**Beta₂-Selectivity of Fenoterol**

**COMPARISON OF INTRAVENOUS AND AEROSOL ADMINISTRATION**

M. H. ĐÜRŘ, P. BAİLLIE

**SUMMARY**

Aerosol administration of fenoterol was compared with intravenous infusion in 30 patients who were undergoing induction of labour. In 11 cases, an increased uterine β₂-selectivity was demonstrated. This, apart from the ease of administration, makes aerosol the mode of administration of choice in some cases. Possible reasons for this are discussed.


The treatment of presumed premature labour with β-adrenergics has gained acceptance. The standard method of administration is intravenous infusion. Because aerosol usage is far more convenient, it was decided to assess whether it was as efficient as intravenous administration.

**PATIENTS AND METHODS**

Thirty patients, in whom labour was induced at gestational stages ranging from 36 to 42 weeks, were studied.

Fenoterol 0.4 mg was administered after painful uterine activity had been induced with oxytocin. When the uterine activity returned to its initial level (±10%), fenoterol 400 μg was administered as an aerosol. In 10 cases, the order of administration was reversed.

The maternal pulse rate was recorded phonocardiographically and the uterine activity was recorded by means of an intra-amniotic polythene cannula, and calculated as Alexandra units. In 22 instances, there was ultrasonic detection of the fetal heart rate, which was recorded simultaneously.

After the termination of the procedure, the membranes were ruptured and normal labour ward procedures were followed.

The effects of the two forms of administration on the maternal heart rate, the fetal rate, and the uterine activity, were compared.

**RESULTS**

All the women were delivered within 18 hours, and 2 neonates were depressed at birth. The types of response to the aerosol could be grouped into two broad categories (Table 1): group A, comprising 11 patients, in whom the effect on uterine activity was similar to that with intravenous administration and group B comprising 10 patients on whom the effect was less (>1½ min difference in return to initial uterine activity).

A further 9 patients experienced no effect. These were excluded from further analysis. In 2 of these the maternal cardiovascular system responded, but the uterine activity did not.

In 6 instances, the fetal heart rate responded by an increase in rate of more than 10 beats per minute, after intravenous administration. No alteration in the fetal heart rate was recorded after aerosol administration.

The aerosol always had less effect on the heart rate than did intravenous administration. Therefore, a distinct uterine β₂-selectivity was displayed in group A.

**DISCUSSION**

The major limitation of the clinical use of β-adrenergic agents is the β₂-inotrophic and chronotrophic effect, which results in severe maternal symptoms. The attainment of uterine β₂-selectivity would, therefore, be a considerable advance in therapy. Newer agents such as salbutamol, ritodrine and fenoterol are far more selective than drugs used previously, but they still have a considerable β₂-effect. The alternative use of β₂-blockers is not satisfactory, since they are also not completely selective, and propranolol increases uterine activity considerably. Furthermore, this drug may be deleterious to the fetus. β Practolol has better β₂-selectivity, but no reports of its use in connection with uterine activity have been published. Verapamil has been used with success.

It was surprising, therefore, to discover that the aerosol had an apparent increased uterine β₂-selectivity in group A. The reason for this is uncertain. The most likely possibility is that the bolus effect of intravenous infusion, which must affect the β₂ cardiac receptors first, is avoided. Absorption occurs slowly and some 10% of the administered dosage is found in the blood. Alternatively, a reflex action may bypass cardiac stimulation.

The reasons for the lack of response, or partial response, are also unclear. Unskilled use of the inhaler, with visible escape of aerosol, was noted on several occasions. In other instances, local barriers to absorption must be postulated, although no pathology was clinically obvious.

At one stage, aerosols were suspected of causing sudden death in asthmatics. Both the propellant and the β₂-adrenergic agent have been incriminated.
TABLE I. RESPONSE TO AEROSOL ADMINISTRATION OF FENOTEROL

<table>
<thead>
<tr>
<th>Group</th>
<th>Highest rate</th>
<th>Time to rise</th>
<th>Return to uterine activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intravenous</td>
<td>Clear rise</td>
<td>Peak</td>
</tr>
<tr>
<td>Group A</td>
<td>Mean</td>
<td>128.6</td>
<td>32.3 sec</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>9.5</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>Mean</td>
<td>105.9</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>10.0</td>
<td>18.2</td>
</tr>
<tr>
<td></td>
<td>Number of patients</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Paired t-test</td>
<td>$t = 10.47$</td>
<td>$t = 8.78$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P &lt; 0.001$</td>
<td>$P &lt; 0.001$</td>
</tr>
<tr>
<td>Group B</td>
<td>Intravenous</td>
<td>Mean</td>
<td>130.0</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>8.8</td>
<td>13.3</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>Mean</td>
<td>112.0</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>5.9</td>
<td>80.62</td>
</tr>
<tr>
<td></td>
<td>Number of patients</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Paired t-test</td>
<td>$t = 6.00$</td>
<td>$t = 4.07$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P &lt; 0.001$</td>
<td>$P &lt; 0.001$</td>
</tr>
</tbody>
</table>

One high-dosage aerosol was withdrawn from the market as a result of investigations such as that of Stolley. Most deaths occurred in older patients who had electrocardiographic abnormalities. Such patients are extremely rare in obstetric practice, because most of the patients are fit young women. Acidemia, another cause of increased myocardial sensitivity to β-adrenergics, is also very unusual in pregnancy, as the pCO₂ is decreased by hyperventilation.

Recent evidence suggests that β-adrenergic aerosols are safe. An extensive clinical usage of β-adrenergic aerosols in cases of threatened premature labour has confirmed this.

In addition to acceptance by the patient and ease of usage, the aerosol administration of fenoterol actually has an increased uterine selectivity when compared with the intravenous form in many cases, making it the preferred type of administration. It is likely that a better technique for its use by the patient will increase its acceptance.

REFERENCES