Postoperative Sedation with Propofol Infusion
Haemodynamics and Pharmacokinetics

Carlo Sorbara, Gabriele Armellin, Raffaele Bonato, Lino Callegher and Giampiero Giron

Department of Anesthesiology and Intensive Care, University of Padova, School of Medicine, Padova, Italy

Abstract

Objective: This study was designed to investigate the haemodynamic response and pharmacokinetics of a low-dose propofol continuous infusion in providing sedation in patients who required mechanical ventilation after coronary artery bypass grafting surgery.

Patients: 22 male patients, aged between 45 and 65 years, were evaluated in an open, uncontrolled study.

Interventions: At the end of the surgical procedure, a low-dose (1 mg/kg/h) propofol infusion was started and adjusted to optimise sedation according to the Ramsay scale. The mean propofol infusion rate was 1.42 ± 0.4 mg/kg/h.

Main Outcome Measures: Electrocardiogram, systemic and pulmonary arterial pressure, and central venous pressure were monitored continuously. Left ventricular shortening fraction was calculated by transoesophageal echocardiography. Propofol plasma levels were calculated in 10 patients to evaluate the pharmacokinetics.

Results: Throughout the duration of the study all patients were haemodynamically stable. Sedation was maintained for 363 ± 244 minutes and was adequate in all patients. The clinical recovery time (postsedation responsiveness) was 15.7 ± 6.2 minutes, after infusion suspension. There was no correlation between propofol plasma levels or propofol infusion rate and the depth of sedation (respectively, r = 0.39 and r = 0.23), while there was a good correlation (r = 0.62) between propofol infusion rate and plasma levels. Open two-compartment model pharmacokinetics were demonstrated.

Conclusion: Low-dose propofol infusion (1 to 2 mg/kg/h) proved to be well tolerated and effective in maintaining sedation after cardiac surgery. Sedation was quickly obtained without a propofol loading dose; steady-state plasma concentrations of 0.6 to 0.8 mg/L were rapidly achieved. Propofol pharmacokinetics ensure rapid clearance with rapid clinical recovery.
Patients admitted to an intensive care unit (ICU) after cardiac surgery often require analgesia, sedation or both during the early postoperative period because they may be hypothermic, haemodynamically unstable and exposed to a number of distressing stimuli such as pain resulting from surgery, distress from the presence of a tracheal tube, mechanical ventilation, and nursing procedures such as tracheal suction, turning and changing of dressings.

Adequate treatment of these patients with sedative-hypnotic drugs can help to minimise the physiological and adrenergic responses to such stimuli, which otherwise may lead to unwanted agitation and cardiovascular instability.\textsuperscript{[1]} Propofol is an intravenous short-acting hypnotic drug with moderate anxiolytic and amnesic effects.\textsuperscript{[2]} It is characterised by a short half-life\textsuperscript{[3]} and is associated with a virtual lack of cumulative effects after incremental administration and with rapid, clear-headed recovery when the drug is administered as a continuous infusion.\textsuperscript{[4,5]}

Moreover, propofol has an apparent metabolic effect independent of its sedative effects, resulting in significant reduction in peripheral oxygen consumption and carbon dioxide production.\textsuperscript{[6,7]} These pharmacokinetic and pharmacodynamic characteristics should make this drug suitable for providing sedation after cardiac surgery. However, the hypotensive effect of this agent, even though due to a fall in systemic vascular resistance rather than to a reduction in cardiac output,\textsuperscript{[8]} has limited its usage in ischaemic patients in the past.

In the present study, we performed a clinical and pharmacokinetic trial that investigated the tolerability and effectiveness of a continuous infusion of propofol in providing sedation in patients who required mechanical ventilation after coronary artery bypass grafting (CABG) surgery.

**Patients and Methods**

**Study Participants**

After Hospital Ethics Committee approval, 22 male patients, aged between 45 and 65 years, scheduled for elective myocardial revascularisation, were selected for the trial after giving informed written consent. Demographic data of the patient population are listed in table I.

Patients with severe renal or hepatic dysfunction (noted on routine biochemical screening), a central nervous system disease, gross obesity (20% above their ideal bodyweight) and with known allergy to propofol were excluded. Patients with severe left ventricular (LV) dysfunction (ejection fraction <40%), based on preoperative angiographic assessment, or patients who had undergone previous heart procedures, were also excluded from the study.

**Methods**

All patients received their normal cardiac medications up to the day of surgery and received oral premedication with flunitrazepam 2mg approximately 1 hour before induction. Induction of anaesthesia included the administration of fentanyl 0.01 mg/kg and thiopental 1 mg/kg.

Anaesthesia was maintained with multiple bolus doses of fentanyl 0.005 mg/kg up to a total dose of about 0.05 to 0.06 mg/kg combined with isoflurane inhalation 0.6 to 0.8% in an oxygen/air mix (50%). During the rewarming period at the end of cardiopulmonary bypass (CPB) all patients received diazepam 0.3 mg/kg to prevent awareness and to secure amnesia.

Neuromuscular blockade was produced with vecuronium bromide and pancuronium bromide, as

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Patients enrolled (no.) & 20 \\
Age (y) & 59.5 (5.7) \\
Weight (kg) & 71.5 (8.6) \\
Height (cm) & 170.7 (7) \\
Prior myocardial infarction (%) & 75 \\
Fentanyl amount during anaesthesia (mg) & 3.27 (1.33) \\
Anaesthesia (min) & 294 (42) \\
Cardiopulmonary bypass-time (min) & 105 (29.6) \\
Aortic cross-clamp time (min) & 61.1 (21.9) \\
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\caption{Demographic and clinical characteristics of the patient population. Values are expressed as mean (SD)}
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