A comparative study of Nifedipine and isoxsuprine hydrochloride in the management of preterm labour.

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Summary: **Pregnancies between 28-36 weeks in preterm labour were randomized to either sublingual nifedipine or intravenous isoxsuprine. After labour was arrested, the patients in the nifedipine group were treated with nifedipine for 3 days and those in the isoxsuprine group were treated with oral isoxsuprine for 3 weeks. 50 cases were considered eligible of whom 25 were randomized to the nifedipine and other 25 were treated with isoxsuprine. We have observed that the mean duration of prolongation of pregnancy was 31.68±10.2 days with nifedipine and 23.08± 9.3 days with isoxsuprine hydrochloride. Maternal side effects were common in isoxsuprine group, as compared to nifedipine group. None of the cases in both groups required discontinuation of therapy due to side effects. Side effects were minimized by reduction of dosage. Nifedipine is significantly more effectively well tolerated tocolytic agent than isoxsuprine hydrochloride.**

Introduction

Being a major cause of perinatal morbidity and mortality prematurity has become the largest single problem in the contemporary paediatrics and obstetrics practice as well as one of the major public health problem of the present time. Therefore, prevention of preterm delivery with tocolytic agent is necessary. Hence, we at the Gauhati Medical College, decided to tackle preterm labour cases by using a relatively new drug, nifedipine, a calcium channel blocker and comparing its tocolytic efficacy and side effects (maternal, fetal and neonatal) with a well known tocolytic isoxsuprine which is commonly used in practice.

Materials and Methods

The study was carried out in the Department of obstetrics and Gynaecology, Gauhati Medical College, Guwahati during the period from 1st Sept' 94 to 31st August '95. The study randomly included 50 patients and they were divided into 2 groups.

Group 'A' :
Included 25 cases treated with Nifedipine.

Group 'B' :
Comprised 25 patients treated with Isoxsuprine hydrochloride.

Criteria for selection of preterm labour
Gestational age - 28 to 36 weeks, documented uterine contraction (8 or more/hr) observing for ½ hr, ruptured membrane or intact membrane, and documented cervical changes/cervical effacement of 80 per cent or more/ cervical dilation upto 3 cms. Patients with following maternal factors are excluded from the study, Diabetes Mellitus, Hyporthyroidism, Cardiac Diseases, Severe preeclampsia and Eclampsia, Abruptio placentae, chorio amnionitis, Hydramnios, Cervical dilation more than 3 cm. The foetal factor considered for exclusion were Foetal distress, severe intrauterine growth retardation, Foetal death, Foetal anomalies incompatible with life.

Management

1. *General:*
   Patient was put on medical treatment as soon as the diagnosis of preterm labour was established. The following regime was adopted routinely in each and every case of preterm labour, bed rest, injection phenergan, intravenous fluid (2400ml/day) and inj.

Dexamethasone for fetal lung maturation if the gestational age is in between 28-34 weeks.

2. *Specific treatment*

Group A - cap Nifedipine 10mg. was given sublingually. If uterine contraction persisted after 20 minutes, this dose was repeated every 20 minutes upto a maximum total dose of 40mg. during the first hour of treatment. If sublingual Nifedipine stopped uterine activity, then oral therapy of 10 mg., 8 hrly. initiated 3 hours after the last sublingual dose. This was continued for 3 days. If uterine contraction did not cease within 1½ hrs. including the initial observation period, patient was deemed a failure and treatment stopped. Treatment was considered successful, if there was abolition of uterine contraction, no progression of cervical dilation, and postponment of labour for at least 72 hrs., and absence of recurrence of uterine contraction within 48 hrs. of cessation of therapy.

Group 'B'

Treated with isoxsuprine, were given a loading dose of 0.2mg/min over 10 minutes and dose was later adjusted according to uterine activity. The maintanence dose was 75 microgram/min. over 24 hrs. Subsequently patients received injectable 10 mg 8 hrly for 2 days followed by oral dose for 2-3 weeks.

Our goal for tocolysis was to delay:

1. Delivery for 48 hours in patients with ruptured membrane.
2. Through 36 completed weeks of gestation in patients in whom the membrane was intact.

Therapy was considered successful when in each respective group, deliveries were delayed for these intervals.

Result and Observation

The patients in nifedipine and isoxsuprine hydrochloride (Group B) were well matched with respect to age, antenatal care, previous obstetric history and socio-economic status.

Table I
Characteristics of Patients

S.No.	Character	Nefidipine	Isoxsuprine
1.	Age (Mean) Years	24.1±2.4	23.8±2.7
2.	Previous Abortion History	24%	36%
3.	Previous preterm delivery	12%	16%
4.	Mean gestational age	32.64±1.8	3.268 ±2.2
5.	On admission (wks) Socio economic status (low)	60%	12%
6.	Mean prolongation of delivery (days)	31.68±10.2	23.08±9.3
7.	Success (no.)	21(84%)	16(64%)
8.	Mean Foetal wt. (kg)	2.5±0.59	2.27±0.63kg.

Characteristic of Patients

In our study, mean gestational age at the time of admission was 32.64±1.8 weeks in group A and 32.68±2.2 weeks in group B. The maximum prolongation of delivery in nifedipine group was 45 days as compared to 49 days in isoxsuprine group. The mean prolongation of delivery in nifedipine group was 31.68±10.2 days as compared to 23.08±9.3 days in isoxsuprine group.

Table II

Prolongation of Pregnancy

Duration of	Nifedipine		Isoxsuprine	
	No.	Group %	No.	Group %
Upto 2 day	-	-	-	-
3-14 days	4	16%	5	20%
15-28 days	6	24%	13	3.2%
29-56 days	15	60%	7	28%
57-84 days		31.68 ± 10.2 days	23.08 ± 9.3 days	

t=3.1 df = 48 p/0.01 - significant.

Table III

Side Effects

Side effects	Nifedipine		Isoxsuprine	
	No. of	%	No. of	%
Headache	5	20	2	8
Flushing	6	24	1	4
Tachycardia	2	8	10	40
Hypotension	1	4	8	32
Nausea & vomitting	1	4	3	12
Palpitation	-	-	1	4

Prolongation of pregnancy

Hence, nifedipine gave a success rate of 84% as compared to 64% in isoxsuprine group. Regarding side effects of both tocolytics, Nifedipine patient experienced much fewer side effects as compared to isoxsuprine group.

The mean birth weight was 2.5±0.59 kg in Nifedipine group as compared to 2.27±0.63 kg in Isoxsuprine group.

There were 2 cases of RDS in Nifedipine group as compared to 4 cases in Isoxsuprine group. There were 2 cases of Hyperbilirubinaemia in Nifedipine group as compared to 3 cases in Isoxsuprine group. There was only one case of birth asphyxia in nifedipine group. There was no significant difference in Apgar scores. There were only 3 neonatal deaths in the nifedipine group as compared to 5 cases in the isoxsuprine group. The commonest cause of death was prematurity and there was no relation with administration of nifedipine or isoxsuprine hydrochloride. There was no still birth or perinatal death.

Discussion

Preterm labour is defined as regular uterine contraction at a frequency of 8 or more per hour with a documented change in cervical dilatation and effacement before 36 completed weeks of gestation.

Beta sympathomimetic drug have been proved not to have any therapeutic value in light of high incidence of side effects. Also they were not suitable for women with significant cardiovascular diseases or diabetes (Hemminki et al, 1978, Spellacy et al, 1979).

Nifedipine, a dehydropyridine derivation was first used clinically in the 1980 by Ultsten et al (1980), Activity in utero in vitro, is much dependent upon extracellular calcium (Boltan 1979) so that it would be anticipated that contraction would be inhibited by calcium antagonist.

Regarding prolongation of delivery after initiation of therapy was 31.16±10.2 days in Nifedipine group as compared to 23.06±9.3 days in isoxsuprine group. These results were very similar to the tocolytic success and postponement of delivery as reported by Read et al (1986), Roy et al (1992), Patki et al (1993) and Menachem et al (1977).

The side effects of Nifedipine and Isoxsuprine hydrochloride are generally tolerable. They are mainly tachycardia, hypotension, flushing, headche, nausea and vomitting etc. The side effects or complications encountered with the present study are almost similar to the side effect that was observed by Patki et al 1993. There was no maternal mortality with any of the regimes.

Conclusion

From the present study, it can be concluded that Nifedipine is significantly more effective, well tolerated tocolytic agent than isoxsuprine hydrochloride and almost devoid of significant maternal or fetal side effects. However, keeping in view, the relatively small number of patients and short periods of study in the present series, further controlled study involving large number of patients, preferably as a co-ordinated multicentric trial, with special attention to a haemodynamic effects of the drug, will be necessary to throw more light on the subject.

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