Validity of Ritodrine as Tocolytic Agent

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Premature delivery represents a serious perinatal event. Overall, about 7% -10% of infants are born prematurely, but they account for about 75% neonatal morbidity and mortality[1].In this study 111 patients with diagnosed, uncomplciated, signleton preterm labour upto 34 weeks gestation were included, managed by intravenous ritodrine (Yutopar) which was found to be an effective treatment. Success rate was related to bishop score at commencement of therapy, the mean time of delivery being 28 days. It was ≥25 days in 63% patients. There were significant differences in the incidence of RDS between the infants of the mothers who received steroid in addition to ritodine and who received ritodrine only.

Key words: Ritodrine, tocolysis, preterm labour

In spite of improvements in antenatal care, preterm labour remains an important obstetric problem and poses the greatest risk to the newborn infant. Over 75% of all first month infant deaths and most infants morbidity occur in premature infants. It has been reported that infants of <750gm at birth have <15% chances of survival[2] (upto 25% in developed countries) compared with 80% of these between 1000gm and 1500gm. The difference between two birth weights in terms of time is only of 4 weeks. Other studies have shown that postponing delivery until 34 weeks, gestation will considerably reduce infant mortality and morbidity[3]. A small increase in the period of gestation (72 hours → 7 days) can therefore have a significant effect on survival.

The main aim of this study was to demonstrate the effect of tocolysis on the prolongation of gestation when administered to the patients in preterm labour before 34 weeks. The tocolytic of choice for this study was Ritodrine (Yutopar). Additional aim was to study different regimens on the incidence of RDS (Respiratory Distress Syndrome).

Ritordine is a β_2-sympathomimetic agent specifically developed for the treatment of uncomplicated preterm labour.

Methods

Patient between 26-34 weeks of gestation inpreterm labour were included in this study. Labour was defined as regular; painful and effective uterine contraction; occurring at a frequency of at least 1 in 5 minutes, or 2 in 10 minutes, and Cx should be 2cm or more dilated of an effaced or partially effaced state. Membranes were to be intact.

Patients who presented with any additional complication were excluded from study like ante-partum haemorrhage; pre-eclampsia; hyperthyroidism; or cardiac/pulmonary lesion; any condition which was contraindicating the prolongation of pregnancy and those receiving simultaneous treatment with other beta-mimetic or β-blockers.

Diagnosis was established on three parameters i.e., confirmation of gestational age, regular uterine contraction and cervical changes. Then intravenous ritodrine hydrochloride infusion was started. The starting dose was 50μg/min; increasing by 50μg/min every 10 minutes; until contractions were ceased or maternal heart rate was 140 beats/min, or the symptoms and signs of hemodynamic instability prevented further increase of dose. The maximum recommended dose was 350μg/min. If infusion arrested labour then it was continued for an other 12 hours. During this time careful fetal and maternal monitoring was done. Patients were advised strict rest for another week and educated about only early symptoms recognition. If labour restarted before 34 weeks, intravneous therapy was reinstituted. Meanwhile steroid were given to enhance fetal lung maturity. At study inclusion; the patient's age and previous obstetrical history were taken into account; along with additional drug supplied, Bishops score at trial's entry, mode of delivery and other symptoms and signs.

For infant, record was made of sex; birth weight, Apgar score (1 in 5 min), resuscitation if needed; and condition on leaving hospital. This study was conducted in Lady Aitchison Hospital and two other teaching hospitals of Lahore from December 1998 to September 1999.

Results

A total of 111 patients were managed and infusion was withdrawn from 9 women, leaving 102 suitable for the analysis. The infusion was withheld due to unwanted side effects, that could have caused maternal or fetal jeopardy. In 4 patients the reason for withholding regimen was occurrence of APH, UTI and difficult control of B.P.

The mean time between start of management and delivery was 28.7 days. It was ≥25 days in 63% of women; ≥15 days in 80%; ≥2 days in 88.2%. The patient who delivered at a gestational age >34 weeks were 67.3%

Bishop scores were recorded in 83 patients at start of trial. In general; the higher the Bishop score at trial entry, shorter the time to delivery that could be expected. Obstetrical history was recorded in all cases; 28 were primigravidae and 74 were multigravidae. The mean time to delivery was 28.7 days in primigravidae and 36.6 days in multigravidae.

Table.1 Mean time between start of management and delivery.

Infusion to delivery interval	No. of Pts	%age
>5	90	88.2
>10	86	84.3
>15	82	80.3
>20	73	71.5
>25	64	62.7
>45	15	14.7
Total	105	

The distribution of birth weights of all viable infants is shown following table 2.

Table 2 distribution of birth weights

Birth weight (Kg)	No. of Pts.
0.50-0.99	3
1.00 – 1.49	10
1.50 – 1.99	14
2.00 – 2.49	16
2.50 – 2.99	30
3.00 – 3.49	20
3.50 – 3.99	5
≥4.0	2
Total	100

95.6% of all viable infants weighed>1.0-kg and 56.3% ≥2.5kg

An attempt was made to compare the incidence of RDS in infants of the mothers who received corticosteroid in addition to ritodrine and who received ritodrine only. A total of 82 mothers were considered for analysis (whose gestational age was upto 32 weeks) of which 45 were given steroid and 37 were not. In steroid group 7(3.1%) developed RDS and 4(10.6%) in the nitrodrine only group so presenting a statistically a significant difference.

Discussion

The results confirm that intravenous ritordrine is satisfactory treatment for preterm labour. The time between the start of trial and eventual delivery obtained in this study is in accord with other controlled studies of ritodrine.the finding that pregnancy continued for >2days in >88.2% patients is important as this is the minimum time period considered adequate to allow administered steroid to enhance fetal lung maturity, and to reduce the incidence of RDS.

There is lack of comparability between study groups especially with regard to the Bishop scores of patients evening the studies. The importance of this; although predictable, is borne out by this study. It would appear that tocolytic therapy is unlikely to succeed if Bishop score is ≥7 at the start of treatment.

The unwanted effects of ritodrine therapy are mainly result from either stimulation of cardiac β_2 receptors or the mild β_1 stimulating effect of the drug. High doses are reported to accelerate pulmonary edema but none was seen in this study. In such cases patient cardiopulmonary states must by evaluated by a specialist.

Apgar score were satisfactory and were comparable with other studies[4]. A significant reduction in the incidence of RDS is also noticed when mothers were given[5] steroids 24 hours before delivery (especially when gestational age was less than 32 weeks).

References

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