PLACENTAL TRANSFER OF ATROPINE AND THE EFFECT ON FOETAL HEART RATE

BY

A. H. JOHN

Department of Obstetrics and Gynaecology, Welsh National School of Medicine, Cardiff, Wales

SUMMARY

The effect on the foetal heart rate of atropine administered intravenously to the mother is described in 51 cases. In 10 cases no foetal response was obtained within 30 minutes of injection. There was a tachycardia amounting to 10–27 per cent of the pre-test rate in 26 cases, without any initial bradycardia. In 15 cases there was either a bradycardia alone or a bradycardia followed by a tachycardia amounting to 10–29 per cent of the resting rate. The failure of the placenta to transmit atropine suggests that its function is seriously reduced. The effect of atropine, administered to the mother, on the foetal heart rate is of clinical as well as academic interest to the anaesthetist.

The effect of atropine on the heart rate and the mechanism by which this effect is produced is the subject of some conjecture. Tachycardia, without initial slowing, following intravenous atropine has been described by Hunter (1953), while Bain and Broadbent (1949) found that bradycardia preceded the increased heart rate in the same circumstances. Morton and Thomas (1958) clarified this situation by showing that the effect of atropine on the heart rate depends on the total dose and the rate and route of administration. They showed that if given subcutaneously or by slow intravenous injection, atropine causes first slowing and then an increase in heart rate. By increasing the dose and rate of intravenous injection they were able to abolish the bradycardia and produce tachycardia only.

While studying methods of assessing placental function, the writer became interested in the possibility of utilizing the placental transfer of atropine, with its subsequent effect on foetal heart rate, as an index of placental function. According to Snyder (1959), Holzbach in 1907 demonstrated the presence of hyoscine in the infant's urine when delivered 15 minutes after it was given to the mother. Although Moya and Thorndike (1962) state that both hyoscine and atropine have been shown to cross the placenta to the foetal circulation, the writer has found no reference to this in relation to atropine. The dilution of the atropine in the foetal circulation makes its demonstration difficult by the conventional pharmacological tests (e.g., the cat's-eye test or the rabbit ileum motility test). However, by comparison with the passage of substances of high molecular weight such as protein (Clemetson and Churchman, 1954), carbohydrate (Folkart, Dancis and Money, 1960), barbiturates (Flowers, 1959) and antibiotics (Charles, 1954), there seems little doubt that atropine would, in fact, be rapidly transferred from maternal to foetal circulation providing the placenta was normal. There is certainly clinical evidence to support this.

Hon (1962, 1963) and Hon, Bradfield and Hess (1961) have shown that in some cases of foetal bradycardia, normal cardiac rhythm can be restored by the administration of atropine to the mother. Hellman et al. (1961) administered 1 mg of atropine intravenously to each of 13 pregnant patients and produced changes in the foetal heart rate in all but 2 cases. Foetal tachycardia was produced in 11 cases, some of which showed initial bradycardia. The effect began between 10 and 20 minutes after injection. Hellman et al. (1963) reported further cases investigated with atropine, the foetal heart rate being subjected to a computer analysis in order to get a more definite point of change in rate.
The use of atropine to induce foetal heart rate changes, in utero, would thus appear to be a simple procedure. An investigation was undertaken to assess the value of such changes as a test of placental function. It was hoped that the time from intravenous injection to foetal reaction or the type of reaction produced would provide an index of placental bloodflow and so of placental reserve. The results in relation to this aspect of the investigation will be reported elsewhere. However, atropine is commonly given routinely prior to general anaesthesia in pregnancy and particularly before Caesarean section and some other operative deliveries. Any effect of atropine on the foetal heart rate is, therefore, of interest to the anesthesiologist. It is the purpose of this paper to record the changes in foetal heart rate which occurred following the administration of intravenous atropine in a series of 51 pregnant patients.

METHOD

The method of recording the foetal heart rate was by direct counting which has an average error of approximately 5 per cent (Lamkee, Huntington and Alvarez, 1962), due largely to the difficulty in auscultation. To limit this error, a cardiophone with amplifier was used, of the type described by Wilson, Fothergill and Taylor (1956) and MacRae (1959, 1960, 1962). It was found that changes in foetal heart rate produced by atropine, if they were detectable, were always at least 10 per cent of the initial rate so that this reduced error is acceptable.

The test consisted essentially of the intravenous injection of atropine to the mother and subsequent observation of the foetal heart rate for 30 minutes. In order to minimize apprehension at the time of injection, an intravenous infusion of 5 per cent dextrose was set up before the test was started. In this way it was possible to inject the atropine via the rubber tubing of the infusion apparatus without the patient experiencing any pain and being unaware of the actual time of the injection.

The foetal heart rate was recorded for 30 seconds of each minute for 15 minutes before the injection of atropine, and for 30 seconds of each minute for 30 minutes afterwards. In most of the normal cases the test was performed between 38 weeks gestation and term, and in the obstetrically abnormal cases within a few days of the induction of labour. The dose of atropine was based on the patients' weights, 0.6 mg being given to a patient weighing 70 kg, and the others calculated accordingly.

RESULTS

A total of 51 patients was investigated. Any sustained alteration in the foetal heart rate of 10 per cent or more (increase or decrease) of the initial value was regarded as a response induced by the atropine.

Type of response (table I).

In 10 cases, no significant change in the foetal heart rate occurred within 30 minutes of giving the atropine. In 26 patients a foetal tachycardia without initial slowing was observed. Eight cases showed a foetal bradycardia following the injection of atropine, but the rate did not subsequently rise above the pre-test level during the 30 minutes observation. The remaining 7 cases showed foetal bradycardia followed by tachycardia within the test period.

Time of onset of reaction (table I).

The 26 patients showing foetal tachycardia following atropine administration consisted of 6 in which the response began within 5 minutes of the injection, 15 which reacted between 6 and 10 minutes, 4 between 11 and 15 minutes, and 1 case at 17 minutes.

<table>
<thead>
<tr>
<th>Type of reaction</th>
<th>Number of cases</th>
<th>Onset of reaction (in minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>10</td>
<td>0-5, 0, 0, 0, 0</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>26</td>
<td>6-10, 15, 4, 1</td>
</tr>
<tr>
<td>Bradycardia or bradycardia-tachycardia</td>
<td>15</td>
<td>6-10, 15, 8, 1</td>
</tr>
<tr>
<td>Totals</td>
<td>51</td>
<td>12, 23, 5, 1</td>
</tr>
</tbody>
</table>

Table I

Showing type and time of foetal heart change following intravenous atropine to mother.
TABLE II

<table>
<thead>
<tr>
<th>Type of reaction</th>
<th>Number of cases</th>
<th>Degree of reaction (per cent of pre-test rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>10</td>
<td>10-15</td>
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<tr>
<td></td>
<td></td>
<td>16-20</td>
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<td></td>
<td>21-25</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8</td>
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<td></td>
<td></td>
<td>1</td>
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<tr>
<td>Bradycardia or bradycardia-tachycardia</td>
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<td>0</td>
</tr>
<tr>
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<td>2</td>
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<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Totals</td>
<td>51</td>
<td>26</td>
</tr>
<tr>
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<td></td>
<td>10</td>
</tr>
<tr>
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<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

The combined bradycardia and bradycardia-followed-by-tachycardia group consisted of 6 patients in whom the reaction began within 5 minutes, 8 between 6 and 10 minutes, and 1 at 14 minutes.

Degree of response.

The amount of change in the foetal heart rate induced by the atropine (expressed as a percentage of the pre-test level) varied from 10 to 27 per cent in the tachycardia group and from 10 to 29 per cent in the combined bradycardia group (table II).

DISCUSSION

If the foetal reaction to atropine is similar to that in the adult, then in 41 out of the 51 cases there was evidence that the atropine had crossed the placenta to the foetal circulation. In the group of 26 patients in which there was foetal tachycardia without initial bradycardia it is reasonable to assume that the atropine passed through the placentae rapidly to produce this effect. Subsequent analysis of this group showed that only 1 case revealed evidence of placental insufficiency at delivery but in this case the test was performed 3 weeks before delivery (which was postmature) so that the condition of the placenta at the time of the test was not really reflected by the placental state at delivery.

The 15 cases showing either only bradycardia or bradycardia followed by tachycardia can be grouped together, as they probably both represent a slow but steady passage of atropine across the placenta. It might be supposed that the placentae in this group were less efficient than those in the tachycardia group, but subsequent examination did not confirm this. No patient in this group showed evidence of placental insufficiency.

The 10 cases which showed no foetal response after atropine administration to the mother seemed to indicate that the atropine had not reached the foetal circulation in significant amount. This was confirmed by later analysis, for all the patients in this group showed evidence of reduced placental function.

The placental transfer of atropine, and its effect on the foetal heart rate, is of more than academic interest to the anaesthetist, who is often called upon to resuscitate the newborn infant following operative delivery where atropine has been given as a premedicating agent.

ACKNOWLEDGMENTS

I am indebted to Professor A. S. Duncan and Professor W. W. Mushin, for their interest, help and advice while undertaking this investigation and in the preparation of this paper.

Note. The investigation described in this paper forms part of an M.D. thesis which has been submitted to the University of London.

REFERENCES


LE PASSAGE TRANSPLACENTAIRE DE L’ATROPINE ET SON EFFET SUR LE RYTHME DU COEUR FOETAL

SOMMAIRE
On décrit dans 51 cas l’effet sur le rythme du cœur foetal de l’atropine administrée à la mère par voie intraveineuse. Dans 10 cas il n’y a pas eu de réponse foetale dans les 30 minutes qui ont suivi l’injection. Il y a eu une tachycardie de 10 à 27 % du rythme existant avant le test dans 26 cas, sans aucune bradycardie initiale. Dans 15 cas, il y a eu soit une bradycardie seule, soit une bradycardie suivie d’une tachycardie de 10 à 29 % du rythme au repos. Le fait que le placenta ne transmet pas l’atropine suggère que sa fonction est fortement réduite. L’effet de l’atropine, administrée à la mère, sur le cœur foetal présente un intérêt tant clinique que scientifique pour l’anesthésiste.

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