

Title: INFLUENCE OF PROPRANOLOL BLOOD LEVELS ON HEMODYNAMIC RESPONSE TO SURGICAL STIMULATION IN MAN

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**Introduction.** The beneficial effect of propranolol therapy in treatment of ischemic heart disease is well established. Little information relating plasma propranolol level to hemodynamic performance during surgery is available. Numerous studies have compared anesthetics with respect to hemodynamics, not taking actual propranolol levels into account. Patients receiving near-identical anesthetics were investigated to determine whether or not propranolol influences cardiovascular responses to surgical stimulation.

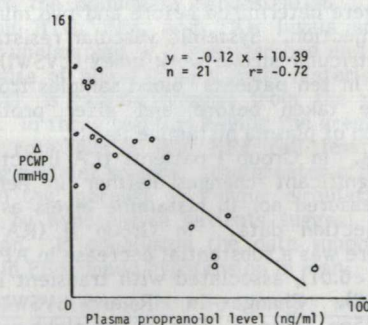
**Methods.** Institutionally approved informed consent was obtained from 21 patients aged 42 to 72 years scheduled for coronary artery surgery. Patients had similar degrees of coronary disease and hemodynamics at catheterization. All patients took propranolol 40 to 160 mg/day until the day before or morning of surgery. All but one took nitrates. All patients received near identical anesthetics, namely morphine 0.5 mg/kg, diazepam 0.5 mg/kg, pancuronium 0.1 mg/kg, and halothane in oxygen-air was added following endotracheal intubation. Inspired halothane concentrations were adjusted to maintain SBP  $\pm$  20% of preoperative value. Plasma propranolol levels were measured on arrival in the operating room, during skin prep, and during rib retraction. Analysis was performed using high-pressure liquid chromatography with fluorescence detection. End-tidal halothane measurements were via calibrated Beckman LB2. Hemodynamics were determined before and after intubation. Hemodynamics and halothane concentration were measured prior to and following skin incision, at maximum rib retraction after sternotomy, and again after 6 minutes of rib retraction. Linear regressions were determined between plasma propranolol level and hemodynamic changes occurring during the above cardiovascular stress periods. In addition, end-tidal halothane concentration was compared to hemodynamic changes and to propranolol levels.

**Results.** Hemodynamic responses to perioperative stressful stimulation were negatively associated with propranolol in proportion to plasma concentrations. Magnitude of change in HR, PCWP, and CI correlated inversely with plasma propranolol. Levels for the 21 patients ranged from 0-113 ng/ml at intubation, 0-92 ng/ml on skin incision and 0-86 ng/ml following rib retraction. Heart rate change correlated inversely with propranolol level on intubation ( $r = -0.77$ ), at skin incision ( $r = -0.66$ ), during maximum rib retraction ( $r = -0.82$ ), 6 minutes of rib spread ( $r = -0.75$ ). PCWP increase correlated inversely with propranolol level on skin incision ( $r = -0.60$ ), during maximum rib retraction ( $r = -0.72$ ) and following 6 minutes of retraction ( $r = -0.71$ ). Cardiac index change and propranolol level were not related at skin incision but had a similar inverse correlation during rib retraction ( $r = -0.66$ ) and following 6 minutes of rib retraction ( $r = -0.66$ ). Systolic blood pressure increase correlated inversely

with plasma propranolol at intubation ( $r = -0.63$ ) but this relationship was lost following the addition of halothane. Halothane end-tidal concentration did not correlate with propranolol level at skin incision ( $r = 0.46$ ) or rib retraction ( $r = 0.42$ ) nor demonstrated a good relationship to hemodynamic changes.

**Discussion.** Propranolol favorably alters cardiovascular response to surgical stress during anesthesia. A similar relationship has been demonstrated between propranolol level and suppression of exercise-induced tachycardia and anginal pain. Amelioration of HR, BP, and PCWP changes by propranolol is beneficial in patients whose coronary vascular reserve is limited and who are susceptible to myocardial ischemia. Provision of adequate  $\beta$ -blockade should be attempted for patients with ischemic heart disease undergoing surgery. We conclude that propranolol blood levels were negatively correlated with hemodynamic response to stress in surgical patients. Degree of  $\beta$ -blockade should not be inferred from preoperative drug dosage, rather, propranolol blood levels should be measured and then should be considered when conclusions are made concerning different anesthetic abilities to abolish hemodynamic responses to stress.

Change in PCWP and plasma propranolol level during rib retraction



Change in HR and plasma propranolol level during endotracheal intubation

