of tocolytic therapy

Prolongation of delivery from admission	Group A Nifedipine n=50	Group B isoxsuprine n=50
< 48 hours (primary failure of treatment)	8(16%)	20(40%)
= 48 hours to < 37 weeks of gestation	20(40%)	16(32%)
=37 week of gestation	22(44%)	14(28%)
Mean prolongation of pregnancy	37.5 days	25.8 days

Table 4: Side effects associated with tocolytic therapy

Side effects	Group A Nifedipine n=50	Group B Isoxsuprine n=50
Palpitation	2(4%)	25(50%)
Hypotension	3(6%)	13(26%)
Breathlessness	nil	3(6%)
Headache	12(24%)	3(6%)
Pulmonary oedema	nil	nil
Flushing	5(10%)	1(2%)
Nausea & vomiting	nil	12(24%)
Maternal tachycardia	4(8%)	13(26%)

Table 5: Outcomes in treatment group

	Group A Nifedipine n=50	Group B Isoxsuprine n=50	P value
Successn(%)	42(84%)	30(60%)	
Failuren(%)	8(16%)	20(40%)	

Table 1 shows distribution of patients according to gestational age in weeks. Gestational age at inclusion varied from 28-36 weeks. Majority of the cases were having gestational age between 30-32 weeks in both groups.

Table 2 shows distribution according to age & parity among two groups. Mean age was 27.1 years in group A and 25.4 years in group B. In both the groups multigravida outnumbered primigravida.

There was no significant difference in both groups with respect to gestational age, patient's age & parity between two groups.

Table 3 shows results of tocolytic therapy. Prolongation of delivery from e" 48 hours to < 37 weeks of gestation was seen in 20 cases (40%) in group A & in 16 cases (32%) in group B. Pregnancy continued beyond 37 weeks of gestation in 22 cases (44%) in group A & in 14 cases (28%) in group B.

Failure to prolong pregnancy beyond 48 hours was seen in 20 cases (40%) in group B, which was more than group A i.e. 8 cases (16%).

Mean prolongation of pregnancy was 37.5 days in group A & 25.8 days in group B. this difference is statistically significant (chi square test- p = 0.03).

Table 4 shows different side effects associated with tocolytic therapy. Overall nifedipine caused mild symptoms as compared to isoxsuprine.

Headache (24%), flushing (10%) were the common side effects in group A & these were not severe enough to discontinue drug therapy.

Palpitation(50%), hypotension(26%),maternal tachycardia(26%) & nausea, vomiting (24%) were the common side effects in group B. 6 cases required stoppage of treatment in view of the side effects, rest of the patients were managed by reducing the frequency of the drug.

Table 5 shows outcome in both treatment groups. Group A treated with nifedipine was associated with higher success rate 42 cases (84%), as compared to group B 30 cases (60%) which is statistically significant (Chi sq value 23.120,P < 0.005).

Discussion

Incidence of preterm labour is quiet high in our country, contributing significantly to the neonatal morbidity & mortality.

Although tocolytics have not been shown to improve neonatal outcomes, they can delay preterm delivery long enough for antenatal corticosteroids to be administered or for the mother to be transported to a tertiary care facility [3].

Many different classes of drugs have been used for tocolytic therapy. These include beta mimetics such as isoxsuprine,ritodrine and terbutaline; magnesium sulfate; prostaglandin inhibitors (for example, indomethacin, ketorolac); calcium channel blockers such as nifedipine; nitrates (nitroglycerine); oxytocin receptor blockers (atosiban) and others. Each tocolytic has a unique mechanism of action, side effects and degree of complexity to administer [4,5].

In our study we have compared two drugs i.e.nifedipine & isoxsuprine for reporting their safety & efficacy in prevention of preterm labour.

Nifedipine is a calcium channel blocker, which directly inhibit calcium influx across the cell membrane causing uterine muscle relaxation.

Isoxsuprine belongs to beta-sympathomimetic drugs, which act through c GMP to inhibit uterine muscle contraction.

100 patients were enrolled in present study. They were divided in two groups as group A (nifedipine) and group B (isoxsuprine). Both groups were well matched for possible confounding factors.

This is supported by well matched randomized controlled trials conducted by Seema B Nagendrappa et al [6], Singh Nisha et al [7], Rayamajhi R et al [8], Kalita D et al [9],Kedar M G et al [10] .

The mean prolongation of pregnancy in the present study was 37.5 days with Nifedipine and 25.8 days with Isoxsuprine. These results were similar to those reported by Kalita D et al study. Kalita et al reported mean prolongation of pregnancy as 31.16 ± 10.2 days with Nifedipine and 23.06 days with Isoxsuprine. Kedar et al reported mean prolongation of pregnancy as 22.4 ± 15.6 days with Nifedipine and 16.5 ± 14.5 days with Isoxsuprine. Raymajhi et al reported mean prolongation of pregnancy as 25.71 days with Nifedipine and 19.18 days with Isoxsuprine. Tewari et al [11] reported mean prolongation of pregnancy as 39.26 ± 25.5 days with Nifedipine and 25.5 ± 15.75 days with Isoxsuprine.

In the present study, successful tocolysis was achieved in 84% with Nifedipine group and 60% with Isoxsuprine group. These results were similar to those reported by Kedar et al, 88% with Nifedipine and 76% with Isoxsuprine group. Rayamajhi et al reported 81.25% successful tocolysis with Nifedipine and 70% with Isoxsuprine group.

In our study nifedipine was overall well tolerated drug than isoxsuprine.

Nifedipine caused few side effects which were not

responsible for discontinuation of therapy.

Isoxsuprine caused palpitation (50%), hypotension (26%), maternal tachycardia (26%) & nausea, vomiting (24%). Out of 50 cases, 6 (12%) required stoppage of treatment to alter the side effects, rest of the patients were managed by reducing the frequency of the drug.

In this respect our study was comparable with other studies, where nifedipine was well tolerated drug.

Conclusion

Nifedipine has been found to be more effective than isoxsuprine in prolongation of pregnancy in patients with threatened and early preterm labour with lesser side effects. Therefore starting tocolysis with oral nifedipine can be a safe option to obtain good outcome in preterm labour.

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