ETOMIDATE AND FENTANYL FOR MAINTENANCE OF ANAESTHESIA

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An infusion of etomidate and fentanyl was compared with halothane or morphine plus nitrous oxide in oxygen for the maintenance of anaesthesia in 200 patients. Cardiovascular and respiratory changes were found to be similar in the two groups. There was a prolongation of recovery time in the etomidate-fentanyl group: this was possibly a result of lack of flexibility in the infusion technique.

Etomidate can be used as an anaesthetic induction agent (Miller, Hendry and Lees, 1978). In this role its major disadvantages are pain on injection and excitatory movements. In the present study etomidate was combined with fentanyl and used, as an infusion, to maintain anaesthesia. This technique was compared with a conventional technique using halothane, or morphine, with nitrous oxide in oxygen.

PATIENTS AND METHODS

Two hundred patients undergoing general surgical or gynaecological operations were allocated to two groups of 100 patients matched for age, sex, weight, body build and operative procedure (tables I, II).

After premedication with a narcotic analgesic and atropine or hyoscine, anaesthesia was induced with thiopentone 6 mg kg⁻¹ and fentanyl 1.2 µg kg⁻¹. When necessary, the trachea was intubated following suxamethonium 100 mg. Tubocurarine 0.5 mg kg⁻¹ was given when prolonged neuromuscular blockade was required and the lungs were ventilated artificially.

The infusion group (A) breathed 40% oxygen in nitrogen. Anaesthesia was maintained with an i.v. infusion of etomidate and fentanyl in normal saline (etomidate 2.5 mg ml⁻¹ and fentanyl 7 µg ml⁻¹) given from a Treonic DC2 rotary pump. Following a rapid initial infusion (3–4 ml min⁻¹ for 2–3 min) the rate of infusion was decreased according to the patient’s response to surgical stimulation as judged by changes in heart rate, arterial pressure, sweating, lachrymation and, in those who were breathing spontaneously, respiratory rate. The mean total doses (± SEM)


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were etomidate $20 \pm 1.6 \mu g kg^{-1} min^{-1}$ and fentanyl $0.053 \pm 0.0045 \mu g kg^{-1} min^{-1}$.

The control group (B) breathed 33% oxygen in nitrous oxide supplemented with halothane during spontaneous ventilation or morphine $0.2 \text{mg kg}^{-1}$ during artificial ventilation. Physiological saline solution was infused i.v. at a rate similar to the rate of fluid administration in group A.

In all patients heart rate, arterial pressure (oscillotonometer) and e.c.g. were monitored. In 20 spontaneously breathing patients from each group arterial blood was sampled before the induction of anaesthesia, 20 min after a steady state of maintenance anaesthesia has been achieved and 15 min after the end of operation. Blood-gas tensions were measured using an ABL1 Automatic Gas Analyser.

The time from the end of anaesthesia until the patient obeyed simple commands was noted by the recovery room staff, who were unaware of the method of anaesthesia. The time of the first administration of analgesia after operation was recorded. All patients were visited on the day after surgery and the infusion site inspected for evidence of damage to veins.

Student’s $t$ test was used to analyse the cardio-vascular, respiratory and recovery data. $\chi^2$ test was used to compare the amounts of analgesia given, and the frequency of venous sequelae.

RESULTS

Quality of anaesthesia

No problems were encountered during anaesthesia in any of the patients receiving artificial ventilation. The maintenance of anaesthesia was unsatisfactory in three men (group A) who were breathing spontaneously and undergoing haemorrhoidectomy. However, there was difficulty also in obtaining a sufficiently deep level of anaesthesia during the maintenance period in two fit young men in group B undergoing the same operation. On no occasion was the chosen method of anaesthesia abandoned.

Time to recovery

Recovery time in group B was shorter ($12.5 \pm 1.8 (\text{SEM}) \text{min}$) than in group A ($15.8 \pm 2.3 (\text{SEM}) \text{min}$). This difference was not significant. In group A 12% of patients receiving IPPV and 25% of those breathing spontaneously had not recovered consciousness within 40 min. Wakening could be produced readily by the injection of naloxone $0.1-0.2 \text{mg i.v.}$ Restlessness occurred in six patients who received an injection of morphine i.m.

Respiration

In patients in whom blood-gas tensions were measured the percentage changes in the mean arterial carbon dioxide tensions in group B were significantly ($P<0.02$) greater than those from group A during surgery but were comparable 15 min after the end of anaesthesia (table III).

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage increase (±SEM)</th>
<th>15 min after op.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>9.8(±1.1*)</td>
<td>8.1(±1.4)</td>
</tr>
<tr>
<td>B</td>
<td>14.6(±1.9*)</td>
<td>8.0(±1.7)</td>
</tr>
</tbody>
</table>

Circulation

Compared with the values before operation no clinically significant changes in mean heart rate or arterial pressure were noted in either group. Group B (halothane) showed significant decreases in systolic and diastolic pressures and heart rate after induction. The values remained significantly ($P<0.05$) lower throughout the operation, except for the systolic pressure, which was not significantly different from group A during the maintenance of anaesthesia.

Nausea and vomiting

Four patients in group A, all of whom had received naloxone, complained of nausea and vomiting, compared with six in group B, four of whom had received morphine anaesthesia.

Postoperative analgesia

There was no significant difference between the groups in the time until the first injection of analgesic: the mean time in group A was $6.8 \pm 1.0 (\text{SEM}) \text{h}$ compared with $6.4 \pm 0.8 (\text{SEM}) \text{h}$ in group B. On direct questioning, no patient had recall of any event after insertion of the "Butterfly" needle until awakening in the ward.

Venous sequelae

Thrombosis of the infused vein occurred in 15 patients being ventilated artificially in group A, compared with seven patients breathing spontaneously. In the majority of the 15 patients...
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2.5–5 cm of the vein was hard, and there was neither tenderness nor inflammation. However in six patients a more extensive thrombophlebitis was observed. In group B, six patients being ventilated artificially and four breathing spontaneously had evidence of venous thrombosis.

DISCUSSION

The infusion of etomidate and fentanyl produced satisfactory maintenance of anaesthesia in most patients. Irrespective of the mode of ventilation, cardiovascular stability was comparable to that obtained in the artificially ventilated patients in group B and superior to that in the patients in group B receiving halothane. Mean $P_{a\text{CO}_2}$ was lower in the infusion group compared with the halothane group.

The venous sequelae may have been related to the longer duration of infusion into relatively small veins. Our previous experience (unpublished) of infusion via a fast-running i.v. infusion caused a much lower frequency of venous sequelae.

T. M. O'Carroll (personal communication) using a maintenance dose of etomidate 42 $\mu$g kg$^{-1}$ min$^{-1}$ and fentanyl 0.033 $\mu$g kg$^{-1}$ min$^{-1}$ found an increase in muscle movement and muscle tone during anaesthesia. Since muscle movement is a feature of etomidate infusion without fentanyl (Kay and Rolly, 1977), and as it was conspicuously absent in this series, it may be that lower doses of etomidate and larger doses of fentanyl give better conditions.

The combination of thiopentone as an induction agent and an etomidate–fentanyl infusion to maintain anaesthesia provides a practical, pollution-free anaesthetic technique with satisfactory conditions for patient and surgeon. However, the use of a fixed ratio of the two drugs, although satisfactory for the majority of patients, does not allow titration of analgesia and hypnosis in the individual patient. Further studies are required to determine the optimal dosage scheme.

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REFERENCES


ETomidate et fentanyl pour maintenir l'anesthésie

RESUME

On compara une infusion d'etomidate et de fentanyl avec de l'halothane ou de la morphine avec du protoxyde d'azote dans de l'oxygène aux fins du maintien de l'anesthésie, chez 200 patients. Les changements cardiovasculaires et respiratoires s'avèrent analogues chez les deux groupes. Il y eut une prolongation de la période de récupération dans le groupe à l'etomidate–fentanyl: c'est peut-être là le résultat du manque de flexibilité de la technique d'infusion.

ETOMIDATE ET FENTANYL POUR MAINTENIR L'ANESTHESIE

ZUSAMMENFASSUNG


ETOMIDATE UND FENTANYL ZUR AUFRÄHTERHALTUNG DER NARKOSE

SUMARIO

Se procedió a la comparación, con el propósito de mantener la anestesia en 200 pacientes, de una infusión de etomidato y fentanilo con halotano y morfina con óxido nitroso. Se comprobó que los cambios cardiovaskulares y respiratorios eran similares en los dos grupos. Hubo una prolongación del tiempo de recuperación en el grupo etomidato–fentanilo: es posible que esto resultase de la falta de flexibilidad en la técnica de infusión.

EL ETOMIDATO Y EL FENTANILO PARA LA MANTENCIÓN DE LA ANESTESIA