HAS DROPERIDOL AN ATROPINIC EFFECT?

P. PARMENTIER AND P. DAGNELIE

SUMMARY

The action of droperidol on the tachycardia produced by atropine and on the serum concentration of cholinesterases was observed during balanced anaesthesia. Without atropine, the mean heart rates of patients who received fentanyl or fentanyl plus droperidol were similar. Atropine increased heart rate only in the presence of droperidol ($P<0.001$) (fentanyl v. fentanyl plus droperidol: $P<0.05$). Droperidol inhibited serum cholinesterases ($P<0.05$); this effect was independent of atropine.

Some authors claim that butyrophenones have no anti-muscarinic action (Janssen et al., 1963); others that there is a weak anti-muscarinic effect (Byck, 1975; Stanley, 1978). We observed the effect of droperidol on the tachycardia produced by atropine, and on the serum cholinesterase concentrations during anaesthesia with nitrous oxide and fentanyl.

METHODS

Twenty-four unselected adults of either sex, free from cardiac disease, were studied during elective surgery. Premedication was with diazepam 10 mg i.m. After 30 min thiopentone 3.5 mg kg$^{-1}$ followed by suxamethonium 1 mg kg$^{-1}$ were given i.v. The trachea was intubated and the lungs were ventilated mechanically with 40% oxygen in nitrous oxide. Twelve patients received fentanyl 0.003 mg kg$^{-1}$ i.v. and 12 received fentanyl 0.003 mg kg$^{-1}$ plus droperidol 0.15 mg kg$^{-1}$.

Each group of 12 was separated randomly into subgroups of six who received either atropine 0.007 mg kg$^{-1}$ i.v. 5 min after the induction of anaesthesia or no treatment. The heart rate (displayed on an electrocardioscope) was recorded for 4 min. All observations were made before surgery, the patients being free from external stimulation. The minute volume of ventilation was determined using the Engström nomogram (Engström and Herzog, 1959).

Commercial drug preparations were used. Linear regression coefficients of heart rate against time were computed for each patient, and these coefficients were submitted to a two-way analysis of variance (Dagnelie, 1973).

In a second study of 28 patients, grouped and treated as in the first study, atropine was injected at the time of induction of anaesthesia rather than 5 min later. Venous blood was sampled immediately before induction for the determination of cholinesterase activity (control). A second sample was taken 10 min later. Less than 50 ml of saline was administered i.v. between sampling times. A Biochemica test kit (Boehringer & Soehne, Mannheim) was used to measure the activity of cholinesterase by a colourimetric method (Ellman et al., 1961). The rate of production of thiocholine was measured as acetylthiocholine was hydrolysed. Thiocholine reacted with dithiobisnitrobenzoate ion to produce a yellow anion of 5-thio-2-nitro-benzoic acid.

Linear regression coefficients of cholinesterase concentration against time were computed for each patient; these coefficients were submitted to a two-way analysis of variance (Dagnelie, 1973).

RESULTS

In the absence of atropine the heart rates of patients who received either fentanyl or fentanyl plus droperidol were similar (table I; fig. 1). Atropine significantly increased the heart rate ($P<0.001$) only in the presence of fentanyl plus droperidol.

Droperidol inhibited the cholinesterases ($P<0.05$) both in the presence of atropine and in its absence (table II). Atropine did not influence the cholinesterase concentration significantly and it did not affect the action of droperidol on cholinesterase.

DISCUSSION

Droperidol enhanced the anti-muscarinic effect of atropine upon heart rate.

© Macmillan Journals Ltd 1979
Table I. Variation in mean heart rate (beat min⁻¹ ± SEM) of four subgroups of six patients with and without atropine 0.007 mg kg⁻¹, or receiving either fentanyl 0.003 mg kg⁻¹ or fentanyl 0.003 mg kg⁻¹ plus droperidol 0.15 mg kg⁻¹. The statistical significance of the differences between the subgroups is indicated. $p = a + bt$: Equation of the best fitting line joining the corresponding group of means.

<table>
<thead>
<tr>
<th>Minutes after atropine</th>
<th>Fentanyl</th>
<th>Statistical significance</th>
<th>Fentanyl + droperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (beat min⁻¹) ± SEM</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
<td></td>
</tr>
<tr>
<td>$p = a + bt$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>69.2 66.3 65.5 64.8 63.8</td>
<td>70.2 68.7 66.0 64.3 63.7</td>
<td></td>
</tr>
<tr>
<td>$±3.7 ±3.3 ±3.4 ±3.0 ±2.6</td>
<td>±2.6 ±1.9 ±2.4 ±2.2 ±2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$p = 68.37 - 1.22t$</td>
<td>$p = 70.03 - 1.73t$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical significance:
- n.s.
- $P < 0.001$

Table II. Mean variations (mu. ± SEM) of the serum cholinesterases of four subgroups, of seven patients each, 10 min after the administration of one of the following combinations of drugs: fentanyl 0.003 mg kg⁻¹; fentanyl 0.003 mg kg⁻¹ + droperidol 0.15 mg kg⁻¹; fentanyl 0.003 mg kg⁻¹ + droperidol 0.15 mg kg⁻¹ + atropine 0.007 mg kg⁻¹. The statistical significance of the differences between the subgroups is indicated.

<table>
<thead>
<tr>
<th>Mean variation of cholinesterase concn from control ± SEM</th>
<th>Fentanyl</th>
<th>Statistical significance</th>
<th>Fentanyl + droperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-27 mu. (−1.2%) ±65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical significance: n.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-70 mu. (−3.2%) ±77</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Two aspects of the programme of study may compromise the conclusions. The effect of fentanyl, droperidol and atropine on heart rate was studied in patients who were receiving other drugs: diazepam, thiopentone, suxamethonium and nitrous oxide. On the other hand, it appeared from our results that a stable heart rate was not achieved when atropine was injected. The demonstration that fentanyl and droperidol exert their maximal effect within 5 min (Edmond-Seal and Prys-Roberts, 1970; Price, 1975) justified our choice of a 5-min interval between either fentanyl or fentanyl-droperidol and atropine.

Droperidol increases heart rate (Schaper, Jageneau and Bogaard, 1963; Morrison, Clarke and Dundee, 1970; Ferrari et al., 1974), and this effect is generally attributed to a reflex response following...
HAS DROPERIDOL AN ATROPINIC EFFECT?

Droperidol was the only drug which inhibited the serum cholinesterases (table II). Fortes, Scivoletto and Reis (1978) have demonstrated the anticholinesterase activity of droperidol and other butyrophenones. Todrick (1954) showed the selective affinity to serum cholinesterases of drugs with an antimuscarinic action.

We conclude that droperidol may have a mild atropinic action as this drug increases heart rate (Schaper, Jageneau and Bogaard, 1963; Morrison, Clarke and Dundee, 1970; Ferrari et al., 1974) provokes mental restlessness (Morrison, Clarke and Dundee, 1970; Ferrari et al., 1974), inhibits the increase of bronchial tone after fentanyl (Yasuda et al., 1978), enhances the anti-muscarinic effect of atropine on heart rate (table I and fig. 1) and inhibits serum cholinesterases (Fortes, Scivoletto and Reis, 1978) (table II). It may be added that haloperidol, a closely related drug, causes blurring of vision (Byck, 1975).

REFERENCES


Fig. 1. Variations in mean heart rate of four groups of six patients, either in the presence of atropine 0.007 mg kg\(^{-1}\) or in its absence, after either fentanyl 0.003 mg kg\(^{-1}\) or fentanyl 0.003 mg kg\(^{-1}\) plus droperidol 0.15 mg kg\(^{-1}\). (SEM are shown in table I).

small reductions in arterial pressure (Schaper, Jageneau and Bogaard, 1963).

The addition of a baroreflex to the anti-muscarinic action of atropine is improbable, since in the absence of atropine the heart rate of the patients who received fentanyl did not differ from the rate of those who received fentanyl plus droperidol. For the same reason a difference in vagal tone which could explain a stronger effect of atropine upon heart rate of one group as compared with another (Innes and Nickerson, 1975) is difficult to accept. A mild anti-muscarinic effect of droperidol is not incompatible with our observation. A small amount of atropine may have no effect upon heart rate or may even decrease it (Innes and Nickerson, 1975).

We can exclude the role of anxiety following the use of droperidol (Morrison, Clarke and Dundee, 1970) since our patients were asleep.


LE DROPERIDOL A-T-IL UN EFFET ATROPINIQUE?

RESUME
L'action du droperidol sur la tachycardie produite par l'atropine et sur les concentrations de cholinestérase dans le sérum a été observée au cours d'une anesthésie équilibrée. Sans atropine, les fréquences cardiaques moyennes des malades ayant reçu du fentanyl ou du fentanyl additionné de droperidol ont été similaires. L'atropine n'a augmenté la fréquence cardiaque qu'en présence de droperidol ($P < 0,001$) (fentanyl v. fentanyl plus droperidol: $P < 0,05$).