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Title : PROPRANOLOL DURING NITROPRUSSIDE HYPOTENSION

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Introduction. Sodium nitroprusside (SNP) is frequently used to induce deliberate hypotension despite the fact that it is metabolized to cyanide, and large doses may be toxic. Propranolol, a beta-blocking drug, has been observed to decrease SNP dose-requirements, and thus reduces blood cyanide levels in man, but the mechanism of this action has not been defined.[1] In large doses propranolol decreases heart rate and/or cardiac output in man, and also decreases plasma renin activity (PRA) which is known to support the blood pressure during SNP induced hypotension in the rat.[2] This study examines the impact of propranolol on both the cardiovascular and renin-angiotensin systems during controlled hypotension in man.

Methods. The subjects were ten consecutive patients, aged 13-36 years, undergoing operation for posterior spinal fusion. Premedication consisted of morphine (0.1 mg/kg) and scopolamine (0.005 mg/kg) IM one hour prior to induction. Anesthesia was induced with sodium thiopental (3-4 mg/kg) IV and intubation was accomplished with succinylcholine (1 mg/kg) IV. Anesthesia was maintained with 70% N_2O in O_2, morphine (0.5 mg/kg), and curare (0.3 mg/kg initial dose). All patients were mechanically ventilated to maintain an arterial PCO_2 of 34.5 torr ± 0.7 SEM. A radial artery and a thermistor-tipped Swan-Ganz pulmonary artery catheter were placed after induction. The following parameters were determined: Heart rate (H.R.), mean systemic arterial pressure (SAP), cardiac index (C.I.; measured by thermal dilution technique in triplicate), pulmonary capillary wedge pressure (PCWP), hematocrit (Hct), central venous pressure (CVP), systemic vascular resistance index (SVRI), and PRA (measured using radioimmunoassay; New England Nuclear). Control data were obtained 10 minutes after incision, and repeat measurements were made after 40 minutes of SNP infusion (mean dose = 4.1 µg/kg/min ± .53 SEM). Propranolol, 0.03 mg/kg IV, was then administered as a bolus while SNP infusion rate was held constant. All measurements were repeated 10 and 40 minutes after propranolol. Each patient served as his own control and all data were analyzed using Student's t-test for paired data; $p < .05$ was regarded as significant. This protocol was reviewed and approved by the institution's Human Studies Committee, and informed consent was obtained.

Results. Hemodynamic data and hematocrits are summarized in Table 1. SNP infusion caused significant decreases in SAP, SVRI, and PCWP, and significant increases in H.R. and C.I. (Fig. 1). Propranolol administration had two effects: after 10 minutes, C.I. and H.R. were significantly decreased; later, after 40 minutes, PRA was significantly decreased. (Fig. 1).

Discussion. Our data suggest a dual effect for propranolol during SNP-induced hypotension: a) an early direct effect on the heart, causing a decrease in H.R. and C.I.; b) decreased PRA, occurring later presumably as a result of inhibition of renin release from the kidney. SNP is a vasodilator which decreases arterial pressure and increases cardiac output by decreasing systemic vascular resistance (SVR). The increased H.R. and PRA are thought to be reflex responses to decreased SAP. The fact that we did not observe a significant increase in PRA during SNP is probably due to a near-maximal increase in PRA which occurred after anesthesia, pronation and incision. Although SNP infusion was held constant during the present study, we believe that the reduced SNP requirement seen previously when propranolol was given in a dose sufficient to lower heart rate[1] was caused by decreasing both cardiac output and plasma renin activity toward normal values.

References.

1. Bedford RF, Berry FA, Longnecker DE: Impact of propranolol on hemodynamic response and blood cyanide levels during nitroprusside infusion: A prospective study in anesthetized man. Anesth Analg 58:466-469, 1979

2. Miller ED, Ackerly JA, Vaughn ED, et al.: The renin-angiotensin system during controlled hypotension with sodium nitroprusside. Anesthesiology 47:257-262, 1977

	Surg. + 10 min	SNP + 40 min	Propranolol + 10 min	Propranolol + 40 min
Heart Rate (Beats/min)	64 ± 6	80* ± 7	70** ± 6	69** ± 5
$\overline{SAP}$ (Torr)	99 ± 3	74* ± 3	76 ± 2	74 ± 3
SVRI (Dyne-sec-cm^5-m^2)	2502 ± 163	1389* ± 114	1695** ± 137	1574 ± 129
PCWP (Torr)	16 ± 2	12 ± 2	13 ± 2	13 ± 2
Hct	36 ± 1	34 ± 1	34 ± 1	34 ± 1

N=10 All values mean ± standard error of the mean
* values significantly different from surg. + 10 min. $P < .02$
**values significantly different from SNP + 40 min. $P < .02$