PERINATAL SALVAGE FOLLOWING SALBUTAMOL THERAPY

by

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The occurence of preterm labour, and delivery prior to fetal maturity remains the primary cause of perinatal mortality in our country. Eventhough effective labour inhibition by currently available tocolytic agents is possible the common dilemma of the obstetrician are (1) a definitive diagnosis of preterm labour, and (ii) contraindications for labour inhibition.

Caldeyro-Barcia and Poseiro (1960) quantitated the contraction pressure and found that above 10 mm Hg contractions are perceptible by palpation, contractions are associated with pain above 15 mm Hg. and contractions unindentable by finger pressure above 40 mm Hg. Cervical dilatation has been shown to occur only when contraction pressures exceed 24 mm Hg with a contraction frequency greater than 11 per hour (Lindgren, 1973). From, the foregoing observations it is evident that uterine contractions, even when regular and somewhat painful, need not by associated with progressive cervical dilatation; and these contractions frequently cease spontaneously. Nor cervical dilatation alone, in the absence of uterine activity, correlated with preterm labour.

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Preterm labour may in all probability be diagnosed with contractions set in before 37 weeks at a rate of 4 in 20 minutes or 8 in 60 minutes, if (i) membranes are ruptured, (ii) cervix is dilated at least 2 cm or is effaced at least 80%, or (iii) progressive cervical changes over an observation interval (Creasy and Herron, 1981). This criterion does not exclude false labour. At the same time, if cervical dilatation has progressed more than 3-4 cm and nearly completely effaced with regular and strong contractions labour will generally prove unstoppable. And again the dilemma, if one is too quick to make a diagnosis of preterm labour and to treat, many women and their fetuses will be exposed unnecessarily to the known and unknown dangers of tocolytic drugs; on the other hand, to await obvious clinical confirmation of preterm labour eliminates the chance for successful inhibition, (Huddleston, 1982).

In the management of preterm labour determination of duration of gestation should be done accurately; and growth-retarded fetus near term must not be mistaken for preterm fetus. When the common causes for preterm labour such as maternal vascular or cardiac diseases, diabetes, rupture of membranes, foetal death and anomalies, and antepartum haemorrhage, where labour inhibition is un-

warranted or tocolytic agents are contra-indicated, and those in advanced labour when preterm contractions cannot be effectively abolished by tocolytic agents are categorically excluded, there remains only about 20% of women in preterm labour who are reasonable candidates for tocolytic therapy (Zlatnik, 1972).

According to recent reports (Tejani and Varma, 1983), despite the extensive use of tocolytic agents, no substantial pregnancy prolongation and significant reduction in low birth weight deliveries have been achieved in the larger sense. Improved perinatal mortality rate have been obtained in preterm labour even without the use of tocolytic agents (Boylan, and O'Driscoll, 1983), and hence current enthusiasm for tocolytic agents should be tempered until they can be shown to produce further reduction in perinatal deaths. Among the available tocolytic agents such as bed rest, fluid load, magnesium sulfate, sedatives, ethanol and prostaglandin synthetase inhibitors, $Beta_2$ — sympathomimetic agents have a possible added benefit of release of surfactant from fetal lung and there by decrease the risk of respiratory distress syndrome (Enhorning *et al.*, 1977, and Bergman and Hedner, 1978). $Beta_2$ — sympathomimetic agents also favour fetal growth and wellbeing by improving uteroplacental blood flow and stimulating mild hyperglycemia.

Despite the awareness to all these controversies, and even when effective pregnancy prolongation could not be achieved, aiming at quick improvement in fetal lung maturity and consequent improved perinatal salvage we have preferred the liberal use of Beta-sympathomimetic drug, namely, salbutamol, in preterm gestations. Our experience in terms of labour inhibition, pregnancy prolongation, complications of salbutamol and perinatal outcome are discussed in this communication.

Materials and Methods

Since December, 1981 we have been employing salbutamol in preterm gestations with labour contractions, uterine irritability, premature rupture of membranes, multiple pregnancies, and suspected placenta praevia (Table I), and over this period uptil July, 1984, we have treated 129 subjects.

TABLE I

Indications For Salbutamol In Preterm Gestation

Total patients treated	129
Preterm uterine contractions and cervical dilatation	11
Preterm uterine contractility (No cervical dilatation)	27
Premature rupture of membranes	26
Ante-partum haemorrhage	12
Multiple pregnancy	5
Labor contractions between 36 and 38 weeks	

Salbutamol was started as a slow intravenous infusion at a rate of 2.5 microgram per minute and the dose adjusted depending on uterine response and maternal cardiac rate. After abolishion of uterine activity an oral maintenance dose was advocated to prevent recurrence of uterine contractions, and was continued till 38 weeks. The details of dose schedule and patient monitoring are doccumented in our earlier communication (Rajan *et al.*, 1984).

Observations

Among the 129 subjects treated, 113 had uterine contractions and 84 were relieved of the uterine contractions (74.34%). There were 27 subjects with regular painful uterine contractions but no cervical dilatation. Of these subjects with high

risk for preterm labour, painful contractions could be abolished in all 27, and pregnancy prolongation obtained for 7 days in 22 subjects (81.48%) and for 15 days in 20 subjects (74.07%).

When those with cervical dilatation were considered, for the 65 total women treated, contractions could not be abolished in 5 (7.69%) and pregnancy could be prolonged beyond 15 days only in 10 subjects (15.39%). Tocolysis was relatively effective when cervical dilatation was 1-2 cm and effacement was 50-100%, where pregnancy prolongation was obtained for 4 to 7 days in 22 to 52%. Pregnancy could be prolonged beyond 15 days only 17 to 22% in this group. When the cervix was 2 cm dilated or more and almost nearly fully effaced tocolytic therapy totally failed to achieve any desired effect on pregnancy prolongation (Table III)

Patients on salbutamol were carefully monitored by regular recording of maternal heart rate pattern and for evidence of pulmonary oedema. A pulse rate between 130 to 140 per minute was considered an indication for not increasing the drug dose or preferably to reduce the dose. Inspite of this schedule, 13 subjects developed complications due to drug therapy. Major complications were hypotension and shock in one subject and pulmonary congestion in 5 subjects. Hypotension was promptly corrected by administration of antidote propranolol which is a beta blocker. Pulmonary congestion was managed by discontinuation of infusion and administration of diuretics. The minor complications encountered were dyspnoea, palpitation and vomiting, and in all these subjects relief was achieved by discontinuation of medication. (Table IV).

For the 129 subjects treated with salbutamol we have records for deliveries of 108 infants, and among them there were

TABLE II

Pregnancy Prolongation in Subjects with Cervical Dilatation

(Total No. = 64)

Nature of cervix		No. of patients	Not responding		4 days		7 days		15 days and more	
Effacement	dilatation		No.	%	No.	%	No.	%	No.	%
50%	1 c.m.	23	Nil		12	52.17	11	47.83	4	17.39
50%	2 cms	17	Nil		6	35.29	5	29.41	4	23.53
100%	1 cm	9	3	33.33	2	22.22	2	22.22	2	22.22
100%	2 cms	8	Nil		2	25.00	Nil		Nil	
100%	3 cms	4	1	25.00	2	50.00	Nil		Nil	
100%	4 cms	4	1	25.00	Nil		Nil		Nil	
Total	subjects	65	5	7.69	24	36.92	18	27.69	10	15.39

TABLE III
Complications of Salbutamol Therapy

Hypotension and shock	Pulmonary congestion	Dysponea	Palpitation	Vomiting
1	5	6	4	3

TABLE IV
Perinatal Mortality In Low Birth Weight Deliveries

Perinatal mortality (Not receiving Salbutamol) 1983-84	Neonatal deaths and still births (Not receiving Salbutamol) 1983-84	Neonatal deaths (Not receiving Salbutamol) 1983-84	Neontal deaths (Received Salbutamol infusion for 6 hrs.) and more 1981-84	Neonatal deaths (Received Salbutamol infusion for less than 6 hrs.) 1981-84
125|403 31.02%	85|363 23.42%	66|344 19.17%	5|40 12.50%	4|8 50.00%

11 neonatal deaths (10.19%). In order to calculate the perinatal salvage associated with salbutamol therapy we evaluated the perinatal mortaliy in the low birth weight group (below 2.5 kg) who have not received salbutamol and those who have received salbutamol. During the period 1983 — 84 there were 403 low birth weight (LBW) deliveries with a perinatal loss of 125 babies (31.02%), and none of them have received salbutamol. In this group when intra-uterine deaths were excluded there were 65 deaths for 363 births (23.42%); whereas in the salbutamol treated group, if the subject had received medication for 6 hours or more, there have been 5 neonatal deaths for 40 infants born (12.50%). It is also interesting to note that in the group requiring salbutamol therapy, but could not be administered even for 6 hours due to complications the perinatal loss was 4 for 8 (50%) (Table V).

Discussion

It is evident from our study that no substantial pregnancy prolongation, significant enough to reduce the incidence of low birth weight infants, have been achieved by administration of beta$_2$ sympathomimetic agent, salbutamol, as a tocolytic agent. The study also cautions one against the possible complications, and hence the need for careful surveillance; however, the complications could be treated effectively without allowing for deterioration of maternal or foetal conditions. Despite these disadvantages what is remarkably evident is the reduced perinatal mortality for the low birth weight infants associated with salbutamol therapy. We have to infer the probable means of achieving this result is through improvement of pulmonary maturity of the premature infants and the added well-being ensured by increased utero-placental blood supply and hyperglycaemia.

This, while we anticipate improved perinatal survival by the tocolytic effect of the drug and prolongation of gestational age, what we really achieve quite often is improved salvage through fetal lung maturity improvement and to some extend

through marginal prolongation of pregnancy.

As a fetal lung maturing agent salbutamol is effective even when administered only for less than 24 hours; and as tocolytic agent it is least effective when contractions are established and cervix is completely effaced and 2 cm or more dilated. However, even in these subjects if salbutamol could be administered atleast for 6 hours or more reasonable perinatal salvage could be anticipated.

Because of the metabolic derangements and cardiovascular adjustments associated with salbutamol this drug is containdicated in diabetes, heart disease and hypertension. These derangements are of no consequence in healthy subjects and hence salbutamol can be confidently and safely administered in healthy subjects for management of problems of preterm gestations unless there is a contraindication for labour inhibition.

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