SEDATION AFTER CARDIAC BYPASS SURGERY: COMPARISON OF PROPOFOL AND MIDAZOLAM IN THE PRESENCE OF A COMPUTERIZED CLOSED LOOP ARTERIAL PRESSURE CONTROLLER

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SUMMARY
Forty patients who had undergone coronary artery graft surgery and who required vasodilator therapy for postoperative hypertension were given infusions of either propofol (2,6,di-isopropylphenol) or midazolam, together with an infusion of morphine for analgesia while ventilation was controlled artificially. Sodium nitroprusside was administered to patients in both groups using a computer-controlled closed loop system. Both agents produced good quality of sedation. Overall times to spontaneous ventilation and tracheal extubation were shorter in the propofol group, but this was not statistically significant. Ease of control of arterial pressure was satisfactory clinically with both agents, although propofol appeared to be associated with a statistically greater incidence of hypotension.

KEY WORDS

The ease of control of arterial pressure using vasodilators can be a useful method of assessing adequacy of sedation. An unbiased assessment of the quality of control is possible using a computer-controlled closed loop system such as that developed in our department [1].

The objectives of the present study were to compare the sedative and cardiovascular effects of propofol (2,6,di-isopropylphenol) and midazolam in patients who required vasodilators for control of arterial hypertension after coronary artery surgery.

METHODS AND RESULTS
The study was approved by the Hospital Ethics Committee and written informed consent obtained from 40 patients of ASA grade III and between the ages of 30 and 70 yr. Exclusion criteria included a weight less than 40 kg or greater than 100 kg, severe respiratory, renal and hepatic disease, or blood loss of more than 1 litre after operation.

All patients received continuous ECG, core temperature and central venous pressure monitoring, and arterial pressure was measured directly via the radial artery. Sodium nitroprusside (SNP) was administered by the computer-controlled closed loop system. When the patients were able to move all four limbs to command, they were allocated randomly to two groups: group 1 received a bolus of propofol 10-40 mg followed by a continuous infusion of 1% propofol 0.5-2.0 mg kg⁻¹ h⁻¹; group 2 received a bolus of midazolam 1-4 mg followed by a continuous infusion of midazolam 0.1-0.2 mg kg⁻¹ h⁻¹. All patients received a bolus of morphine 2 mg followed by an infusion of 2 mg h⁻¹.

A six point scoring system was used to assess the level of sedation every 30 min for 3 h and hourly thereafter until sedation was discontinued or for a maximum total of 8 h: 1 = sedated, no response; 2 = responds only to painful stimuli; 3 = responds to verbal commands, but cannot indicate awareness of the surroundings; 4 = rouseable, comfortable and responds to commands; 5 = moderately agitated; 6 = distressed and very restless. The infusion rates were adjusted and additional bolus doses of sedative or morphine administered by the nursing staff, to maintain the optimal level of sedation (score 4)—that at which the patient was rouseable, responded to verbal commands and was comfortable. The same group of nurses assessed the patients in both groups.

When the patient had a stable cardiovascular system, the infusions were discontinued and times to recovery of spontaneous ventilation and extubation of the trachea recorded.

Percentage time spent outside the target pressure ±10, 20 and 30 mm Hg, during sedation and for 30 min before the study commenced, peak SNP requirements, total dose administered and duration of the SNP infusion were noted.

Data from the two groups were compared using the unpaired t test and the Mann-Whitney U test as appropriate. \( P < 0.05 \) was considered statistically significant.

There were no significant differences in patient characteristics. Anaesthetic regimens were not stan-
Propofol
Midazolam

Fig. 1. Percentage of total time spent at each sedation level. Significant difference between levels 1+2 and 3+4: *P < 0.05.

dardized, but differences between the two groups were not significant, apart from a four-fold greater amount of fentanyl administered in the midazolam group (P < 0.05). There were no significant differences between the two groups in the duration of the sedative infusions, the number of alterations in infusion rate, or additional bolus doses of sedative or morphine administered. There were no significant differences between the two groups in the percentage of time spent at each sedation level (fig. 1). Overall times to spontaneous ventilation and tracheal extubation were shorter in the propofol group, but not significantly so.

There were no significant differences in cardiovascular stability between the two groups before the study commenced. During the study there were no significant differences between the groups for time spent with arterial pressure greater than target. Patients who received propofol spent significantly more time with arterial pressure less than target minus 10 mm Hg (median 26 %) and minus 20 mm Hg (median 3.3 %) compared with those who received midazolam (medians 20.1 % and 1.7 %, respectively). The median total and peak requirement for SNP and the duration of SNP infusion were less for patients in the propofol group, but the differences were not significant.

COMMENT

Both propofol and midazolam produced good quality sedation. The infusion rate of midazolam was that which was used routinely in our intensive care unit for sedation after coronary artery bypass surgery. Equipotent doses for propofol and midazolam have not been defined clearly, but other intensive care units have used propofol infusions with a mean dose in the range 0.79–3 mg kg\(^{-1}\) h\(^{-1}\) [2–5]. A smaller dose was chosen in our study to take into account residual sedation from the opioid-based anaesthetic. A greater amount of fentanyl was received during operation by the midazolam group, but a possible influence on the pharmacokinetics of propofol by fentanyl has not been confirmed by recent work [6] and, after operation, there were no significant differences in ease of control of sedation between the two groups. Times to spontaneous ventilation and tracheal extubation were shorter in the propofol group, but this did not reach statistical significance.

The ease of control of arterial pressure was satisfactory clinically with both sedatives, although propofol used in this manner has a greater tendency to produce hypotension. It is possible that propofol produces less stable conditions than midazolam which the closed loop system fails to modify. However, clinically, the difference between the two groups was not obvious. The attenuation of hypertensive responses to noxious or other stimuli by the sedative infusions would confirm the clinical measurements of the good quality of sedation which was achieved.

REFERENCES