USE OF SIMPLE TESTS TO DETERMINE THE RESIDUAL EFFECTS OF THE ANALGESIC COMPONENT OF BALANCED ANAESTHESIA

T. MANNER, J. KANTO AND M. SALONEN

Many attempts have been made to define the best methods with which to evaluate recovery from anaesthesia, and the effects of the different drugs used during anaesthesia. In our earlier study (Manner, Kanto and Salonen, 1987) simple tests (Maddox wing apparatus, critical flicker fusion threshold test, visual analogue scale ratings for subjective sensations) differentiated clearly between the effects of fentanyl and those of buprenorphine and, especially, from those of a placebo. We have used the same simple tests to evaluate the difference in the rate of recovery after general anaesthesia when fentanyl or buprenorphine were used as the analgesic component of balanced anaesthesia. The "postanaesthetic recovery score", which has been widely used since 1970, was recorded and used as a reference.

PATIENTS AND METHODS

In a randomized, double-blind study the per- and postoperative effects of fentanyl (n = 15) and buprenorphine (n = 15) (as the analgesic component of a balanced anaesthetic technique) were recorded in healthy women undergoing elective Caesarean section. The patients were at term, and none had any signs of placental dysfunction. The most common indications for Caesarean section were cephalo–pelvic disproportion and previous Caesarean section. In group 1, after the clamping of the umbilical cord, fentanyl 2.5 μg kg⁻¹ was injected i.v. and in group 2, buprenorphine 7.5 μg kg⁻¹ i.v. Based on clinical studies (Heel et al., 1979; Mather, 1983), and our own experiences with healthy volunteers (Manner, Kanto and Salonen, 1987), the doses chosen were expected to produce a comparable maximal analgesic effect. Otherwise, the anaesthesia (routine technique of J. Kanto) was similar in both groups: no premedication; vecuronium 120 μg kg⁻¹ i.v. followed after 15–30 s by rapidly injected thiopentone 4 mg kg⁻¹ i.v. + nitrous oxide in oxygen (40 : 60) + 0.5 % halothane (until delivery); maintenance of anaesthesia: nitrous oxide in oxygen + opioid + dihydrobenzperidol 20 μg kg⁻¹

SUMMARY

In order to evaluate simple means of determining the rate of recovery after general anaesthesia, the usefulness of the critical flicker fusion threshold test, the Maddox wing apparatus and the visual analogue scale were compared. The postanaesthetic recovery score was used as a reference. Two patient groups (n = 15 in each) received, in a randomized double-blind study, a similar balanced anaesthesia for Caesarean section, except that the analgesic component was either fentanyl 2.5 μg kg⁻¹ i.v. or buprenorphine 7.5 μg kg⁻¹ i.v. Maddox wing apparatus and visual analogue scale were sensitive enough to differentiate between the postanaesthetic residual effects of the two opioids, but critical flicker fusion threshold and, especially, postanaesthetic recovery score were insensitive in this respect. There was no difference between the two patient groups in mean arterial pressure and heart rate. Our results show that the residual effects of different kinds of opioids as an analgesic component of balanced anaesthesia can be differentiated using simple means like Maddox wing apparatus and visual analogue scales.
EFFECTS OF THE ANALGESIC COMPONENT OF BALANCED ANAESTHESIA

i.v.; glycopyrrolate 0.4 mg + neostigmine 2.5 mg i.v. After cord clamping, oxytocin 5 iu was injected i.v. If required, additional doses of thiopentone 1 mg kg\(^{-1}\), fentanyl 0.5 \(\mu\)g kg\(^{-1}\), buprenorphine 1.5 \(\mu\)g kg\(^{-1}\) or vecuronium 30 \(\mu\)g kg\(^{-1}\) were administered.

The following measurements were undertaken just before the induction of anaesthesia and 15, 30, 45, 60 and 120 min after the end of anaesthesia: critical flicker fusion frequency (CFF-threshold) (Smith and Misiak, 1976); relaxation of ocular muscles with Maddox wing apparatus (Hannington-Kiff, 1970a, b); subjective sedation: quite alert to extremely tired; analgesia: no pain to very severe pain; nausea: none to vomiting. (The last three assessments by 10-cm visual analogue scales marked 0–10 (Bond and Lader, 1974; Maxwell, 1978).) In addition, as a reference, in order to test the postoperative state of the patients, the postanaesthetic recovery score was recorded by the anaesthesist in the recovery room by evaluating muscle activity, ventilation, circulation, consciousness and skin colour (maximum 10 points (Aldrete and Kroulik, 1970)). Heart rate, and systolic and diastolic arterial pressures (sphygmonometer) were monitored as depicted in figure 1. The expiratory end-tidal carbon dioxide was monitored during anaesthesia (Datex, Normocap, Espoo, Finland) and maintained at 5 ± 0.5% to maintain normoventilation. The degree of neuromuscular blockade was assessed by observing movements of the fingers following four successive supramaximal stimuli administered to the ulnar nerve near the wrist via surface electrodes at a frequency of 2 Hz (Myotest, Biometer, Odense, Denmark). An additional dose of vecuronium was administered when a weak but still visible twitch from the second stimulus was observed. Exubation of the trachea was performed when all four twitches were seen with no or only slight fade, and when the end-tidal carbon dioxide concentration remained less than 7%, while the patients were breathing spontaneously (Salmenperä and Tammisto, 1980). During the anaesthesia, lactated Ringer’s solution (without glucose) was infused—approximately 1000 ml followed by Normosol-type infusion of 1000 ml. In no patient was the estimated blood loss more than 500–600 ml. If required, in the recovery area, buprenorphine 4 \(\mu\)g kg\(^{-1}\) was injected i.m. for severe pain.

Normally distributed data were analysed using Student’s \(t\) test and two way ANOVA (Cohen and Holliday, 1982) with repeated measures on one factor. On the ordinal data Mann–Whitney \(U\) test (Glantz, 1981) and Chi-square test were used.

RESULTS

The two groups were comparable in respect to age, weight, height, ASA classification, induction–delivery time, intubation time and the duration of anaesthesia: there were no significant differences (table I). All newborns had Apgar scores ≥ 7. During anaesthesia only two of the patients in the buprenorphine group needed a single additional dose of vecuronium, compared with 12 patients in the fentanyl group (\(P = 0.0035\)). There were no significant differences between the two groups in the cardiovascular variables (mean arterial pressure, heart rate), but there were similar, statistically significant time-related changes (\(P < 0.001\)) in both groups during anaesthesia and in the recovery period (fig. 1, table II), but neither drug had any significant influence on these variables. In the recovery room six of the 15 patients in the fentanyl group asked for an...
TABLE I. Comparison of the two study groups. The values are mean ± SD. Probability tested by Student’s t test (non-paired data) and † Chi-square test

<table>
<thead>
<tr>
<th></th>
<th>Fentanyl group</th>
<th>Buprenorphine group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>15</td>
<td>15</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>31.1±6.3</td>
<td>29.8±6.4</td>
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<tr>
<td>Weight (kg)</td>
<td>75.2±12.9</td>
<td>79.5±18.7</td>
<td>ns</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.4±5.8</td>
<td>162.9±5.9</td>
<td>ns</td>
</tr>
<tr>
<td>ASA class I</td>
<td>13</td>
<td>14</td>
<td>ns</td>
</tr>
<tr>
<td>class II</td>
<td>2</td>
<td>1</td>
<td>ns</td>
</tr>
<tr>
<td>Induction-delivery time (min)</td>
<td>4.6±1.0</td>
<td>4.0±0.8</td>
<td>ns</td>
</tr>
<tr>
<td>Intubation time (s)</td>
<td>126.1±20.0</td>
<td>118.2±21.5</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>58.1±7.8</td>
<td>58.1±7.7</td>
<td>ns</td>
</tr>
<tr>
<td>Patients needing additional neuromuscular blocker</td>
<td>12/15</td>
<td>2/15</td>
<td>P = 0.0035†</td>
</tr>
<tr>
<td>Patients needing analgesic in the recovery room</td>
<td>6/15</td>
<td>0/15</td>
<td>P = 0.022‡</td>
</tr>
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TABLE II. F-values and probability levels using two-way analysis of variance (ANOVA) with repeated measures on one factor (time)

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Interaction</th>
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<tr>
<td></td>
<td>= drug</td>
<td>= time</td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>0.977</td>
<td>30.85</td>
<td>0.926</td>
</tr>
<tr>
<td>P</td>
<td>0.66</td>
<td>&lt; 0.001***</td>
<td>0.54</td>
</tr>
<tr>
<td>Arterial pressure</td>
<td>0.950</td>
<td>9.33</td>
<td>0.126</td>
</tr>
<tr>
<td>P</td>
<td>0.66</td>
<td>&lt; 0.001***</td>
<td>0.99</td>
</tr>
</tbody>
</table>

additional analgesic (buprenorphine 4 µg kg⁻¹ i.m.) from 30 to 95 min (mean 61 min) after the end of anaesthesia. Values of the postoperative measurements, however, did not differ statistically from those of the other patients in the fentanyl group and, therefore, the results of the 15 patients of this group were combined.

In the CFF-threshold test the patients showed a wide inter-individual variation in preanaesthetic values and no statistically significant differences in the absolute values were found between the two groups in the recovery period (table III). The CFF-readings did not reach the pre-anaesthetic values during the 2-h study period in either group. When results were expressed as relative changes in CFF-threshold, the buprenorphine group showed a statistically significantly (P = 0.027) lower value at 90 min (table III).

The measurements with Maddox wing apparatus showed evidence of more rapid recovery in the fentanyl group. The difference between the two study groups increased significantly from 30 min to 120 min (table III). However, no statistically significant differences were found in the PARS values (table III).

Results of subjective expressions of postoperative sedation, pain and nausea (measured by visual analogue scales) are summarized in table III. Following the equal maximum values of sedation at 15 min after surgery, the patients in the fentanyl group showed a more rapid recovery with significant differences at 60 and 90 min. At 120 min the difference did not reach statistical significance.

The most striking difference between the two groups was found in subjective pain rating (table III). In both groups the scores stayed at a relatively constant value (variation in means from 7.1 to 5.1 for the fentanyl group and from 3.4 to 3.9 for the buprenorphine group). Patients in the fentanyl group expressed markedly higher scores at every time point in the postoperative period (P values from 0.001 to 0.003, table III). There were no differences between the two groups in nausea scores, although two patients in the buprenorphine group vomited (table III).
TABLE III. The postanaesthetic recovery of the patients measured with both objective methods (CFF, ΔCFF, Maddox wing, postanaesthetic recovery score (PARS)) and subjective methods (visual analogue scale (VAS) for sedation, pain and nausea).
  \[\text{Mann-Whitney } U \text{ test, mean±SD}\]

<table>
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<tr>
<th></th>
<th>Before anaesth.</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
</tr>
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<td><strong>CFF (Hz)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Fentanyl</td>
<td>30.2±2</td>
<td>24.4±3.2</td>
<td>25.1±2.8</td>
<td>26.1±2.9</td>
<td>26.4±3.1</td>
<td>27.3±3.1</td>
<td>27.6±2.9</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>32.0±2.6</td>
<td>25.7±3</td>
<td>26.6±3.4</td>
<td>26.9±3.5</td>
<td>26.9±3.2</td>
<td>27.1±2.9</td>
<td>28.5±3.1</td>
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<tr>
<td>(P = 0.02)</td>
<td>ns</td>
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<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td><strong>CFF relat. (Δ Hz)</strong></td>
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<tr>
<td>Fentanyl</td>
<td>0</td>
<td>5.8±2.6</td>
<td>5.1±2.4</td>
<td>4.1±2.4</td>
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<td>2.6±2</td>
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<td>5.8±3.4</td>
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<td><strong>Maddox wing (d)</strong></td>
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<tr>
<td>Fentanyl</td>
<td>1.7±2.4</td>
<td>16.4±4.7</td>
<td>13.3±5.1</td>
<td>10.9±4.3</td>
<td>9.1±5.3</td>
<td>7.1±4.7</td>
<td>4.9±4.1</td>
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<td>Buprenorphine</td>
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<td>17.9±5.6</td>
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<td><strong>PARS (points)</strong></td>
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<td>Fentanyl</td>
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<tr>
<td>Buprenorphine</td>
<td>10±0</td>
<td>8.3±1.0</td>
<td>8.9±1.0</td>
<td>9.3±0.9</td>
<td>9.5±0.8</td>
<td>9.7±0.6</td>
<td>9.9±0.4</td>
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<tr>
<td>(P = 0.001)</td>
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<tr>
<td><strong>VAS (cm)</strong></td>
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<tr>
<td>Sedation</td>
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<td>7.7±2</td>
<td>6.2±2</td>
<td>5.3±1.8</td>
<td>4.5±2.3</td>
<td>3.9±2.2</td>
<td>4.2±1.8</td>
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<tr>
<td>Buprenorphine</td>
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<td>7.7±1.8</td>
<td>6.8±1.9</td>
<td>6.1±1.9</td>
<td>5.9±1.6</td>
<td>5.4±1.9</td>
<td>5.0±1.3</td>
</tr>
<tr>
<td>(P = 0.02)</td>
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<td>ns</td>
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</tr>
<tr>
<td>Pain</td>
<td>0.4±0.7</td>
<td>7.1±2.3</td>
<td>6.9±1.9</td>
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<td>(P = 0.0001)</td>
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<td>P = 0.0001</td>
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<tr>
<td>Nausea</td>
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<td>1.2±1.6</td>
<td>1.1±1.5</td>
<td>0.7±1.3</td>
<td>0.5±0.9</td>
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<tr>
<td>Buprenorphine</td>
<td>0±0</td>
<td>1.2±3.2</td>
<td>0.5±1.5</td>
<td>1.3±2.9</td>
<td>0.4±1.5</td>
<td>1.3±1.3</td>
<td>0.7±1.5</td>
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<tr>
<td>(P = 0.02)</td>
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**DISCUSSION**

The measurement of the balance of the extraocular muscles with a Maddox wing apparatus has been shown to be a very sensitive indicator of the rate of recovery from general anaesthesia (Hannington-Kiff, 1970a), and in differentiating between the changes associated with i.v. or inhalation agents (Hannington-Kiff, 1970b). However, in the assessment of changes in CNS arousal produced by a variety of psychotropic (Smith and Misiaik, 1976; Hindmarch, 1980) and anaesthetic (Hovorka, Lehtinen and Kalli, 1983) agents, the critical flicker fusion threshold test has been used more widely. Currently, the visual analogue scale is, apparently, the most widely used method with which to rate different subjective sensations of psychoactive agents (Bond and Lader, 1974; Maxwell, 1978; Hindmarch, 1980) with good reproducibility (Revill et al., 1976) especially if numerical scales are used (Downie et al., 1978; Kremer, Atkinson and Ignelzi, 1981). In the present study we compared the usefulness of these three simple devices with that of the postanaesthetic recovery score (Aldrete and Kroulik, 1970) in evaluating the difference in the rate of recovery after the technique of general anaesthesia described above.

We found the Maddox wing apparatus and the visual analogue scale to be the most sensitive tests. Their usefulness became most evident in the late recovery states, once patients had achieved normal postanaesthetic recovery scores. The latter method, and the critical flicker fusion threshold method, appeared to be too insensitive in differentiating between the residual effects of the analgesics used during the anaesthetic.

Apparently, the residual extraocular muscle imbalance after anaesthesia is not only the result of the use of neuromuscular blocking agents, but...
is also influenced by peroperative analgesics. In the fentanyl group the divergence of the eyes decreased significantly more rapidly, but neither group had attained the preanaesthetic reference value by 2 h after operation. The critical flicker fusion threshold test showed poor sensitivity in distinguishing between the residual effects of the two opioids. A wide inter-individual variation persisted throughout the whole study period and, even when these values were expressed as individual relative changes, no differences were found between the two patient groups, with the exception of slightly higher values for buprenorphine 90 min after anaesthesia. Thus, this method seems to be almost as insensitive as the postanaesthetic recovery score in determining the residual effects of opioids administered during anaesthesia. Improving the accuracy of CFF-measurement by fixing the pupil size with special eye-glasses might be helpful, but this is impossible in the recovery room environment.

Visual analogue scales proved to be valid in evaluating the subjective sensations of pain, sedation and nausea. Pain scales were significantly greater in the fentanyl group during the 2-h study period in the recovery room, which confirms the previously known durations of action of these two analgesics (Kay, 1980). In addition to this, the administration i.m. of buprenorphine to six patients in the fentanyl group should be taken into consideration. As expected, buprenorphine caused more postoperative sedation than fentanyl (Heel et al., 1979; Sjövall, 1983).

The insignificantly greater mean values of heart rate and mean arterial pressure during and after anaesthesia in patients receiving fentanyl are apparently attributable to the shorter analgesic action of this agent.

Surprisingly, nausea and vomiting occurred infrequently in both groups, and were not associated with the longer duration of action of buprenorphine.

The requirement for additional neuromuscular blocker during anaesthesia was decreased in the patients receiving buprenorphine. This finding confirms the previous studies with this long-acting analgesic (Sjövall, 1983).

In conclusion, the Maddox wing apparatus appears to be a useful clinical test with which to evaluate the residual postanaesthetic effects of opioids. It is much more sensitive than the traditionally used postanaesthetic recovery score and the less-used critical flicker fusion threshold method. However, the simplest device, the visual analogue scale, proved to be sensitive as well.

REFERENCES


