No effect of cardiopulmonary bypass on hypnosis in patients anaesthetized with propofol and alfentanil

J. Ahonen1*, A. Sahlman2, A. Yli-Hankala3, H. Eriksson1, A. Nemlander2, J. Rämo2 and M. Salmenperä1

Departments of 1Anaesthesia and Intensive Care Medicine, and 2Thoracic and Cardiovascular Surgery, Helsinki University Hospital, Helsinki, Finland. 3Department of Anaesthesiology, Medical School, University of Tampere, and Department of Anaesthesia, Tampere University Hospital, Tampere, Finland

*Corresponding author. E-mail: jouni.ahonen@fimnet.fi

Background. The effect of cardiopulmonary bypass (CPB) on the level of anaesthetic depth has not been studied previously in a randomized way.

Methods. We assessed the effect of CPB on the propofol needed to maintain a fixed bispectral index score, and on the recovery from anaesthesia in 22 patients undergoing coronary artery bypass graft surgery with CPB (on-pump) compared with 18 patients operated on without CPB (off-pump). Anaesthesia was induced and maintained with propofol and alfentanil. Throughout the procedure, the infusion rate of propofol was adjusted to keep the BIS value at 40 ± 5.

Results. With the off-pump technique, the duration of surgery and anaesthetic administration were significantly greater. The need for propofol in proportion to time was exactly the same in both groups. During anaesthesia and the first 3 h thereafter, the BIS recordings were similar in both groups. No differences were detected in the time to awakening or tracheal extubation.

Conclusions. CPB does not affect propofol requirements or immediate postoperative recovery compared with the off-pump technique.

Br J Anaesth 2004; 92: 137–9

Keywords: anaesthetics i.v., propofol; analgesics opioid, alfentanil; heart, cardiopulmonary bypass; hypnosis; monitoring, bispectral index

Accepted for publication: August 7, 2003

In coronary artery bypass graft (CABG) surgery, cardiac stabilizing devices have made the avoidance of cardiopulmonary bypass (CPB) a realistic alternative. Accordingly, about 20% of all CABG operations are currently performed off-pump.1 Early postoperative recovery2 including the time to extubation2,5 is better in off-pump patients than in patients undergoing conventional CABG with CPB (on-pump).

The effect of CPB on the level of anaesthetic depth has not been studied previously in a randomized way. Therefore, we decided to measure propofol requirements during surgery and immediate postoperative recovery in patients undergoing on-pump surgery compared with those operated on using an off-pump technique. Our hypothesis was that the effect of CPB on cerebral circulation and brain water content4,5 would impair cortical neuronal integrity resulting in reduced propofol requirements and prolonged patient recovery when compared with off-pump surgery.

Methods and results

According to our previous study,6 18 patients per group would be needed to show a 20% difference in propofol consumption at a level of significance where \( P < 0.05 \) with a power of 80%. After institutional approval and informed consent, 40 patients were assigned randomly to either an on-pump or an off-pump group. Exclusion criteria were: left ventricular ejection fraction <40%; significant valvular dysfunction; renal or liver insufficiency; treatment with any known inhibitor or inducer of cytochrome P450IIIA enzymes;7 or body mass index >35.

© The Board of Management and Trustees of the British Journal of Anaesthesia 2004
After premedication with lorazepam 40 μg kg⁻¹, anaesthesia was induced and maintained with propofol and alfentanil. After induction doses of propofol 1.0–1.5 mg kg⁻¹ and alfentanil 50 μg kg⁻¹, the infusion rate of propofol was adjusted to keep the BIS (A-2000, Aspect Medical System, Natick, MA, USA) value at 40±5. Before skin incision, a second bolus dose of alfentanil 50 μg kg⁻¹ was given followed by an infusion of 1.5 μg kg⁻¹ min⁻¹ for 30 min and thereafter 1.0 μg kg⁻¹ min⁻¹ until the beginning of sternal closure. Blood pressure was adjusted with bolus doses of nitroglycerin, ephedrine, or norepinephrine. Rocuronium was given for neuromuscular block. The lungs were ventilated with a mixture of oxygen 50% in air.

In CPB patients, the pump flow was set at 2.4 litre min⁻¹ m⁻² and the perfusion pressure between 50 and 80 mm Hg. A cold crystalloid cardioplegic solution was used. In both groups the surgical procedures were performed under moderate hypothermia (core temperature 35-37°C) and a forced-air warmer was used during and after the operation. Postoperative sedation was provided by propofol 25 μg kg⁻¹ min⁻¹ for 2 h. If rewarming was inadequate, the sedation was prolonged. Awakening was defined as the return of appropriate responses to the command ‘move your right and left arm and your legs’ and to the question ‘do you feel any pain?’. Ketorolac 30 mg i.v. was administered 1, 7 and 15 h after the operation. After awakening, additional analgesia was provided by i.v. bolus doses of morphine 0.05 mg kg⁻¹. Mechanical ventilation was stopped when the patient was awake and calm. We used the same weaning procedure and extubation criteria as in our previous studies with CABG patients. The morning after surgery, the patients were asked if they recalled any awareness during the anaesthetic.

The total dose of propofol was recorded. To assess exactly the effect of CPB we also determined the amount of propofol given from the time of heparinization to the end of the anaesthesia. We also calculated propofol requirements in proportion to time. To compare the BIS values and the core temperature between the groups, we determined the area under the BIS value/core temperature–time curve (AUC) using the trapezoidal rule. BIS values and the core temperature were compared during the anaesthetic as well as during the recovery phase. BIS values were recorded at intervals of 5 min, each value representing the median for 30 s. Core temperature (nasopharyngeal temperature during the anaesthetic and the tip of the pulmonary artery catheter thereafter) was recorded at 30 min intervals, starting 30 min after the induction of anaesthesia.

Results are expressed as mean (SD). Patient characteristics were compared using the χ²-test or Student’s t-test. Other variables were compared using the two samples, two-tailed Student’s t-test assuming unequal variances.

Patient characteristics in the 22 on-pump and the 18 off-pump patients did not differ (Table 1). After tracheal extubation, one off-pump patient was returned for re-
operation because of haemodynamic collapse; no graft complications were detected and an intra-aortic balloon pump was inserted allowing uneventful recovery. An additional off-pump patient had a repeat sternotomy after awakening but before tracheal extubation, because of bleeding. This patient was excluded from the analysis of the time to tracheal extubation.

During the anaesthetic, BIS recordings were similar in both groups. Because of the off-pump technique, the length of surgery and thus the length of the anaesthetic were significantly longer in off-pump patients. Total doses of propofol did not differ between the groups and the need for propofol in proportion to time was exactly the same in both groups. The dose of lorazepam or that of alfentanil did not differ between the groups. After the end of the anaesthetic, BIS recordings did not differ between the groups. Core temperature was less in off-pump patients during the recovery phase, so the duration of sedation was longer (not significantly) in these patients. No differences were detected in the time to awakening or tracheal extubation, nor in the need for postoperative morphine (Table 1). None of the patients reported awareness during the anaesthetic.

**Comment**

We found no effect of CPB on propofol requirements or on immediate postoperative recovery in our patients randomized to on-pump surgery compared with those operated on by an off-pump technique. After equal doses of lorazepam premedication and equal doses of alfentanil, the need for propofol was similar in both groups. In the light of the BIS values and the time to awakening and tracheal extubation, the immediate postoperative recovery was similar in on-pump and off-pump patients.

Propofol plasma concentration decreases at the start of CPB because of haemodilution and binding of propofol to the extracorporeal circuit.8,9 In spite of this decrease in total propofol plasma concentration, there was no decrease in the unbound propofol concentration after the start of CPB. Accordingly, the Nb-wave latencies of the auditory evoked potentials remained significantly prolonged also during and after CPB, suggesting adequate anaesthesia.9 We thus believe that changes in the pharmacokinetics of propofol during CPB did not affect our results.

In CABG patients anaesthetized with propofol and fentanyl, hypothermic CPB can cause significantly smaller BIS values compared with normothermic CPB.10 During anaesthesia and surgery before and after CPB, however, BIS values were comparable with previously published data from non-cardiac surgery. In our off-pump patients, the core temperature was less at the end of the anaesthetic and during recovery because rewarming with the CPB machine was better compared with the forced-air warmer. However, during the anaesthetic, when the propofol dose was adjusted according to the BIS recordings, the core temperature did not differ significantly between the groups. Therefore, we do not believe that the core temperature had a significant impact on our results.

The BIS index is derived from the spontaneous EEG, which is sensitive to electrical artefacts in an operating room. Recently, case reports of an interference of various medical devices on BIS recordings have been reported.11 Roller pump artefact disturbing all kinds of EEG monitoring during cardiac surgery is a well-known phenomenon. Therefore, caution is needed when EEG-derived indices are used during CPB or with other extracorporeal roller pumps. In this study, we did not detect any unexpected sudden changes or ‘freezing’ of BIS values during CPB or any other parts of the procedures.

In conclusion, we could not show an effect of CPB with crystalloid prime on perioperative hypnosis or on immediate postoperative recovery in our patients undergoing CABG with CPB compared with those operated on by off-pump technique.

**References**