TITLE: CLONIDINE DECREASES ISCHEMIC EVENTS DURING CORONARY ARTERY SURGERY

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Postoperative myocardial infarction accounts for up to 40% of deaths following CABG surgery, and is reported to occur three times more frequently in patients who develop intraoperative ECG signs of ischemia.[1] The alpha 2 agonist clonidine has been shown to blunt reflex tachycardia and to reduce intraoperative lability of systolic and diastolic blood pressure[2,4], and to reduce the frequency of angina in patients with chronic angina.[3] We evaluated the effects of clonidine on myocardial ischemia in patients undergoing CABG surgery.

After obtaining V.A. IRB approval and the patient's informed consent 23 consecutive patients scheduled for CABG were randomized to receive either a standard preoperative medication (morphine with scopolamine) or the standard preoperative medication with 200 micrograms of clonidine PO. Anesthesia was induced and maintained with sufentanil and versed and pavulon. ST segment trend analysis in lead II and V5 were continuously monitored with the Marquette microcomputer augmented ST segment analyzer. Ischemia was considered present when greater than one mm of ST segment depression or elevation occurred. Minutes of ischemia with regards to total exposure time of all patients at four intervals: (arrival to induction; induction to skin incision; skin incision to sternotomy; and sternotomy to bypass), as well as the number of patients experiencing ischemia were compared.

Heart rate, mean arterial blood pressure, PCWP, and cardiac index did not differ between groups. Minutes of ischemic time was significantly higher at all intervals in the control group when compared to patients receiving clonidine (see Figure).

Despite the small numbers of patients in this study statistically significant differences in ischemic events and duration of ischemia was seen. We found less overall ischemia in the clonidine treated group and fewer ischemic patients from induction of anesthesia to cardiopulmonary bypass. Preoperative clonidine may decrease the incidence of perioperative myocardial infarction.

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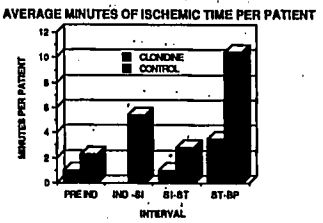

Ischemic time was significantly lower for patients receiving clonidine ($p<0.05$, unpaired t-test).at all intervals (preinduction, induction - skin incision, skin incision - sternotomy, sternotomy - bypass).

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TITLE: ROLE OF BENZYL ALCOHOL PRESERVATIVE IN HEPARIN-INDUCED HYPOTENSION PRIOR TO CARDIOPULMONARY BYPASS

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A bolus dose of 300 U/kg IV heparin given prior to cardiopulmonary bypass causes transient hypotension.[1] Possible mechanisms for this effect include calcium binding, "direct" action, and histamine release,[2,3] but the issue has not been settled. Benzyl alcohol is a common heparin preservative, and is known to be a vasodilator.[4] We asked whether the presence of benzyl alcohol preservative might account for the hemodynamic perturbations attributed to heparin.

METHODS: Institutional Review Committee approval was obtained. Each of 10 subjects scheduled for myocardial revascularization was randomly allocated to receive 330 U/kg of either bovine heparin with 1.5% benzyl alcohol (HBA) or bovine heparin without preservative (HPF). Subjects with a history of prior myocardial infarction, congestive heart failure, or arrhythmia were excluded. Pre-op medications, including calcium-channel and beta-blockers, were continued to the time of operation. Anesthesia was induced with oxygen, either midazolam or diazepam, and either fentanyl or sufentanil. Prior to cannulation for bypass, right atrial injection of heparin was performed in double-blind fashion.

Heart rate (HR, min^{-1}), mean systemic arterial pressure (MAP, mmHg), central venous pressure (CVP, mmHg), mean pulmonary arterial pressure (MPAP, mmHg), pulmonary capillary wedge pressure (PCWP, mmHg), cardiac index (CI, L min^{-1} m^{-2}), systemic and pulmonary vascular resistance indices (SVRI and PVRI, dyn sec cm^{-5} m^{-2}), and mixed venous oxygen saturation (SvO_2, %) were measured or calculated at 1" before, and at 1", 3", and (when possible) 5" after, injection. For each patient, the maximum change in each parameter from baseline was noted. Analysis was by Student's t-test.

RESULTS: No significant difference was evident in any hemodynamic parameter between subjects receiving HBA and those receiving HPF. Mean (SD) changes after heparin injection were as follows:

	HBA (n=5)	HPF (n=5)	p
HR	-0.4 (6.8)	2.8 (6.5)	0.47
MAP	-10.0 (5.4)	-15.0 (4.0)	0.11
CVP	1.0 (1.2)	2.0 (2.6)	0.45
MPAP	-0.2 (1.1)	-2.2 (2.5)	0.13
PCWP	1.2 (4.2)	-0.2 (1.9)	0.51
CI	0 (0.50)	0.32 (0.48)	0.34
SVRI	0 (626)	-342 (218)	0.28
PVRI	10.0 (76.0)	-35.4 (56.9)	0.31
SvO_2	0.2 (4.1)	2.2 (5.1)	0.51

DISCUSSION: Bolus IV heparin causes hypotension, but the mechanism is unclear. Conflicting outcomes have been reported regarding the roles of histamine,[2,5] calcium,[3,6] and even the source (bovine vs. porcine) of the drug.[1,2,5] However, it is likely that all of these studies used heparin with preservative.

Our data suggest that benzyl alcohol, a standard preservative and a recognized vasodilator, does not play a role in heparin-induced hemodynamic perturbations, even though the dose of benzyl alcohol administered in this study exceeded recommended safe dosage by roughly 50%.[4]

Combined findings from both groups show trends similar to those found in previous investigations. For example, MAP decreased in each of our 10 subjects (mean -12.7, SD 5.33). SVRI also decreased, with one striking exception (an increase of 1111 dyn sec cm^{-5} m^2 in a subject who received HBA); in the remaining subjects, the mean decrease in SVRI was 313 (SD 55.8). These findings, like those of other studies,[1-3] suggest that the heparin effect has a vasodilatory component.

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