Salbutamol in Premature Labour – a preliminary Report

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ONE OF the most important causes of fetal wastage is prematurity. Attempts at stopping premature labour so that the fetus can reach an age when its chances of surviving are better have only been effective to a limited degree, and the search for better methods continues. Among the drugs that have been used in recent years are intravenous alcohol (Fuchs et al., 1967), Orciprenaline (Baillie et al., 1970), Ritodrine (Wesselius-de Casparis et al., 1971) and Fenoterol (Baillie et al., 1972).

Intravenous alcohol is not often successful when the cervix is dilated more than four centimetres (Fuchs et al. 1967). Orciprenaline shows a rapid tachyphylaxis so that within 30 to 60 minutes of continuous administration further use of the drug is ineffective (Zilianti et al., 1971). Furthermore there are side effects mainly on the cardio-vascular system which limit the use of the drug.

The advent of Salbutamol (Ventolin, Glaxo), a B-adrenergic stimulant with selective action on B^2 endings and reports of its use in asthmatics without causing significant cardiovascular side effects prompted the clinical trial of the drug in inhibiting uterine contractions in patients with premature labour.

This paper is a preliminary report outlining our experiences with the first 10 cases of premature labour. The purpose of this part of the study is to look specifically at immediate effectiveness, side-effects, and safety, so as to determine the feasibility of more prolonged and thorough study of its use in the management of this important problem.

Materials and methods

The patients were selected to include only cases in uncomplicated premature labour between 30 and 35 weeks' gestation, selected at random from cases admitted during 1972 into the labour unit of the department of Obstetrics, University Hospital, University of Malaya, Kuala Lumpur. Cases associated with premature rupture of membranes, pre-eclamptic toxaemia, antepartum haemorrhage or essential hypertension were not included in the series.

Because of difficulty in ascertaining whether premature onset of labour or false labour is present, only cases where regular palpable uterine contractions associated with pain, and with a cervical dilatation of more than 3 cm were accepted for the study. Thus patients were only selected where they were known to be less than 36 weeks pregnant, and had no obstetric complications apart from the premature onset of labour. External tocography was used to monitor cases wherever possible.

Tables I to IV show the distribution of age, parity, and period of gestation at which treatment was started in these patients, and the degree of cervical dilatation at the onset of treatment.

Table I
Age distribution of patients on Salbutamol therapy.

Age in years	No. of cases
15 to 20	2
21 to 25	4
26 to 30	3
31 to 35	1
Total	10

Table II

Parity distribution of patients on Salbutamol therapy.

Para	No. of cases
0	3
1	2
2	3
3	0
4	1
4 +	1
Total	10

Table III

Period of gestation at which Salbutamol was administered.

Period of gestation in weeks	No. of cases
32	2
33	1
34	4
35	3
36	0
Total	10

Table IV

Cervical dilatation at onset of therapy.

Cervical dilatation in cm	No. of cases
0 – 3	0
3 – 4	6
4 – 5	3
5 +	1
Total	10

After the preliminary examination, an intravenous drip was set up with 25 mg of Salbutamol in 500 ml of 5% dextrose solution. The drip was started at an initial rate of 10 drops a minute, and stepped up after every 10 minutes by 10 drops per minute till maintenance doses were reached. The drip rate was kept constant when (a) the uterine contractions ceased, (b) a maximum of 40 drops per minute was reached, or (c) the pulse rate reached 140 per minute, whichever end-point was reached earlier. The above regime gave an approximate initial dosage of 8.9 ug per minute and maintenance of 38.9 ug per minute.

The patient was watched, the following being noted: pulse rate, blood pressure, uterine contractions, and side-effects. After uterine contractions had ceased for 4 hours, the infusion was discontinued.

Results

Tables V to VII show the effectiveness of the drug in stopping uterine contractions, the duration of effectiveness after a single administration of the drug by intravenous infusion, and the side-effects encountered.

Table V

Effectiveness of Salbutamol in Stopping uterine contractions.

Contractions	No. of cases
stopped	6
continued	4
Total	10

Table VI

Duration of uterine quiescence after single infusion of Salbutamol. (Ventolin).

Contractions ceased	No. of cases
0 – 12 hrs.	5
12 – 24 hrs.	2
24 hrs. – 6 days	2
over 7 days	1
Total	10

It will be seen (Table V) that in 6 out of 10 cases uterine quiescence was obtained while the patient was on Salbutamol drip. This compares with the results of Fuchs et al. (1967) using alcohol. However, Liggins et al. (1973) using Salbutamol have better results than the present series in so far as 85% of their patients obtained uterine quiescence for over 24 hours. However, cervical dilatation was less than 3 cm in about 65% of their cases. As has been pointed out by them, comparison between series has been difficult as criteria for case selection and judgement of success have been different in the various groups investigated.

In our series, contractions started again within 24 hours in 7 out of 10 cases. The implications of this will be considered later. In the one patient whose cervical dilatation was more than 5 cm, labour continued unabated despite the Salbutamol drip. In one case when definite uterine contractions subsided, labour was arrested for over a week. In 2 cases the uterine contractions ceased for periods of 4 and 6 days respectively.

Side-effects were present in 9 out of the 10 patients. In 4 of these this consisted only of tachycardia upto 120 per minute. This was not considered sufficiently severe to stop the administration of the drug.

In 5 patients the pulse rate rose to over 120 beats per minute. Three of these complained of palpitations, and in these the drip rate had to be slowed down. There were no cases of precordial pains, nor of muscular twitchings, though these latter have been described by Liggins et al. (1973).

Changes in blood pressure consisted of either a transient rise of systolic blood pressure by 10 mm Hg., or what was far more common, a drop of diastolic blood pressure to about 70 mm Hg. One patient had a major drop in blood pressure to 80/40 mm Hg. This was treated by discontinuing the drip and replacing the Salbutamol with a rapid infusion of 5% destrose solution, a total of 600 ml of fluid having been run in before the blood pressure stabilised at 110/80 mm Hg. On review it was found that the patient had been given pethidine and sparine 2 hours prior to the setting up of the drip, and as all cases who had been put on sedation were not selected for study, this patient was removed from the series and does not show up in the analyses, except in Table VII.

Table VII
Side effects of therapy.

Tachycardia upto 120 per min.	4
,, 120 – 140 per min.	5
Palpitations	3
Hypotension	1
Precordial pain	0

Discussion

The test to which the drug was submitted is a severe one as it has been shown that results are poor with all drugs once the cervical dilatation has reached 3 cm (Liggins et al., 1973).

It was felt that though the criteria would necessarily have to be widened in clinical practice, the initial test should be a severe one. It appears from our experience and those of Liggins et al. (1973) that the effectiveness bears comparison with that of intravenous alcohol. Whether it is superior to alcohol requires a carefully controlled trial. The workers previously mentioned suggest that it is superior to alcohol in cases where membranes have been ruptured.

It is also possible that one of the drugs will work where the other will not, and that Salbutamol and Ethanol may be most effective when used as complementary to each other rather than in competition. This is undergoing study at the present moment.

The relatively short duration of action of the drug used intravenously means that it must be continued to be administered, possibly orally (Dellenback et al., 1972) after the initial effect of stopping the uterine contractions has been obtained by intravenous infusion. The alternative use of Salbutamol in premature labour may well be that suggested by Liggins et al. (1972): i.e. the use of continuous infusion to stay the onset of labour for 24 to 48 hours until antepartum glucocorticoid therapy is established for a sufficiently long period to significantly reduce the chances of the fetus developing respiratory distress syndrome.

It will be seen that there is sufficient indication of the effectiveness and utility of Salbutamol to warrant extension of clinical trials along the lines suggested and along the lines already being followed up by other workers. The final outcome of these will establish the definitive place of this drug in the armamentarium of the obstetrician.

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