SEDATION DURING SPINAL ANAESTHESIA: COMPARISON OF PROPOFOL AND MIDAZOLAM

E. WILSON, A. DAVID, N. MACKENZIE AND I. S. GRANT

SUMMARY

Propofol and midazolam were compared in 40 patients undergoing orthopaedic surgery under spinal anaesthesia. An infusion of either 1% propofol or 0.1% midazolam was given at a rate adjusted to maintain a similar level of sedation. The mean time to reach this required level was similar in both groups. Quality and ease of control of sedation were good in all patients. A mean infusion rate of 3.63 mg kg⁻¹ h⁻¹ was required for propofol and 0.26 mg kg⁻¹ h⁻¹ for midazolam. Immediate recovery, as judged by ability to open eyes and recall date of birth, was significantly more rapid following propofol (P < 0.0001). Similarly, restoration of higher mental function was significantly faster following propofol, measured by choice reaction time and critical flicker fusion threshold. Amnesia for the immediate postoperative period was significantly greater after midazolam (P = 0.0001).

KEY WORDS

Previous work has shown that propofol is a good agent for use by infusion to provide sedation as an adjunct to regional anaesthesia [1]. It is metabolized rapidly, with little evidence of cumulation and recovery is rapid, with minimal side effects.

This study was designed to compare infusions of propofol and midazolam in the provision of sedation for spinal anaesthesia.

PATIENTS AND METHODS

We studied 40 patients of ASA grade I or II, aged at least 16 yr, scheduled for orthopaedic surgery under spinal anaesthesia. Patients were assigned randomly to receive i.v. sedation by a continuous infusion of 1% propofol or 0.1% midazolam.

Informed consent was obtained from each patient and the study was approved by the Hospital Ethics Committee.

Before operation each patient was instructed in the use of the Leeds Psychomotor Tester. This apparatus allows measurement of Critical Flicker Fusion Threshold (CFFT) and Choice Reaction Time (CRT). These assessments give accurate and reproducible information on the effects of psychoactive drugs on normal central nervous system function [2, 3].

For CRT measurement, the subject scans an array of six small lights which are randomly illuminated. As soon as the subject detects the light he extinguishes it by touching the appropriate button. The latency of this response provides an assessment of the integrity of sensory-motor function. The CFFT is an index of CNS arousal and of the subject's ability to integrate discrete units of sensory data. For determination of CFFT, four light-emitting diodes are arranged 1 m from the subject's eyes. The frequency of flicker is increased from 10 Hz to 50 Hz and decreased in a similar fashion, the point at which the subject detects either flicker or fusion being recorded.

Each patient was made familiar with the apparatus and then had 50 practice attempts with the CRT component before preoperative baseline CFFT and CRT scores were recorded. These practice attempts are recommended by the de-
signers to preclude possible learning effects from interfering with the assessments. The CRT was taken as a mean of 25 response times following five practice attempts at each assessment and the CFFT as a mean of six results, three each on the ascending and descending frequency scales. For every subject, care was taken to ensure correct positioning of the apparatus and a constant level of ambient lighting.

All patients were premedicated with temazepam 10–20 mg orally, according to bodyweight and age, 1–2 h before the procedure. On arrival of the patient in the anaesthetic room, baseline heart rate and arterial pressure were recorded and an i.v. infusion of Hartmann’s solution was commenced via a peripheral vein in the dorsum of the hand. An infusion of 1% propofol or 0.1% midazolam was started via syringe pump into the i.v. cannula. Spinal anaesthesia was produced by an intrathecal injection of plain 0.75% bupivacaine 2.5–3.0 ml via a 25-gauge spinal needle.

As in a previous open study, the propofol infusion was commenced at 6 mg kg\(^{-1}\) h\(^{-1}\) and reduced to 4 mg kg\(^{-1}\) h\(^{-1}\) after 10 min. The midazolam infusion was started at 0.5 mg kg\(^{-1}\) h\(^{-1}\) and reduced to approximately 0.2 mg kg\(^{-1}\) h\(^{-1}\) when the patient began to feel drowsy. Thereafter, the infusion rates were adjusted to maintain an appropriate level of sedation (level 4) on a five-point sedation scale (table I).

The times to reach each level of sedation were noted. Conscious level, heart rate and arterial pressure were noted at 5-min intervals for the first 30 min and at 10-min intervals thereafter. All patients breathed oxygen 4 litre min\(^{-1}\) through a Hudson mask and no other anaesthetic or analgesic drugs were given. I.v. fluids were given as Hartmann’s solution or blood as indicated clinically. The sedative infusion was discontinued 10 min before the anticipated end of the procedure.

The overall quality and ease of control of sedation were graded by the anaesthetist. The presence of any side effects was noted, particularly in relation to respiratory or airway problems and to excitatory phenomena.

The times taken from the end of the infusion for the patients to open their eyes on command and to give their correct date of birth were noted. All these assessments were carried out in theatre by the anaesthetist, who obviously could not be blinded to the drugs being administered. However, recovery was assessed further by psychometric testing performed at 30, 60, 90, 120, 180 and 240 min after the end of the infusion by an independent investigator who was unaware of the sedative agent used. Patients whose spinal anaesthesia had worn off and who had received further analgesia were excluded from subsequent assessments. The patients were questioned at 4 h for perioperative recall. This included arrival in the anaesthetic room, the lumbar puncture, intraoperative awareness and of being shown two simple pictures 10 and 20 min after awakening. The presence of any postoperative side effects was noted.

The results were analysed statistically using Student’s t test and Chi-square tests where appropriate.

**RESULTS**

There were no significant differences between the groups with respect to patient age, weight or sex (table II).

The mean duration of the procedure was similar in the propofol and midazolam groups: 77 and 72 min, respectively. The mean duration of infusion was also comparable in each group: 106 min for propofol and 93 min for midazolam. In both groups the mean time to reach the required level of sedation was approximately 24 min. There were no significant differences between the groups in the intervals from the start of the infusion to injection of the spinal anaesthetic and to skin incision. The overall mean infusion rate was 3.6 mg kg\(^{-1}\) h\(^{-1}\) for propofol (range 2.4–4.5) and 0.26 mg kg\(^{-1}\) h\(^{-1}\) for midazolam (range 0.14–0.43). The steady state infusion rates were 2.84 mg kg\(^{-1}\) h\(^{-1}\) for propofol and 0.15 mg kg\(^{-1}\) h\(^{-1}\) for midazolam.

Quality and ease of control of sedation were good in both groups. Airway maintenance was excellent in all patients, with no evidence of coughing, laryngospasm, ventilatory obstruction or apnoea. The frequency of side effects during
the infusion was low in both groups. One patient in each group had restlessness of the arms which required no action. Two other patients in the propofol group had complaints related to the infusion, one of coldness in the arm and the other of a slight burning pain in the arm. These settled within 5 min of the infusion commencing.

There was a slight decrease in heart rate in both groups, of approximately 5 beat min$^{-1}$ during the first 1 h of the infusion. There were no significant differences between the agents with respect to systolic and diastolic pressures, there being a slight reduction in both variables of the order of 15% over the first 1 h (fig. 1).

The mean interval from the end of the infusion until patients opened the eyes and gave the correct date of birth was significantly shorter with propofol than with midazolam: 2 and 10 min, respectively (table III). The frequency of side effects in the postoperative period was low, with only one case of nausea or vomiting in each group. In both cases this occurred when the spinal anaesthesia had worn off. Patient recall of the perioperative period was also noted. Most patients remembered arrival in the anaesthetic room (19 propofol, 17 midazolam). Twelve of the propofol group remembered injection of the spinal anaesthetic, compared with nine in the midazolam group. Two patients in each group had some intraoperative awareness consisting of background theatre noise, but none found this distressing. Postoperative amnesia was significantly greater after midazolam. No patient had recall of pictures shown to them 10 and 20 min after awakening, compared with 12 and 13 patients, respectively in the propofol group.

All patients in the propofol group were satisfied with their anaesthetic and would choose the same technique again. Two patients in the midazolam group would prefer an alternative technique in the future, one because of postoperative nausea and vomiting.

Six patients who received midazolam were too sedated 30 min after operation to co-operate with psychometric testing, and in four this persisted.

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**Table II. Patient and infusion data (mean (SEM))**

<table>
<thead>
<tr>
<th></th>
<th>Propofol ($n = 20$)</th>
<th>Midazolam ($n = 20$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>57.2 (4.18)</td>
<td>51.1 (4.48)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.4 (2.94)</td>
<td>68.1 (3.03)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/11</td>
<td>7/13</td>
</tr>
<tr>
<td>Duration of procedure (min)</td>
<td>76.5 (7.71)</td>
<td>72.4 (8.26)</td>
</tr>
<tr>
<td>Duration of infusion (min)</td>
<td>106.0 (9.22)</td>
<td>93.4 (8.46)</td>
</tr>
<tr>
<td>Start infusion to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal (min)</td>
<td>7.8 (0.73)</td>
<td>7.4 (0.56)</td>
</tr>
<tr>
<td>Incision (min)</td>
<td>37.0 (2.77)</td>
<td>30.1 (1.35)</td>
</tr>
<tr>
<td>Level 4 sedation (min)</td>
<td>23.7 (2.22)</td>
<td>24.8 (2.54)</td>
</tr>
<tr>
<td>Infusion rate (mg kg$^{-1}$ h$^{-1}$)</td>
<td>3.63 (0.151)</td>
<td>0.26 (0.023)</td>
</tr>
<tr>
<td>Steady state infusion (mg kg$^{-1}$ h$^{-1}$)</td>
<td>2.84 (0.216)</td>
<td>0.15 (0.020)</td>
</tr>
</tbody>
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**Fig. 1.** Mean (SEM) heart rate, systolic and diastolic pressures during infusion of sedative. • = Midazolam; ▲ = propofol.
for 1 h. In contrast, all patients in the propofol group were able to co-operate fully with testing. Some slight impairment of CRT at 30 min was seen following propofol, reverting to normal by 1 h. With midazolam, however, significant impairment of CRT persisted for 3 h (fig. 2). With respect to the more sensitive CFFT, significant impairment was seen for 90 min with propofol and 2 h with midazolam (fig. 3).

**DISCUSSION**

We have shown that both propofol and midazolam by infusion produced excellent and easily controllable sedation as an adjunct to spinal block. Onset of sedation was smooth and depth was controlled easily. The frequency of side effects was low in both groups, both during operation and in the recovery period. However, recovery, as judged by immediate return of consciousness and orientation and by performance in psychometric testing, was significantly faster with propofol. Early postoperative amnesia was significantly greater with midazolam.

The infusion rates selected for this study were chosen to provide a deep level of sedation with definite end-points to allow comparison of the two agents. This level guaranteed hypnosis, but patients remained rousable readily with mild physical stimulation. Lighter levels of sedation may be deemed appropriate in many instances, particularly for less invasive surgery. Even at our
chosen depth of sedation, however, two patients in each group reported some awareness during operation and there was no significant cardio-respiratory depression.

In a recent study using a similar level of sedation, Negus and White [4] found broadly equivalent drug requirements for both agents; there was rapid recovery and relative freedom from side effects following propofol.

Low dose infusion of propofol appears to avoid the cardiorespiratory depressant effects of higher doses of the agent. Indeed, a recently published animal study suggests that the ideal clinical use of propofol may be to supplement regional anaesthesia, rather than as a component of general anaesthesia [5].

Another attractive feature of propofol is the ease of conversion from sedation to general anaesthesia, should the surgery extend outwith the analgesic field of the regional block, simply by increasing the rate of infusion [1] and supplementing with an appropriate analgesic such as nitrous oxide or alfentanil.

This study shows that both propofol and midazolam by i.v. infusion provide highly satisfactory sedation as an adjunct to spinal anaesthesia. Recovery is significantly faster following propofol, with regard to both return of consciousness and restoration of higher mental function. This may be of significant benefit in certain patients, for example those with pulmonary disease to allow early co-operation with chest physiotherapy or in diabetes where early return to normal diet is desirable.

ACKNOWLEDGEMENT
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REFERENCES