COMPARATIVE EVALUATION OF TERBUTALINE, SALBUTAMOL AND ISOXSUPRINE IN PRETERM LABOUR

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SUMMARY

75 cases with imminent preterm labour of 20-36 weeks gestation were studied. Cases were randomly allocated into three groups of 25 each and were given terbutaline, salbutamol and Isoxsuprine by oral (15 cases) and I/V (10 cases) routes. The results showed that with oral therapy prolongation of pregnancy for more than 24 hours was 80%, 73.4% and 80% with Salbutamol, Terbutaline and Isoxsuprine respectively. Mean prolongation of pregnancy was maximum with Salbutamol i.e. 5.50 ± 5.27 weeks while with Terbutaline and Isoxsuprine it was 2.77 ± 3.38 weeks and 2.07 ± 2.41 weeks respectively.

With I/V therapy the prolongation of pregnancy for more than 24 hours was 90% with Salbutamol, 90% with Terbutaline and 50% with Isoxsuprine.

Cervical dilatation and status of membranes were important determinants. Side effects were minimal. Palpitation, and foetal and material tachycardia were more with terbutaline and Salbutamol and hypotension was more with Isoxsuprine.

Introduction

Preterm labour occurs in 5-10% of all births. It accounts for about 75% of perinatal deaths (Fuchs, 1976). Apart from high mortality it is also responsible for perinatal morbidity. Residual mental and motor handicaps are the major deterrents to the optimal development of a preterm infant (Lubchenco et al, 1972).

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The use of drugs for the prevention of preterm labour has been in vogue for a long time. Many drugs have been used but none proved to be a complete answer.

Better understanding of the catecholamine receptor system by Ahlquist, 1948 showed that B_2 receptors stimulation accounts for uterine relaxation. B_2 agonist compunds like isoxsuprine, salbutamol, ritodrine and terbutaline have come up. These have shown a variable efficacy and

safety. Thus a comparative trial is warranted to test the efficacy, safety and the most favourable route of adminstration of these drugs for prevention of preterm labour.

Material and methods

The present study was carried out in the Department of Obstetrics and Gynaecology, S.N.Medical College, Agra.

A total of 75 cases of preterm labour were included in the study, they were divided in three groups A, B and C, each group comprised of 25 cases. These groups were given terbutaline, salbutamol and isoxsuprine respectively. Each group was further divided into two subgroups. 15 patients in each subgroup were given oral therapy, while remaining 10 patients were given parenteral therapy.

Criteria for selecting cases:

1. Cases of 20-36 weeks gestation with
   a) painful intermittent uterine contraction with show,
   b) closed cervix or dilated upto 4 cm.
2. Cases with formation of bag of waters.
3. Cases with leaking without uterine contraction.
4. Cases with longitudinal lie either vertex or breech.
5. Both primipara and multipara between 16-38 years were selected.

A detailed history was taken and complete obstetrical examination carried out.

Adminstration of drugs:

Oral therapy: Terbutaline was given in the doses of 5 mg. 6 hourly. Salbutamol 4 mg. 6 hourly and Isoxsuprine was given as 10 mg. every 6 hourly. Dose was reduced according to response and continued till term.

Parentral therapy: All the drugs were given in the form of diluted infusion in various concentration and was started slowly at rate of 4-8 drops/mt. Rate of infusion was increased gradually 4 drops every 15 mts.till the desired effect has reached or to the maximum of 30-40 drops/mt. Subsequently patient was put on oral therapy. Concentration of various drugs used were as follows:

Terbutaline — 20 mg/l

Salbutamol — 10 mg/l

Isoxsuprine — 120 mg/l

During drug therapy careful watch for pulse, B. P. uterine contraction cervical dilation and foetal heart was taken. Therapy was suspended in the event of any of the following:

1. Progression of cervical dilatation beyond 6 cm.
2. Excessive tremors.
3. Severe hypotension
4. Maternal tachycardia above 140/mt.
5. Foetal heart rate above 160/mt. persisting beyond 30 mts.
6. Heavy vaginal bleeding.

Observations

The present study shows that success rate of tocolytic therapy with sympathomimetic drugs depend on initial cervical dilatation. When cervical dialation was 2 cm. or less, prolongation of pregnancy for more than 24 hours with oral therapy was 100% with salbutamol, 91.7% with terbutaline and 86.7% with Isoxsuprine while

with dilatation more than 2 cm. prolongation of pregnancy was not achieved more than 24 hours in any case with terbutaline and Isoxsuprine and in only one case with salbutamol. With intravenous therapy in these cases sucess rate was 75%. 6.6% and nil with terbutaline. Salbutamol and Isoxsuprine respectively. In contrast to this in cases with cervical dilation less than 2 cm.it was 100% with I/V salbutamol and terbutaline and 62.5% with I/V Isoxuprime (Table 1,2, and 3).

TABLE 1
PROLONGATION OF PREGNANCY IN RELATION TO INITIAL CERVICAL DILATATION WITH TERBUTALINE THERAPY

Initial Cervical Dilatation	*Route*	*No.of cases*	*Prolongation of pregnancy*							
			<24 Hours		*1 - 7 days*		*8 - 14 days*		*>14 days*	
			No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
No. dilatation	0	4	1	25	–	–	–	–	3	75
	I/V	–	–	–	–	–	–	–	–	–
1 - 2 Cm	0	8	–	–	3	37.5	2	25	3	37.5
	I/V	6	–	–	–	–	1	16.7	5	83.3
3 - 4 Cm.	0	3	3	100	–	–	–	–	–	
	I/V	4	1	25	3	75.0	–	–	–	–

TABLE 2
PROLONGATION OF PREGNANCY IN RELATION TO INITIAL CERVICAL DILATATION WITH SALBUTAMOL THERAPY

Initial Cervical Dilatation	*Route*	*No.of cases*	*Prolongation of pregnancy*							
			<24 Hours		*1 - 7 days*		*8 - 14 days*		*>14 days*	
			No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
No dilatation	0	1	–	–	–	–	–	–	1	100
	I/V	2	–	–	1	50	1	50	–	–
1 2 Cm	0	10	–	–	3	30	–	–	7	70
	I/V	5	–	–	1	20	–	–	4	80
3 - 4 Cm	0	4	3	75	1	25	–	–	–	–
	I/V	3	1	33.3	2	66.6	–	–	–	–

TABLE 3
PROLONGATION OF PREGNANCY IN RELATION TO INTIAL CERVICAL DILATATION WITH ISOXSUPRINE THERAPY

Initial Cervical Dilatation	*Route*	*No.of cases*	*Prolongation of pregnancy*							
			<24 Hours		*1 - 7 days*		*8 - 14 days*		*>14 days*	
			No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
No dilatation	0	2	–	–	–	–	1	50	1	50
	I/V	2	–	–	–	–	1	50	1	50
1 - 2 Cm	0	12	2	16.6	5	41.7	2	16.6	3	25
	I/V	6	3	50	3	–	–	–	–	–
3-4 Cm.	0	1	1	100	–	–	–	–	–	–

In case of intact membranes success rate was 100% with oral salbutamol and isoxsuprine and 70% with terbutaline. When membranes were absent or patient had leaking it was only 57.1% with salbutamol and isoxsuprine and 80% with Terbutaline while with I/V therapy all the drugs had 100% success rate with intact membrane and 66.6% success with absent membranes (Table 4).

On comparing the three drugs irrespective of cervical dilation, status of membranes or gestation age, Salbutamol shows best results with 80% cases prolonged more than 24 hours and 53.3% more than 14 days and mean prolongation of 5.50 weeks. In Terbutaline group with oral therapy success rate was 73.4% with mean prolongation of only 2.77 weeks. Though in Isoxsuprine group 80% showed success but only 26.7% cases could be prolonged for more than 14 days and mean prolongation was only 2.07 weeks.

This shows that oral salbutamol is significantly better ($p<0.01$) than terbutaline and isoxsuprine (Table 5&6)

TABLE 4
PROLONGATION OF PREGNANCY IN RELATION TO STATUS OF MEMBRANE IN VARIOUS GROUPS

Status of Membrane	*Route*	*Terbutaline Group*			*Salbutamol Group*			*Isoxsuprine Group*		
		No.of cases	*> 24 Hours*		*No.of cases*	*> 24 Hours*		*No. of cases*	*> 24 Hours*	
			No.	*%*		*No.*	*%*		*No.*	*%*
Intact	0	10	7	70	8	8	100	8	8	100
	I/V	7	7	100	7	7	100	7	7	100
Leaking	0	5	4	80	7	4	57.1	7	4	57.1
Absent	I/V	3	2	66.6	3	2	66.6	3	2	66.6

TABLE 5
PROLONGATION OF PREGNANCY BY DIFFERENT DRUGS

Groups	Route	No. of cases	Prolongation of Pregnancy					
			>24 hours		>7 days		>14 days	
			No.	%	No.	%	No.	%
Terbutaline	0	15	11	73.4	8	53.4	6	40
	I/V	10	9	90	6	60	5	50
Salbutamol	0	15	12	80	8	53.4	8	53.3
	I/V	10	9	90	5	50	4	40
Isoxsuprine	0	15	12	80	7	46.7	4	26.7
	I/V	10	5	50	2	20	1	10

TABLE 6
MEAN PROLONGATION OF PREGNANCY IN WEEKS BY DIFFERENT DRUGS

Groups	Route	Mean Prolongation of Pregnancy in weeks
Terbutaline	Oral	2.77 ± 3.38
	I/V	2.70 ± 2.35
Salbutamol	Oral	5.50 ± 5.27
	I/V	3.64 ± 4.84
Isoxsuprine	Oral	2.07 ± 2.41
	I/V	1.56 ± 3.36

In patients placed on I/V therapy success rate was 80% for both salbutamol and terbutaline and 50% with Isoxsuprine but mean prolongation was 3.64 weeks, 2.70 weeks and 1.56 weeks with salbutamol, terbutaline and isoxsuprine respectively. Clearly showing that salbutamol is more effective, terbutaline is next and isoxsuprine is least effective when given parenterally (Table 5 and 6).

On comparing the results of oral and I/V salbutamol therapy mean prolongation of pregnancy was more with oral therapy i.e. 5.50 weeks in comparision to 3.64 weeks by I/V drug.

Gray et al (1978) also advocated the oral regime from start thus minimising the discomfort of I/v therapy. The side effects with Salbutamol and terbutaline were more in the form of palpitation, restlessness tremors and foetal tachycardia. Isoxsuprine group showed more hypotension (Table 7).

Conclusions

From the present study it can be concluded that success of preterm labour inhibition therapy is dependent on the degree of cervical dilatation and status of membranes. Poor results are observed when cervical dilation is more than 2 cm. or membranes are absent.

TABLE 7
SIDE EFFECTS IN DIFFERENT GROUPS

Side effects	*Number of cases*					
	Terbutaline		*Salbutamol*		*Isoxsuprine*	
	Oral	*I/V*	*Oral*	*I/V*	*Oral*	*I/V*
1. Palpitation	3	6	3	5	1	1
2. Restlessness	2	3	2	2	1	3
3. Hypotension	–	1	–	1	1	2
4.Nausea	1	1	1	1	1	1
5.Tremors	2	2	2	–	–	–
6.Postpartum haemorrhage	–	–	–	1	1	1
7. Foetal tachycardia.	–	3	–	1	–	1

Oral salbutamol therapy is a satisfactory method for long term inhibtion of preterm labour in early stages. While intravenous salbutamol is reserved for cases hospitalised in a state of advanced labour.

Of the other two drugs terbutaline was found to be better than isoxsuprine in both efficacy and safety.

References

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