A RANDOMIZED CONTROLLED STUDY OF NIFEDIPINE AND ISOXUPRINE IN THE TREATMENT OF PRETERM LABOR

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SUMMARY

A prospective randomised controlled study was conducted to evaluate the efficacy of nifedipine in delaying preterm labor in comparison with isoxuprine. There were 14 patients in nifedipine group and 11 in isoxuprine group. Nifedipine is found to be as effective as isoxuprine. Isoxuprine had more side effects.

INTRODUCTION

The incidence of low birth weight in India is around 30-40% of which 12-18% are associated with gestational age less than 37 weeks (hospital statistics)(krishna menon 1982). Between 30-36 weeks of gestation the incidence of Idiopathic Respiratory Distress Syndrome (IRDS) is 15% to 20%(Behrman 1983). It is a major cause of perinatal morbidity and mortality. If preterm labour can be delayed by 48 hours, fetal lung maturity can be accelerated with betamethasone(Block 1977). If the pregnancy proceeds to term the perinatal complications are significantly decreased. These facts are of special importance in developing countries where neonatal facilities are limited. Isoxuprine is an accepted tocolytic agent requiring initial parenteral administration and rigorous monitoring. Calcium channel blockers on the other hand are good tocolytic agents with a few and easily reversible side effects and are easily administered. Hence the latter was compared with the former in this study.

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PATIENTS AND METHODS

A prospective study was conducted on consecutive patients with preterm labour ad-

mitted in C.M.C.Hospital over a period of 10 months. The inclusion criteria were a) cases with known dates or where gestational age was confirmed by ultrasound scan before 20 weeks. b) gestational age between 28 -36 weeks. c) singleton pregnancies. d) uterine contractions occurring atleast once every 10 minutes and lasting for 30 seconds or more recorded on external tocography. e) cervical dilatation less than 2 cm. Women who had premature rupture of membranes, intrauterine infections, malformed foetus, hydramnios and medical complications were excluded from the trial. The patients were assigned to the two groups using a table of random numbers. All patients were rested in bed and sedated with Inj. Pethidine 75 mg and Inj. Promethazine 25 mg. Two doses of Inj. Betamethasone 12 mg each were given intramuscularly at 12 hourly interval. Nifedipine was administered as capsules orally; initially 30 mg, followed by 20 mg every 8 hours for 48 hours. Maternal blood pressure and pulse rate and fetal heart rate were monitored every 15 min. for the first 2 hours; hourly for 24 hours and subsequently before the drug administration. Calcium gluconate and IV fluids were kept ready at hand (Hurst 1985). Isoxuprine 40 mg in 500 ml of D5W was started at a drip rate of 30 drops/mt and accelerated with close monitoring to achieve tocolysis, then continued for 4 hours. Subsequently the drug was administered intramuscularly at a dose of 30 mg/24 hours for 2 days. Maternal blood pressure and pulse rate and fetal heart rate monitoring was done every 15 mts. while on the IV drip and subsequently before each intramuscular injection and oral dosing.

The treatment was considered successful if the pregnancy was prolonged for 48 hours from the beginning of therapy.

RESULTS

Fourteen patients received nifedipine and 11 controls isoxuprine. The two groups were comparable for age, weight, height

TABLE I

CLINICAL DETAILS

	Nifedipine (n = 14)	Isoxpurine (n = 11)	Significance
Age (Years)	23.03±3.98	25.5±5.8	NS
Maternal wt (kg)	49.79±9.7	54.2±8.9	NS
Maternal Height (cm)	150.89±7.1	152.7±4.8	NS
Gestation at treatment (weeks)	33.7±1.7	33.7±1.9	NS
Bishop's Score	4.85±2.3	4.0±1.9	NS
Tocolytic Index	3.28±1.06	2.9±1.0	NS

NS - Not Significant.

TABLE II

BISHOP'S SCORES AND TOCOLYTIC INDICES

Drug	Successful Tocolysis	Failed Tocolysis	Significance
Bishop's Score			
Nifedipine	8,1,7,3,5,2,2,5,4,4,5	8,8,7	p< .05
Isoxuprine	4,3,3,4,0,6,7,4,4,3	6	NS
Tocolytic Index			
Nifedipine	3,3,4,3,4,3,1,3,3,2,3	5,5,4	p< .01
Isoxuprine	2,3,2,4,1,4,4,3,3,2	4	NS

parity, gestational age, Bishop's score (1984) and Tocolytic index Richter 1977) (Table I). In the nifedipine group 11/14 patients had tocolysis while in the isoxuprine group 10/11 had successful treatment (p = 0.4 N.S.).

There were 4 primigravidae in the nifedipine group and 1 in the isoxuprine group. The mean Bishop's scores and Tocolytic indices of patients are shown in Table II. Lower indices were significantly associated with successful nifedipine tocolysis (Mann-Whitney U test). Tachycardia was significantly higher in the isoxuprine group (5/11) compared to the nifedipine group (1/14) (P<0.04). Hypotension was recorded only in one patient who had received isoxuprine. In the isoxuprine group, 10/11 patients were discharged following successful tocolysis after 72 hours, of these 8/10 delivered at term in this hospital, and 2/10 went elsewhere for delivery. Of the nifedipine group 11/14 were discharged after tocolysis. Of these, 8 patients delivered at term, 1 delivered after 4 days, 2 delivered elsewhere. There were no neonatal complications in any of infants.

DISCUSSION

Due to strict inclusion criteria the patients studied are limited as in previous studies (Read 1986 Ulmsten 1980, 1984). However the treatment and control groups were comparable for the mean Tocolytic index and Bishop's score. Successful nifedipine tocolysis is associated with lower scores as previously shown with other tocolytic agents Hurst (1985).

Fetal survival is directly related to fetal birth weight and age. Due to small numbers we did not experience IRDS or other complications in infants born preterm following unsuccessful tocolysis. Eight out of 10 patients in the isoxuprine group and 8 out of 14 in the nifedipine group delivered at term following successful tocolysis. In this regard both the

drugs were equally effective. Nifedipine had significantly less side effects compared to Isoxuprine. These side effects are easily reversible with intravenous saline and calcium Hurst (1985). Hence nifedipine can be an effective alternative for Isoxuprine in tocolytic therapy.

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