Date

Title : MAINTENANCE OF PROPRANOLOL THERAPY BY IV INFUSION

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It is often desirable to maintain chronic propranolol (P) therapy in the postoperative period when patients cannot take drugs orally. One means of doing so is to infuse P continuously to produce a steady plasma concentration within the therapeutic range. This study examined the feasibility of P infusion in patients who had undergone coronary artery bypass surgery (CABG). Such patients may require P to control tachycardia, dysrhythmias, and hypertension in the postoperative period.

METHODS. Twelve patients (34-61 yrs) scheduled for elective CABG gave informed consent to this study which was approved by the Human Investigations Committee. All patients had coronary artery disease as their only significant illness and were not taking drugs other than those for angina pectoris. All had normal ventricular function (ejection fraction > 0.5, end-diastolic pressure < 15 torr) and were taking P (160mg/day in 4 doses). They received their last dose at 10pm the night before surgery (scheduled for 8am). Infusion of P was begun postoperatively at approximately 2pm when the patients were normothermic and had normal blood gases with intermittent mandatory ventilation. Mean arterial (MAP), central venous (CVP), pulmonary artery (PAP) and capillary wedge pressures (PCWP) were monitored continuously along with heart rate (HR) and the ECG. Cardiac output (CO) was estimated by thermodilution. Systemic vascular resistance (SVR) and stroke work index (SWI) were calculated. Blood samples were taken at 9:55pm, 8am, just before starting the infusion and intermittently thereafter (see Figure). The constant infusion was continued for 7 hours (n=3) or for 4 hours followed by a 3-hour period of blood sampling (n=4). Plasma, was separated from blood and analysed for P.[1] Results are expressed as the mean ± S.E..

RESULTS. Based on a P clearance (Cl) of 1.2 L/kg/hr,[2] an infusion rate (Q) of 0.65µg/kg/min should produce a steady-state plasma concentration (Cpss) of 53ng/ml (Q ÷ Cl = Cpss). The observed Cpss was 54±4ng/ml in 9 patients (Figure). In 3 other patients, infusion of 0.32µg/kg/min produced a Cpss at 3.5 hours of 23±2ng/ml vs an estimated Cpss of 26ng/ml. The half-time for P elimination ($t_{\frac{1}{2}\beta}$) was approximately 5 hours before the infusion (n=9) and 4 hours after the infusion was stopped (n=4). Hemodynamic variables did not change during the infusion (Table).

DISCUSSION. Plasma P concentrations of 14 to 90 ng/ml are associated with optimal relief of angina pectoris and with a 64 to 98% blockade of exercise-induced tachycardia.[3] It was anticipated that these levels of propranolol would reduce the cardiac response to stress without affecting hemodynamics in the resting state. We were able to maintain P levels in the therapeutic range by a constant infusion of P in the postoperative period. The time required to achieve therapeutic levels was less than that usually predicted (4 x $t_{\frac{1}{2}\beta}$), probably because of the residual P from preoperative therapy. If necessary, the level can be achieved more rapidly by an IV volus dose and maintained by an infusion. It is anticipated that infusion rates will have to be modified for patients in certain disease states.[4]

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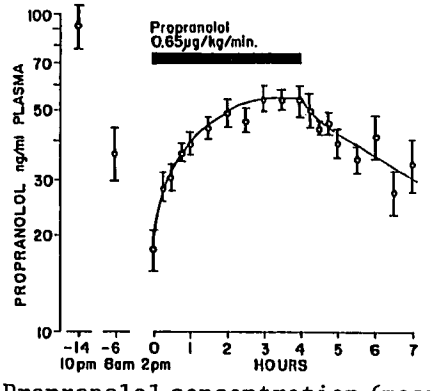

Figure. Propranolol concentration (mean±SE) in plasma of 9 patients before and during a 4-hour constant infusion. Elimination of propranolol after stopping the infusion is shown for 4 patients; 3 others had a level of 56±8ng/ml at the end of a 7-hour infusion.

Table. HEMODYNAMIC FUNCTION (MEAN ± SE) BEFORE AND DURING PROPRANOLOL INFUSION

Hemodynamic Variable		Before Infusion (18 ± 3ng/ml*)	Infusion for 3hrs (55 ± 3ng/ml*)
HR	(bpm)	91±5	88±4
MAP	(torr)	91±4	86±3
CO	(L/min)	4.9±0.5	5.0±0.4
LVSWI	(gM/M^2)	37±5	34±8
PCWP	(torr)	7.0±1.3	11±1
CVP	(torr)	8.3±0.7	9.4±0.8
SVR	($d\text{-}s/cm^{-5}$)	1432±115	1278±93

*Propranolol concentration in plasma at time of measurements.