ISOXSUPRINE AND PREMATURE LABOUR

By

V. K. Singh, M. Sharma, Anjoo Malhotra and P. Rohatgi

SUMMARY

Isoxsuprine, a betamimetic receptor stimulant has been used to prevent premature labour in 40 patients. 40-60 mg of drug in 540 ml of 50% dextrose was infused intravenously at the rate of 10 drops per min. and increased to 60 drops per min. depending on maternal cardiovascular and uterine response. The intravenous infusion of drug was then gradually withdrawn and substituted by intramuscular therapy for 24 hours. After this the patient was maintained on oral therapy till 37 weeks of gestation. 85% of patients had prolongation of pregnancy for more than 3 days and 70% for more than 7 days. 45% patients reached maturity. Mean gain in days was 28.41, maximum gain being 70 days. The drug was more effective in patients with cervical dilatation less than 2 cms and uterine contractions less than 3 per 10 min.

Introduction

Despite considerable gains in neonatal outcome due to tremendous improvement in neonatal intensive care the impact of preterm delivery on the perinatal mortality is staggering. Infants born prior to term account for majority of neonatal deaths. In addition, a disproportionately large percentage of mature infants suffer significant neonatal morbidity and long term sequelae such as motor and intellectual handicaps.

The incidence of preterm birth can be reduced by adequate prenatal care and active treatment of factors that predispose pregnant women to preterm labour. When preventive measures fail, pharmacological suppression of preterm labour is commonly undertaken since significant decrease in neonatal morbidity and death may be realised with addition of one or two weeks of intrauterine existence.

In our study we have evaluated the efficacy of isoxsuprine in inhibiting uterine contractions in premature labour and also studied its side effects on the mother and baby.

Material and Methods

The cases for the study were selected from patients admitted in U.I.S.E. Maternity hospital, Kanpur during the year 1984-85. The cases presented in gestation period between 20-36 weeks with regular uterine contractions at least one in every 10 min, lasting for atleast 30 seconds with cervical effacement and

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dilatation upto 3 cm. The patients with ruptured membranes were also included. The patients suffering from hyperthyroidism, diabetes mellitus, cardiac disease, hypertension, severe pre-eclampsia, abruptio placentae and chorio-amnionitis were excluded from our study.

80 cases were selected out of which 40 were controls. All patients were subjected to detailed history and examination. Necessary investigations were done.

In control group, only bed rest and sedatives were prescribed.

In study group, 40-60 mg of isoxsuprine diluted in 540 ml of 5% dextrose solution was started at rate of 10 drops/min and increased further by 10 drops/min. every 5-10 min. upto 60 drops/min. depending on maternal cardio vascular and uterine response. The patient was placed in left lateral position. During administration of drug, maternal pulse rate, blood pressure, uterine contractions and foetal heart rate were noted every 15 min. The drug was discontinued if cervix dilated further after 6 hrs. of treatment or if maternal pulse rate exceeded 140 beats/min. In other cases the drug was gradually withdrawn over next 12 hours after cessation of contractions. For next 24 hours, the drug was given intramuscularly—10 mg every 6 hours. Then the patient was maintained on oral dose of 10 mg every 6 hours till 37 weeks.

In patients with intact membranes, our aim was to prolong pregnancy upto 37 weeks. In patients with ruptured membranes, our aim was to prolong pregnancy for atleast 48 hours while corticosteroids were administered in form of injection decadron 4 mg every 8 hours upto total of 6 doses.

These patients were given antibiotics in form of capsule ampicillin 500 mg every 8 hours to minimize risk of chorio-amnionitis.

Observations and Results

Mean age of patients of study group was 25.45 ± 3.498 years, while it was 23.25 ± 4.35 years in control group. The gestational age at which drugs were started ranged between 20-36 weeks. The mean gestational age of study group was 30.05 ± 4.05 weeks and control group was 29.3 ± 3.28 weeks. There was no relationship between age and parity of patients and incidence of prematurity, while there was rise in number of preterm births with declining socio-economic status.

In our study, 85% of patients treated with isoxsuprine had prolongation of pregnancy for more than 3 weeks and 70% had prolongation of pregnancy for more than 1 week while with placebo therapy only 55% and 25% had prolongation of pregnancy for more than 3 days and 7 days respectively. The results are in acordance with those of Das (1969, prolongation of pregnancy in 72% of cases was more than 7 days). The mean gain in days with isoxsuprine was 28.41 ± 21.87 days (with maximum gain of 70 days) whereas it was only 4.4 ± 2.71 days (with maximum days gain of 14) in control group (Table I). The conclusion that isoxsuprine is better than placebo for prolonging pregnancy is also supported by results of Csapo and Herczeg (1977, pregnancy was prolonged for an average of 51 days by treatment with isoxsuprine as compared to 13 days in controls).

45% of cases of isoxsuprine group while only 5% of cases of control group reached maturity. Although Castren

TABLE I
Prolongation of Pregnancy in Control and Study Group

S.N.	No. of days gained	Study group No.	%	Control group No.	%
1.	Less than 3	6	15	18	45
2.	3 - 7	6	15	12	30 t=6.8
3.	8 - 14	4	10	10	25 p<.001
4.	15 - 28	4	10		highly
5.	29 - 56	14	35		significant
6.	57 - 84	6	15		
Mean & S.D.		28.41 ± 21.87 days		4.4 ± 2.71 days	

and associates (1975) reported that isoxsuprine was no better than placebo in prolonging pregnancy upto 37 weeks but these investigators have infused isoxsuprine for only one hour as compared to 12-24 hours in our study and then we maintained patient on intramuscular and oral therapy. On the other hand Anwar Khatoon (1977) who has used similar doses as used by us has shown much better results than us (in 85% of cases pregnancy could be prolonged to 37 weeks).

The mean gestational age at the time of delivery was more when isoxsuprine was used (34.4 ± 4.476 weeks) as compared to placebo group (30.1 ± 4.96 weeks). There was no significant increase in gestational age after treatment with placebo ($t = .838$, $p > .05$) where as by the use of isoxsuprine this increase was statistically highly significant of ($t = 4.51$ $p < .001$).

Isoxsuprine is more effective when cervix was less than 2 cm dilated. Mean gain in days was 36.33 ± 19.44 days when cervix was less than 2 cm while it was only 4.65 ± 5.07 days when cervical dilatation was more than 2 cm.

In cases with cervical dilatation 2 cm or less, all the cases had prolongation of pregnancy for more than 3 days, 86.67% had prolongation of pregnancy for more than 7 days and 53.33% cases reached maturity. While in cases with cervical dilatation more than 2 cm, only 60% of cases had prolongation of pregnancy for more than 3 days, 20% had prolongation of pregnancy for more than 7 days and none of the cases reached maturity.

On comparing the effect of isoxsuprine with placebo, we found that by isoxsuprine gain in days was statistically more than days gained with placebo when cervix was 2 cm or less than 2 cm dilated ($t = 5.0287$ $p < .001$, highly significant) but when drug was given in patients with cervical dilatation more than 2 cm mean gain in days was not more than mean no. of days gained in patients of control group ($t = 0.99$ $p > 0.5$, not significant).

From our study it is evident that isoxsuprine is more effective when used in patients having uterine contractions less than 3 per 10 min as compared to those with contraction frequency of more than 3 per 10 min. With isoxsuprine mean gain in days was 43.33 ± 14.98 when frequency of contractions were less than 3 per 10 min while it was only 4.59 ± 5.17 days when contractions were 3 or more than 3 per 10 min. In cases with frequency of contractions less than 3/10 min. all the cases had prolongation of pregnancy for more than 1 week and

50% reached maturity, while in patients with contraction frequency 3 or more than 3 per 10 min. 62.5% had prolongation of pregnancy for more than 3 days, 25% had prolongation of pregnancy for more than 7 days and 25% reached maturity.

In patients with ruptured membranes isoxsuprine, could prolong pregnancy beyond 48 hours in 30% of cases while in the placebo group pregnancy could be prolonged in only 10% cases beyond 48 hours.

Side effects noted were tachycardia (more than 140/min.) in 20% of cases, palpitation in 27.5% hypotension (fall in systolic BP to less than 90 mm of Hg) in 20% of cases and nausea and vomiting in 10% cases. Our results are similar to those of Stander and associates (1964, increase in maternal heart rate by 30-50 beats/min in 20% cases and severe hypotension leading to discontinuation of infusion in 20% cases).

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