A COMAPARATIVE STUDY OF EFFICACY OF TERBUTALINE AND NIFEDIPINE AS TOCOLYTICS IN PRETERM LABOUR

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SUMMARY

Prevention of preterm births remains one of the major challenges, the obstetrician is confronted with. A number of tocolytic agents have been used so far. The present study was conducted on patients of preterm labour between 27-36 weeks of gestation, to compare the efficacy of terbutaline and nifedipine as tocolytics.

We observed that the mean duration of prolongation of pregnancy was 34.50 ± 26.61 days with terbutaline and 24.18 ± 20.68 days with nifedipine. Number of cases reaching maturity was 15/28 (53.6%) with terbutaline and 13/28 (46.42%) with nifedipine. Cervical dilatation and presence or absence of leaking were found to be important prognostic factors in arrest of preterm labour. None of the cases in terbutaline group required discontinuation of therapy due to side effects; side effects were minimized by reduction of dosage. In nifedipine group, one patient had marked hypotension (systolic BP < 80 mm of Hg) which necessitated discontinuation of nifedipine.

INTRODUCTION

Prematurity, together with its complications, remains the most important preventable cause of perinatal mortality and morbidity. Therefore, prevention of preterm delivery with tocolytic agents is necessary.

Since human uterus contains $ß_2$ receptors (Anderson *et.al.* 1973), $ß_2$ receptor stimulants are preferred tocolytic agents over nonspecific ß-receptor stimulants.

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Terbutaline has been proved to have selective effects on β_2-receptors (Person & Olsson, 1970).

Tocolytic effects of nifedipine have been studied Read & Wellby, 1986. Meyer *et. al.* (1990) have reported nifedipine to have similar tocolytic effects as compared to ritodrine in suppression of preterm labour without side effects.

MATERIAL AND METHODS

The study was conducted on 56 patients of preterm labour with gestational age between 27-36 weeks, persistent painful uterine contractions occuring at least once in every 10 minutes after ½ hour rest, cervical dilatation between 1-4 cm and estimated foetal weight on admission < 2500 gm based on Johnson's formula (Table I).

The patients with absent membranes or any contraindication to tocolysis e.g., I.U.D., lethal congenital anomaly, APH etc., or any contraindication to drug e.g., heart, kidney and liver diseases were excluded from the study.

The patients were kept on absolute bed rest in Trendelenburg position. Antibiotics and corticosteroids were given whenever indicated. Patients were randomnly divided into 2 groups.

Group 1 patients were given terbutaline in 5% dextrose infusion at a rate of 10 μg/min followed by an increase in dose by 5 μg/min every 15 minutes till uterine contractions ceased or maximum of 25 μg/min was reached which was continued for 4 hours. This was followed by half hourly reduction in dosage in the same concentration as it was increased, until minimum effective dose was achieved. This dose was maintained for 8 hours, followed by subcutaneous injection of 250 μg 6 hourly for 3 days. This was followed by 15 mg oral dose till end of 36 weeks.

Group 2 patients were given nifedipine 30 mg orally followed by 20 mg thrice daily for 3 days.

A close monitoring of vitals, uterine contractions and foetal heart rate was done. The side effects were noted. Patients during their stay in hospital were monitored for any recurrence of preterm labour, foetal wellbeing and continued foetal growth.

OBSERVATIONS AND DISCUSSION

The patients in terbutaline and nifedipine group were matched with respect to age, parity, gestational age, Bishop scoring, cervical dilatation and estimated foetal weight on admission (Table I). Mean duration by which pregnancy was prolonged was 34.5 ± 26.1 days in terbutaline group (Table II). This is similar to reports of and Stubblefield and Hely (1982). In nifedipine group, mean days gained were 24.1 ± 20.68 days (Table II). Our studies have shown better results as compared to Ulmten *et. al.* (1980), who have reported prolongation of pregnancy by 15 days only. There was no significant difference in prolongation of pregnancy by two drugs ($p > 0.05$) (Table II). No data are available on comparative study of terbutaline and nifedipine to the best of our knowledge.

Arrest of preterm labour could be achieved till the end of 36th week in 53.6% (15/28) cases in terbutaline group and 46.42% (13.28) cases in nifedipine

Table I

Showing characteristics of patients of terbutaline and nifedipine group

Sl. No.	Character	Terbutaline Group	Nifedipine Group
1.	Mean Age	23.5 ± 3.76 years	22.71 ± 3.39 years
2.	Most Frequent para	2 (53.55%)	2 (46.44%)
3.	Mean Gestational age on admission	30.21 ± 1.93 week	30.75 ± 2.10 weeks
4.	Patients with Bishop Score < 6	67.8%	75.0%
5.	Patients with Cervical Dilatation ≤ 2cm	75%	85.7%
6.	Patients with no leaking PV	82.15%	78.5%
7.	Estimated fetal Weight	1404 ± 521gm	1606 ± 463.11gm
8.	Mean Gestational age at delivery	34.96 ± 3.14 weeks	34.19 ± 3.22 weeks

Table II

Showing duration for which pregnancy was prolonged in terbutaline and nifedipine group

Sl. No.	Duration for which pregnancy (In days)	Terbutaline Group		Nifedipine Group	
		Number	Percentage	Number	Percentage
1.	< 4 Days	2	7.14	3	10.71
2.	2 - 7 Days	7	25.0	7	25.0
3.	8 - 14 Days	4	14.28	5	17.85
4.	15 - 28 Days	—	—	1	3.57
5.	29 - 56 Days	9	32.12	11	39.3
6.	57 - 84 Days	6	21.46	1	3.57
	Mean ± S. D.	34.50 ± 26.61 Days		24.18 ± 20.68 Days	

t = 1.592; p > 0.05 not significant.

Table III

Showing percentage of cases with arrest of preterm labour till the end of 36 weeks in two groups

	Terbutaline Group		Nifedipine Group	
	Number	Percentage	Number	Percentage
Cases with arrest of PTL till end of 36 weeks	15	53.6%	13	46.42%

Table IV

Showing duration for which pregnancy was prolonged in relation to cervical dilatation in two groups

Sl. No.	Time for Which pregnancy prolonged (In Days)	Terbutaline Group				Nifedipine Group			
		≤ 2 cm		> 2 cm		≤ 2 cm		> 2 cm	
		No.	%	No.	%	No.	%	No.	%.
1.	< 1	—	—	2	28.57	—	—	3	75.00
2.	2 - 7	2	9.5	5	71.43	6	25.00	1	25.00
3.	8 - 14	4	19.0	—	—	5	20.8	—	—
4.	15 - 28	—	—	—	—	1	4.2	—	—
5.	29 - 56	9	42.9	—	—	11	45.8	—	—
6.	57 - 84	6	28.6	—	—	1	4.2	—	—
		n = 21	100.00	7	100.00	24	100.00	4	100.00
Mean ± S. D.		44.33 ± 23.39		4.71 ± 2.63		27.79 ± 20.14		2.5 ± 3.0	
Tebutaline Gr.		≤ 2cm Vs > 2 cm,		t = 4.309		p < 0.01 Significant			
Nifedipine Gr.		≤ 2cm Vs 2 cm,		t = 2.415,		p < 0.01 Significant			
Tebutaline Vs Nifedipine Group									
≤ cm dilatation		t = 2.006, p > 0.05, not significant							
< 2 cm dilatation		t = 1.152, p > 0.05, not significant							

group (Table III).

Both terbutaline and nifedipine were found to be more effective with lesser cervical dilatation (Table III), similar to the observations of Caritis *et. al.* (1982). On comparison of efficacy of two drugs on varying cervical dilatation, no difference was found in tocolytic effect of drugs either in lesser (≤ 2 cm) or advanced (> 2 cm) cervical dilatation (Table IV).

There was no change in efficacy of terbutaline in presence of leaking whereas nifedipine was more effective in absence of leaking PV (Table V). On comparison of efficacy of two drugs in relation to leaking PV, no significant difference was found.

Significant maternal tachycardia and foetal tachycardia were encountered in 10.71% (3/28) cases on terbutaline therapy, which responded to reduction in infusion rate (Table VI). Incidence of side effects with terbutaline was lower as compared to studies of Katz *et. al.* (1981). The lower incidence of side effects was probably due to lesser dosage used (25 μg/min.) and due to use of 5% dextrose for infusion in contrast to normal saline in above mentioned study. Facial warmth 35.7% (10/28), headache 25.0% (7/28) and palpitations 17.85% (5.28) were some of the frequent side effects found with use of nifedipine (Table VI).

Table V

Comparative study of two groups showing duration for which pregnancy was prolonged in relation to leaking per vaginum

Sl. No.	Time for Which pregnancy prolonged (In Days)	Group I				Group II			
		No Leaking		Leaking		No Leaking		Leaking	
		No.	%	No.	%	No.	%	No.	%.
1.	< 2	1	4.3	1	20.0	—	—	3	50.00
2.	2 - 7	6	26.1	1	20.00	4	18.2	3	50.00
3.	8 - 14	2	8.7	2	40.0	5	22.7	—	—
4.	15 - 28	—	—	—	—	1	4.54	—	—
5.	29 - 56	8	34.8	1	20.0	11	50.0	—	—
6.	57 - 84	6	26.1	—	—	1	4.54	—	—
		n = 23	100.00	5	100.00	22	100.00	6	100.00
Mean ± S. D.		38 ± 26.5		15 ± 15.85		29.95 ± 19.63		3 ± 2.44	

Tebutaline Gr. — No Leaking Vs Leaking, t = 1.8; p > 0.05, No significant

Nifedipine — No Leaking Vs Leaking, t = 3.23; p < 0.01 significant

Terbutaline Vs. Nifedipine

With No Leaking — t = 1.28, p > 0.05, not significant

With Leaking — t = 1.66, p > 0.05, not significant

Table VI

Side effects with terbutaline and nifedipine therapy

Sl. No.	Side Effects	Terbutaline Group		Nifedipine Group	
		Number	Percentage	Number	Percentage
1.	Nausea	3	10.4	1	3.57
2.	Headache	—	—	7	25.0
3.	Facial Flush & Warmth	—	—	10	35.7
4.	Tremors	4	14.28	—	—
5.	Palpitation	—	—	5	17.85
6.	Maternal Tachycardia > 140/min	3	10.7	4	14.28
7.	Hypotension	—	—	1	3.57
8.	Foetal Tachycardia > 40 beats above baseline	3	10.7	2	7.15

Table VII

Reaons for discontinuation of drug

Sl. No.	Drug	Side Effects		Failure to arrest progress of labour		Therapy Completed	
		No.	%	No.	%	No.	%
1.	Terbutaline	—	—	2	7.14	15	53.6
2.	Nifedipine	1	3.57	2	7.14	25	89.29

None of the patients in terbutaline group required discontinuation of treatment due to side effects, whereas in nifedipine group, 1 of 28 patients (3.57%) required stoppage of nifedipine therapy due to marked hypotension. Percentage of patients requiring discontinuation of treatment due to failure to arrest progress of labour was same in both the groups (2/28, 7.14%). In terbutaline group therapy was completed in 15 of 28 patients (53.6%) whereas 25 of 28 patients (89.29%) had therapy completed in nifedipine group. The reason for apparently lower percentage of cases having therapy completed in terbutaline group is that the therapy was completed at the end of 36th week in this group, whereas treatment was stopped at the end of 3 days of initiation of therapy in nifedipine group (Table VII).

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