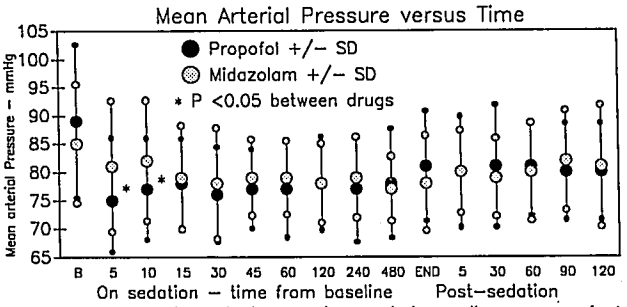
A278

Title: ICU SEDATION FOLLOWING CABG: PROPOFOL vs MIDAZOLAM

Authors: TL Higgins MD, JP Yared MD, FG Estafanous MD, JP Coyle MD, F Vassel; RN, DB Goodale DDS PhD*

Affiliations: Dept of Cardiothoracic Anesthesia, Cleveland Clinic Foundation, Cleveland OH, and *ICI Pharmaceuticals Group, Wilmington, DE.

Introduction: Propofol (Diprivan, 2,6-diisopropylphenol), a short-acting IV hypnotic agent was compared with midazolam for sedation of ventilated patients following coronary artery bypass grafting (CABG).
Methods: After IRB approval and informed consent, ASA 3-4 elective CABG pts aged 40-78 were randomized to receive propofol ≤ 0.5 mg/kg IV bolus plus continuous infusion of 1-4 mg/kg/hr; or midazolam ≤ 0.3 mg/kg IV bolus plus infusion of 0.01-0.04 mg/kg/hr. Infusion rates were titrated by the ICU nurse to keep pts comfortable, drowsy, and responsive to verbal stimulation. Study began postoperatively when pts could open eyes to command; infusion duration averaged 10 hrs. Supplemental prn opioids were given IV. Analysis is based on 42 propofol (P) and 38 midazolam (M) pts including six (4 P, 2 M) in whom drug was discontinued for hypotension or events not necessarily related to the study (ie: return to OR for bleeding; low cardiac output). Continuous variables were evaluated using Wilcoxon rank-sum tests; discrete variables by chi-square, and changes from baseline by ANOVA, with $p<0.05$ considered significant.
Results: Mean age was 63.2 yrs (P) and 59.9 years (M), with matched gender, medical history and CPB time. Mean loading doses for P and M were 0.24 and 0.012 mg/kg respectively; mean maintenance doses 0.76 and 0.017 mg/kg/hr respectively. Total dose per patient varied markedly (P: 21-1932 mg; mean 583 mg, and M: 1-26 mg; mean 12.3 mg). Four M pts and one P pt required repeat bolus for insufficient initial sedation. Mean arterial pressure dropped significantly in P patients after bolus (figure); but no other hemodynamic changes were significant, including SVR, CVP, cardiac index or ECG ST-segment changes during up to 12 hrs of infusion. Only 2 P pts and 3 M pts required vasopressors. Lower total doses of sodium nitroprusside were used in the P group ($p<0.05$). Supplemental opioids were required by 40% of P and 60% of M pts ($p<0.05$). 38% of the P and 34% of the M group were extubated within 2 hrs of stopping infusion.



Discussion: Titration of short acting sedatives allows convenient control of anxiety and agitation during mechanical ventilation. Either P or M can be safely infused with minimal hemodynamic effects in ASA III and IV ventilated pts recovering from high-dose opioid anesthesia for CABG, although a wide dosage range was observed, consistent with residual opioid effects. P pts demonstrated lower opioid and vasodilator requirements, suggesting better sedation at doses used. Transient initial hypotension occurs with P at 0.25 mg/kg, is easily treated with positioning or volume loading, and avoided by using a lower bolus dose (<0.2 mg/kg). Reported negative inotropic effects of P (2) were not evident at the low dose used in this study. Extubation times after discontinuing either P or M may reflect residual operative opioids rather than kinetics of study agents.

References: (1) Seminars in Anesth 7:4, 1988
(2) Anesthesiology 71:260, 1989

A279

APPROPRIATE THERMAL MANIPULATIONS ELIMINATE POST-ANESTHETIC TREMORS IN RATS. D. A. Grahn, PhD., M. C. Heller, and H. C. Heller, PhD. Department of Biological Sciences, Stanford University, Stanford, Ca. 94305

Post-anesthetic tremors, characterized by shivering-like electromyograph (EMG) activity and increased metabolic rate, are common during recovery from surgery. In addition to increasing the acute risks to the patient, these tremors can disrupt wound healing and may increase the recovery time. These tremors may be thermogenic responses to anesthesia induced hypothermia. If so, they should be eliminated by appropriate thermal manipulation. However, if the tremors are nonthermogenic, the thermal condition of the subject should have no effect on the tremors. The hypothesis tested was: Can Post-anesthetic tremor be abolished by appropriate thermal manipulation?

Six Wistar rats, equipped with electroencephlogram (EEG) electrodes, neck muscle EMG electrodes, and a thermocouple reentrant tube to measure brain temperature (T_b), were subjected to 1 hour of halothane anesthesia under various thermal regimes. While anesthetized, the animal's T_b was either: 1) allowed to drop (the animal was placed on a metal plate in a 23°C room), 2) maintained between 37 and 38°C (the animal was wrapped in a controlled temperature water perfusion blanket), or 3) allowed to drop for the first hour and then warmed to 37-38°C. A slow wave sleep (SWS) like EEG pattern and complete suppression of EMG activity were maintained throughout the anesthesia period. During recovery from anesthesia the animals were placed in a 23°C chamber. EEG and EMG activity, T_b, and O_2 consumption were monitored throughout the recovery period.

If external heat was not applied during anesthesia, T_b dropped from 37-38°C to 30-31°C. These hypothermic animals exhibited robust post-anesthetic tremors which persisted until T_b returned to normothermic (up to 80 min). During this time O_2 consumption was elevated, EMG was spastic, EEG was characteristic of wakefulness, and the animals displayed no coordinated movements. When T_b reached normothermia the tremors subsided, O_2 consumption decreased, coordinated movement was initiated and the animal began cycling through normal sleep patterns.

In contrast, the animals which were maintained at normothermia or rewarmed prior to release from anesthesia displayed no tremor responses. When warm, coordinated behaviors were initiated within 5-10 min post anesthesia and SWS was observed within 10 min post anesthesia. Although there were temporal variations in the response patterns, these findings were consistent for all animals tested. We conclude that post-anesthetic tremor is a thermogenic response which can be eliminated by proper thermal manipulation prior to the recovery from anesthesia. This research was supported by a grant from the Upjohn Co.