EFFECT OF PREMEDICATION ON ETOMIDATE ANAESTHESIA

R. CARLOS AND S. INNERARITY

SUMMARY

The effect of premedication upon the induction of anaesthesia with etomidate was studied in 74 adult patients undergoing elective orthopaedic surgery. Premedication with fentanyl plus atropine or with diazepam plus atropine decreased the frequency of involuntary muscle movements without modifying the pattern of the circulatory effects of etomidate, although fentanyl increased the frequency of apnoea. Pain at the site of injection was not modified by premedication.

Etomidate is a recently-introduced water-soluble i.v. anaesthetic agent with minimal actions on the cardiovascular and respiratory systems (Doenicke et al., 1973; Kettler et al., 1974). However, the appearance of myoclonic movements and pain at the site of injection have been reported (Doenicke, 1974; Morgan, Lumley and Whitwam, 1975). This study was undertaken in order to explore the effects of premedication with diazepam plus atropine or with fentanyl plus atropine, on the induction of anaesthesia using etomidate as the induction agent.

PATIENTS AND METHODS

Seventy-four patients (age range 16–65 yr) undergoing elective orthopaedic surgery were studied. In all instances anaesthesia was induced with etomidate* 0.3 mg kg\(^{-1}\) injected over 45 s. The patients were allocated randomly to one of three groups: not pre-treated (n = 26); pretreated with fentanyl 10 \(\mu\)g kg\(^{-1}\) i.v. plus atropine 10 \(\mu\)g kg\(^{-1}\) i.v. (n = 25) or with diazepam 150 \(\mu\)g kg\(^{-1}\) i.v. plus atropine 10 \(\mu\)g kg\(^{-1}\) i.v. (n = 23) 10 min before the administration of the etomidate. All drugs were injected through an Abbocath 16 catheter inserted in an antecubital vein.

Direct arterial pressure, the electrocardiogram (e.c.g.), heart rate and respiratory rate were recorded continuously on a Greantbach 9232/1100 polygraph. Blood-gas tensions were measured in samples withdrawn through an arterial catheter 1 min before the administration of etomidate and 1 and 3 min thereafter.

* Etomidate sulphate (0.2%) in a polyethyleneglycol vehicle.

The time required to induce sleep was measured, and patients were observed for any evidence of pain, muscular movements, cough, hiccup or increased secretions occurring before the continuation of the anaesthetic with other agents. Complaints about pain were recorded, but no direct questions were asked about pain at the site of injection. Emetic sequelae after operation were not investigated.

RESULTS

Loss of consciousness was obtained 25–30 s after the administration of etomidate. No signs of excitation were observed in any patient before loss of consciousness. Eyelash and corneal reflexes were abolished consistently 2 min after termination of the injection. However, the laryngeal and pharyngeal reflexes were not affected in patients receiving etomidate without premedication.

The effects of etomidate on cardiovascular function and its modification by premedication are presented in table I. A slight increase of respiratory rate (lasting about 15–20 s) was detected immediately after the injection in about two-thirds of the unpremedicated patients. Apnoea of less than 15 s duration developed in two patients in this group and cough occurred in four additional patients. Patients premedicated with fentanyl plus atropine showed irregular patterns of breathing after the administration of etomidate. Premedication with diazepam plus atropine resulted in the development of apnoea in three of 23 patients, but in none did this last for more than 15 s. The frequency of apnoea, and the blood-gas tensions in the three groups of patients are presented in table II. Bicarbonate concentration and base excess values were not altered by etomidate.

Myoclonic movements were observed in 14 of 26 patients receiving etomidate alone. Three further patients in this group developed tonic movements.

© Macmillan Journals Ltd 1979
TABLE I. Changes in arterial pressure and heart rate (mean ± SEM) after etomidate 0.3 mg kg⁻¹.

* P<0.05; ** P<0.001; Student's t test of differences from initial values

<table>
<thead>
<tr>
<th></th>
<th>Etomidate</th>
<th>Fentanyl + atropine</th>
<th>Diazepam + atropine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After 1 min</td>
<td>After 3 min</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>138 ±4.6</td>
<td>122 ±3.9*</td>
<td>125 ±5.0*</td>
</tr>
<tr>
<td></td>
<td>133 ±3.0</td>
<td>115 ±2.0**</td>
<td>114 ±2.5**</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>78 ±2.6</td>
<td>71 ±2.6*</td>
<td>72 ±2.6</td>
</tr>
<tr>
<td></td>
<td>79 ±1.6</td>
<td>70 ±1.9**</td>
<td>69 ±2.0**</td>
</tr>
<tr>
<td>Heart rate (beat min⁻¹)</td>
<td>87 ±2.3</td>
<td>107 ±3.0</td>
<td>107 ±3.4</td>
</tr>
<tr>
<td></td>
<td>88 ±2.7*</td>
<td>105 ±2.6</td>
<td>107 ±3.4</td>
</tr>
<tr>
<td></td>
<td>89 ±2.9</td>
<td>102 ±2.3</td>
<td>104 ±5.7</td>
</tr>
</tbody>
</table>

TABLE II. Blood-gas tensions and oxygen saturation (mean ± SEM) and frequency of apnoea after administration of etomidate 0.3 mg kg⁻¹. * P<0.05; ** P<0.001; Student's t test of differences from initial values

<table>
<thead>
<tr>
<th></th>
<th>Etomidate</th>
<th>Fentanyl + atropine</th>
<th>Diazepam + atropine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After 1 min</td>
<td>After 3 min</td>
</tr>
<tr>
<td>pH (unit)</td>
<td>7.42 ±0.007</td>
<td>7.40 ±0.005*</td>
<td>7.40 ±0.007</td>
</tr>
<tr>
<td></td>
<td>7.38 ±0.005</td>
<td>7.37 ±0.001*</td>
<td>7.37 ±0.001</td>
</tr>
<tr>
<td></td>
<td>7.38 ±0.008</td>
<td>7.37 ±0.006</td>
<td></td>
</tr>
<tr>
<td>Pco₂ (kPa)</td>
<td>5.1 ±0.11</td>
<td>4.8 ±0.23</td>
<td>4.4 ±0.2</td>
</tr>
<tr>
<td></td>
<td>5.5 ±0.09*</td>
<td>5.2 ±0.13</td>
<td>4.9 ±0.12</td>
</tr>
<tr>
<td></td>
<td>5.5 ±0.009*</td>
<td>5.3 ±0.16</td>
<td>4.9 ±0.11</td>
</tr>
<tr>
<td>Po₂ (kPa)</td>
<td>10.9 ±0.24</td>
<td>11.8 ±0.55</td>
<td>11.5 ±0.64</td>
</tr>
<tr>
<td></td>
<td>9.2 ±0.29**</td>
<td>8.3 ±0.47**</td>
<td>9.0 ±0.29**</td>
</tr>
<tr>
<td></td>
<td>9.6 ±0.31**</td>
<td>8.5 ±0.47**</td>
<td>10.1 ±0.4</td>
</tr>
<tr>
<td>Oxygen satn (%)</td>
<td>95.0 ±0.3</td>
<td>95.0 ±1.1</td>
<td>95.0 ±0.8</td>
</tr>
<tr>
<td></td>
<td>93.0 ±0.5**</td>
<td>85.0 ±2.5**</td>
<td>91.0 ±1.2*</td>
</tr>
<tr>
<td></td>
<td>92.0 ±0.5**</td>
<td>85.0 ±2.5**</td>
<td>93.0 ±0.8</td>
</tr>
<tr>
<td>Apnoeic periods (%)</td>
<td>Less than 30 s</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Lasting 30–60 s</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>More than 60 s</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Premedication with fentanyl and atropine reduced the appearance of involuntary movements after etomidate (six instances of myoclonic movements and one with tonic movements, of 25 patients). Similar results were obtained following premedication with diazepam and atropine (five patients with myoclonic and one with tonic movements; total of 23). Burning pain at the site of injection was reported spontaneously by about 20% of patients. This side-effect was recorded in five of 26 patients given no premedication, four of 25 receiving fentanyl, and six of 23 premedicated with diazepam. Marked salivation was observed in most patients receiving etomidate alone, but in none of those pretreated with atropine, plus either fentanyl or diazepam. Nausea during induction was recorded in three non-pretreated patients, in three pretreated with fentanyl and in one pretreated with diazepam. Vomiting was observed only in one fentanyl-pretreated patient.

**DISCUSSION**

The frequency of involuntary movements in the induction of anaesthesia with etomidate without sedative premedication has varied from about 18% (Macrez et al., 1976) to 59% (Rifat, Gamulin and Gemperlé, 1976) and even to more than 80% (Zacharias...
PREMEDICATION AND ETOMIDATE

et al., 1978). This may be a result, in part, of the differences in the definition of myoclonia or to dosage or speed of injection, and also to the effects of movement of the patient during anaesthesia. In this study myoclonia was observed in 53% of patients receiving etomidate alone, but its frequency was decreased substantially by premedication with either diazepam or fentanyl. This is in accordance with the results of Ghoneim and Yamada (1977) and Zacharias and co-workers (1979).

The frequency of pain during the injection of etomidate was less in our series than in that of Ghoneim and Yamada (1977) and slightly less than in the series of Zacharias and co-workers (1978) in which polyethylene glycol was used as a solvent. In contrast to the results of Kay (1976) and Zacharias and co-workers (1979) which showed a decrease in pain following premedication with fentanyl or pethidine, analgesic premedication did not influence pain on injection. A similar lack of influence was reported by Ghoneim and Yamada (1977). This discrepancy may be explained in part by differences in methods of evaluating pain or in the dosage of the analgesic drugs, and it is generally agreed that pain is less likely if etomidate is injected into a large vein.

The effects of etomidate on the circulatory and respiratory systems were only moderate when this drug was administered alone. The frequency of apnoea in our patients was of the order reported by Ghoneim and Yamada (1977) and less than in the series of Holdcroft and co-workers (1976), and was not influenced by the prior administration of diazepam. The highest frequency of apnoea was seen in fentanyl-premedicated patients. Since, in these patients, voluntary movements were less frequent than in those receiving etomidate alone, it is difficult to accept the contention (Morgan, Lumley and Whitwam, 1977) that involuntary movements play a major role in the induction of apnoea. Changes in blood-gas tensions were moderate and affected Po2 values mostly. They were more marked in patients premedicated with fentanyl and could be explained by changes in respiratory pattern.

The frequency of nausea and vomiting during the induction of anaesthesia with etomidate in this series is greater than in other reports (Macrez et al., 1976). However, nausea and vomiting after operation were not considered here since it was felt that these are related to the type of intervention and to the agent used for the maintenance of anaesthesia. If the problem of pain at the site of injection can be curtailed by use of an appropriate solvent or technique of administration, and if emetic emergence sequelae are shown to be in the range observed with other induction agents, etomidate, associated with a suitable premedication, may be a valuable i.v. anaesthetic in patients with cardiovascular or respiratory problems.

ACKNOWLEDGEMENTS

We would like to thank Janssen Pharmaceutica, Beerse, for the supply of etomidate.

REFERENCES


EFFET DE LA PREMEDICATION SUR L’ANESTHESIE PAR L’ETOMIDATE

RESUME

L’effet de la prémédication sur l’induction de l’anesthésie par l’etomidate a été étudié sur 74 malades adultes, subissant une intervention chirurgicale orthopédique à froid. La prémédication à base de fentanyl et d’atropine ou de diazepam a réduit la fréquence des mouvements musculaires involontaires sans modifier le mode des effets circulatoires, bien que le fentanyl ait augmenté
la fréquence de l'apnée. La douleur ressentie au point d'injection n'a pas été modifiée par la prémédication.

DIE WIRKUNG VON VORBEHANDLUNG AUF EINE ETOMIDAT-ANÄSTHESIE

ZUSAMMENFASSUNG

EFECTO DE LA PREMEDICACION EN LA ANESTESIA CON ETOMIDATO

SUMARIO
Se estudió el efecto de la premedicación sobre la inducción de la anestesia con etomidato en 74 pacientes adultos sometidos a operaciones quirúrgicas ortopédicas electivas. La premedicación con fentanilo adicionado de atropina o con diazepam adicionado de atropina hizo bajar la frecuencia de los movimientos musculares involuntarios sin modificar el tipo de efectos circulatorios del etomidato, aunque el fentanilo aumentara la frecuencia del apnea. La premedicación no alteró el dolor al punto de la inyección.