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Title: CAN PREOPERATIVE ORAL CLONIDINE REDUCE ANESTHETIC REQUIREMENT FOR CABG SURGERY?
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Introduction: Clonidine (C) has been utilized to reduce anesthetic requirement and decrease intra and postop hypertension in a variety of surgical settings. We are conducting a placebo controlled, double-blinded, randomized trial of C premedication in patients undergoing CABG in order to assess its effect on the induction, maintenance, and total amount of sufentanil required for anesthesia.

Methods: Institutional Human Subjects Review Committee approval was obtained to study relatively good risk patients. After informed consent, twenty patients all undergoing elective CABG surgery were studied. Exclusionary criteria were: high-grade left main coronary artery stenosis, congestive heart failure with LVEF <40%, use of C, alpha-methyl-dopa, or guanibenz within the past week, AV block greater than first degree, renal or hepatic failure, any gastrointestinal disturbance which would hinder enteric absorption of oral medication. Ninety minutes prior to induction, all patients received 40 mcg/kg lorazepam orally, and randomly received C 5 mcg/kg or a placebo (P) by staff not involved in the anesthetic management of the patient. Induction of anesthesia was with an initial 50 mcg of sufentanil (S) and 5 mg of vecuronium. The S was then further titrated to loss of consciousness. A CNS EEG monitor was used to further evaluate S's effect. Muscle relaxation was enhanced with vecuronium or pancuronium as needed. A standard 0.05 mcg/kg/min infusion of S was utilized for maintenance of anesthesia. Thirty minutes prior to cardiopulmonary bypass, a second dose of C at 5 mcg/kg or P was given as a dilute slurry dissolved in 20cc normal saline via theogastric tube. An additional 20 mcg/kg of lorazepam was administered during CPB.

Results: Patient demographics were essentially comparable to an average CABG population. The total induction and intubation dose of sufentanil administered was significantly less ($p < 0.05$) for C patients resulting in half that required for the placebo patients. (Table 1) The anesthesiologists titrated sufentanil to an end point of induction satisfactory to clinical criteria and correlated with EEG and then intubated the patient. Lack of knowledge of the placebo or clonidine status of the patient was successfully maintained. The total amount of sufentanil required for CABG surgery was also significantly less, though not so dramatically as the titrated end point was less defined.

Conclusion: Alpha-2 agents have the combined effect of decreased anesthetic requirement with stable hemodynamics and early awakening (Table 2) and thus C can have useful and positive contributions in CABG surgical patients.

TABLE 1

	Placebo Mean ± SD	Clonidine Mean ± SD
Induction		
S ug/kg	4.5 ± 1.2	2.1 ± 0.8 ^a
Maintenance		
S ug/kg	6.8 ± 3.2	7.0 ± 3.3
Total		
S ug/kg	11 ± 1.5	9 ± 1.3 ^a

Note: ^a is significant $P < 0.05$ difference between study groups.

TABLE 2

	Placebo Mean ± SD	Clonidine Mean ± SD
Time to awakening	283 ± 198	102 ± 48

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TITLE: MODIFYING THE STRESS RESPONSE DURING TOTAL INTRAVENOUS ANESTHESIA
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Total intravenous anesthesia (TIVA) involves the simultaneous administration of sedative-hypnotic, opioid analgesic and muscle relaxant drugs. However, when patients manifest signs of excessive autonomic activity, it is unclear whether one should administer additional sedative or analgesic medication. We designed a randomized, prospective study to evaluate the effectiveness of two different approaches to treating acute hemodynamic responses during TIVA.

22 consenting patients undergoing radical prostatectomy procedures were randomized to one of two treatment groups according to an IRB-approved protocol. All patients were premedicated with midazolam, 2 mg iv. Anesthesia was induced with alfentanil 20 µg/kg, propofol 1.5 mg/kg, and vecuronium 0.1 mg/kg and maintained with alfentanil 0.5 µg/kg/min, propofol 50 µg/kg/min, and vecuronium 0.8 µg/kg/min. Mean arterial pressure (MAP), and heart rate were continuously monitored. Arterial blood samples were obtained 1 min before skin incision (pre-inc) and upon entry into the retroperic space (pre-R). Blood was analyzed for plasma catecholamines, vasopressin (ADH), alfentanil and propofol levels. When the patient exhibited an acute increase in MAP > 25% above the pre-inc value, either alfentanil, 10-30 µg/kg, or propofol, 0.3-1.0 mg/kg, was administered. Repeat blood samples were obtained after returning MAP to within 10% of the pre-inc value (post-R). Recovery times and therapy required in the PACU were recorded. The groups were compared using ANOVA and Chi-square tests, $p < 0.05$ was considered statistically significant (means ± S.D.).

Both treatment groups were comparable with respect to demographic data and time to onset of the hypertensive response (8.2±7.8 vs 8.6±4.2 min). The baseline, pre-inc and pre-R hemodynamic values, as well as steady-state (pre-R) propofol (1.8 ± 0.7 vs 1.5 ± 0.3 µg/ml) and alfentanil (66 ± 16 vs 80 ± 14 ng/ml) levels, were similar in the two (alfentanil vs propofol) groups. Significant elevations in catecholamines, and ADH levels were associated with the acute hypertensive response (table). Alfentanil levels of 162±29 ng/ml or propofol levels of 5.2±1.0 µg/ml were required to return the MAP to pre-inc values. Both treatment regimens suppressed these responses, however, blood pressure control was achieved more rapidly in the alfentanil-treated patients (6.3±2.6 vs 10.2±2.5 min). Awakening was also faster in the alfentanil group (3.4±2.9 vs 9.1±6.8 min). However, there were no differences in postoperative analgesic, antiemetic or vasodilator therapy, or in length of PACU stay.

Hypertensive events during TIVA were associated with acute increases in stress hormone levels. Supplemental doses of either alfentanil or propofol were equally effective in suppressing these neuroendocrine responses. However, recovery was more rapid when supplemental alfentanil was used to treat the acute hemodynamic responses during TIVA.

TABLE	Epinephrine (pg/ml)	Norepinephrine (pg/ml)	ADH (pg/ml)
Alfentanil Group†			
Pre-inc	44 ± 23	220 ± 106	2.5 ± 2.3
Pre-R	122 ± 71*	337 ± 94*	24.7 ± 21.3*
Post-R	51 ± 20	247 ± 75	14.8 ± 19.0
Propofol Group†			
Pre-inc	34 ± 17	225 ± 81	1.7 ± 0.5
Pre-R	118 ± 80*	329 ± 142*	24.4 ± 24.0*
Post-R	39 ± 28	219 ± 59	16.9 ± 29.7

† Mean values ± S.D.; * Significantly different from pre-inc, $p < 0.05$