

SALBUTAMOL IN TREATMENT OF PRETERM LABOUR

(A Preliminary Study)

by

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SUMMARY

Salbutol (Beta₂ sympathomimetic tocolytic agent) was employed in 19 cases of preterm labour. Premature labour contractions could be abolished and pregnancy prolonged by more than 24 hours in 15 cases, by more than 72 hours in 12 cases, by more than 7 days in 8 cases and by more than 15 days in 4 cases.

Introduction

With a significant proportion of perinatal mortality attributable to prematurity and low birth weight, a great deal of effort has been directed to searching for agents to inhibit premature labour. Zlatnik (1972) has pointed out, however, that even if an ideal labour inhibitor were available, the maximum reduction of premature delivery might be only 15 to 20%, as many patients might be considered inappropriate candidates for labour inhibition. Even definition of premature labour is quite arbitrary and diagnosis of premature labour is not made very easily. The criteria for early diagnosis of preterm labour will be: (i) uterine contractions 10 minutes or less apart, and (ii) progressive cervical dilatation and effacement

over an observation interval (Daikoku and Burnhill, 1980), in patients with a gestation of 36 weeks or less and estimated foetal weight of 2300 gms or less.

Multiple factors are involved in the initiation of human parturition. Oxytocin, progesterone withdrawal, elevated oestrogenprogesterone ratio, fetal corticosteroids, prostaglandins, alpha catecholamines, uterine stretching, and changes in uterine blood flow have all been implicated as potential triggers of labour at term and may also be involved in the initiation of premature labour (Niebyl, and Johnson, 1980). Since multiple factors may be operative, different pharmacologic approaches may be required to achieve the successful inhibition of preterm labour.

Various approaches to the management of preterm labour are bed rest and placebo effect, sedation, administration of tocolytic agents such as ethanol, Beta₂ adrenergic receptor stimulants, prostaglandin inhibi-

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tors, magnesium sulphate, progesterone and diazoxide. Beta₂ stimulants with their smooth muscle relaxation effect have been employed with increasing frequency for effective inhibition of preterm labour. The usual Beta₂ sympathomimetic drugs used are salbutamol (Ryden, 1977), Ritodrine (Merkatz *et al* 1980), Terbutaline (Bergman and Hedner, 1978), Fenoterol (Epstein *et al* 1979) and Hexoprenaline (Lipshitz and Vinik, 1978). Chance of success increases with the early detection of preterm labour and early application of optimal dose of the Beta₂ stimulants (Fuller, 1978).

Salbutamol was the Beta₂ sympathomimetic tocolytic agent employed in our series of management of preterm labour. Our experience with this agent in inhibition of preterm labour, which we gained over a period of one year is presented in this communication.

Material and Methods

Among the patients admitted with premature labour, conditions where inhibition of labour was contraindicated were excluded initially. However, premature rupture of membranes and multiple pregnancy were not considered as contraindications for labour inhibition. Onset of premature labour was established when a patient, between 28 to 36 weeks gestational age, was found to have uterine contractions at an interval of 10 mts or less and vaginal examination revealed effacement and dilatation of cervix. Salbutamol was not administered if the cervical dilatation had already progressed to 4 cms or more. In patients admitted with premature rupture of membranes vaginal examination was performed to confirm the state of cervix and the membranes, and cord prolapse was excluded. In none of the patients vaginal examination was repeated unless there were other pressing

indications. A careful systemic examination was performed in all patients and any medical disorders, particularly cardiovascular diseases, were excluded before the subject was considered for salbutamol therapy.

Salbutamol was administered in the form of a slow infusion with 2 mg (4 ampoules) in 500 ml of 5% dextrose. The initial dose was 2.5 gm/10 drops/minute, and the dose was increased by 2.5 μ gm every 10 minutes till adequate inhibition of labour contractions could be achieved or maternal heart rate was 140 per minute. Once the contractions were abolished the rate of infusion was reduced to the optimum level in which contractions will recur. The maximum dose of salbutamol administered was 25 μ gm per minute (100 drops per minute). Patients were carefully monitored with a separate protocol. Maternal heart rate, foetal heart rate, intensity and frequency of uterine contractions, blood pressure, respiratory status and any untoward reactions were carefully recorded.

If labour contractions were effectively inhibited the infusion was stopped at 12 hours, and was followed by oral medication for preventing recurrence of premature labour. If contractions persisted the infusion was continued for 24 hours or more, till the effect was achieved, and subsequently followed by oral prophylaxis. If contractions could not be abolished and labour progressed salbutamol infusion was stopped.

Oral medication with salbutamol was initiated immediately after completion of the intravenous infusion. The drug was administered in a dose of 2 mgs twice a day till she reached 38 weeks gestation. If the patient showed a tendency for recurrence of premature labour the whole regime was repeated.

Results

Beginning in December, 1981, over a period of one year, 19 patients were treated with salbutamol for inhibition of preterm labour. Age group of the patients ranged from 20 to 42 years, with all except 5 below 25 years. There were 8 primigravidae, 8 second gravidae, and the remaining 3 were multiparous subjects.

Duration of pregnancy of these subjects ranged from 28 to 36 weeks. Gestational age, as calculated by menstrual dates, was 36 weeks in 13 subjects, 34 weeks in 2 subjects, 32 weeks in 3 subjects and 28 weeks in one patient.

All patients had uterine contractions at a frequency of 10 minutes or less. Cervix was effaced to 50% or more and cervical os dilated to 1 to 2 cms in 15 subjects, and cervical dilatation was more than 2 cms in the remaining 4 subjects.

There were 2 patients with twin pregnancies, both 36 weeks gestation, with one patient showing less than 2 cm cervical dilatation and the other more than 2 cms. One patient with premature rupture of membranes admitted at 32nd week of gestation with a cervical dilatation 1 cm was also treated with salbutamol.

Premature labour contractions could be effectively abolished and pregnancy prolonged by more than 24 hours in 15 subjects (78.95%), by more than 72 hours in 12 (63.16%), by more than 7 days in 8 (42.11%), and by more than 15 days in 4 subjects (21.05%). Of the 3 patients treated at 32nd week of gestation pregnancy could be prolonged by 30 days in 1 subject, and by 41 days in another patient, both of them having a cervical dilatation of 1 cm. All the 2 patients treated at 34 weeks gestation could prolong their pregnancy by 10 days, and their cervical dilatation was 1 cm. In the patient treated at 28th week of gestation with a cervical dila-

tation of 1 cm, labour could not be inhibited effectively and she delivered after 17 hours.

Among the 4 patients with a cervical dilatation of more than 2 cms pregnancy could be prolonged by more than 7 days in none, the maximum prolongation achieved was 4 and 5 days in 2 subjects, and the remaining 2 delivered within 24 to 36 hours. All the 4 patients were treated at 36 weeks of gestation. Among these with a cervical dilatation of 1 to 2 cms, pregnancy could be prolonged by 7 days in 8 of the 15 subjects (53.33%).

In the patient admitted at 32 weeks with premature rupture of membranes labour was induced by oxytocin infusion. The premature infant born was 2.3 kgs and recorded good appgar and had no neonatal morbidity, particularly RDS. Two subjects with twin pregnancy treated at 36 weeks gained a pregnancy prolongation by 21 days in one (cervical dilatation of 1 cm), the other did not respond to the treatment schedule.

Nineteen patients treated delivered 21 infants (including 2 twins), and the birth weight of infants ranged from 1.3 kg to 2.5 kg, with an average of 2.33 kgs. Two premature infants were lost in the neonatal period (1.3 kg and 2.5 kg). The perinatal outcome was good in subjects with twin pregnancy and premature rupture of membranes.

Discussion

Beta₂ adrenergic receptor stimulating agents such as salbutamol are well recognised tocolytic agents and are employed for inhibition of preterm labour with increasing frequency (Niebyl and Johnson, 1980). While labour inhibition is effected by the smooth muscle relaxation effect of Beta₂ stimulants, various other beneficial effects of these agents on pregnancy have been documented:

Antepartum administration of Beta₂ stimulant (Terbutaline) appears to offer protection against RDS in the premature infants (Bergman and Hedner, 1978, and this effect may be mediated within a shorter period of less than 24 hours by the beta-adrenergic activity promoting lung liquid absorption (Hobel and Oakes, 1980), a mechanism other than stimulation of surfactant synthesis.

By increasing cardiac output and promoting better uterine vascularity, and by increased uterine vasodilatation and reduced uterine activity Beta-adrenergic agents improve the foetal conditions in-utero, avoid further development of foetal distress or acidosis, and also may save a foetus from acute foetal distress (Lipshitz, 1977 and Arias, 1978).

Increase in infant birth weight with long term use of ritodrine hydrochloride (Beta₂ stimulant) has been documented (Spellacy *et al*, 1978). This effect is probably related to the hyperglycemia that usually accompanies treatment. Thus treatment with Beta₂ stimulants has an intra-uterine growth promotion effect, and hence could be tried in conditions of intra-uterine growth retardation.

While the primary role of Beta₂ adrenergic stimulants in obstetric practice is inhibition of preterm labour, even if labour could not be effectively inhibited a 12 to 24 hours treatment with these agents should promote adequate lung maturity for the premature infants. Moreover, foetal distress could be temporarily prevented or treated, and intra-uterine growth of foetus promoted by these drugs. In the present series of 19 patients treated with salbutamol pregnancy could be prolonged by a week or more in 42%. All patients who were benefited had a cervical dilatation of 1 to 2 cms. It was also observed that the perinatal outcome was

good in 1 patient with premature rupture of membranes and 2 subjects with twin gestation. While these are relative contraindications for labour inhibition good results have been documented for twin pregnancies (Bieniarz *et al*, 1978) and premature rupture of membranes (Christensen, 1980) by employing Beta₂ stimulants.

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