TITLE: CAPTOPRIL REDUCES THE DOSE REQUIREMENT FOR SNP-INDUCED HYPOTENSION

AUTHORS: J. R. Woodside, M.D., L. Garner, M.D., R. F. Bedford, M.D., E. D. Miller, Jr., M.D., D. E. Longnecker, M.D., R. M. Epstein, M.D.

AFFILIATION: Department of Anesthesiology, University of Virginia Medical Center, Charlottesville, VA 22908

Introduction. Activation of the renin-angiotensin system is known to cause resistance to nitroprusside (SNP)-induced hypotension.[1] Captopril, an antagonist of angiotensin converting enzyme, has been shown to potentiate SNP in awake volunteers.[2] The present study was designed to examine the impact of captopril on the cardiovascular and renin-angiotensin systems in patients receiving SNP for controlled intraoperative hypotension.

Methods. The subjects of the study were 12 patients (50-80 kg) scheduled for major elective cerebrovascular or spinal operations. The protocol was approved by the local human studies committee and informed consent was obtained from each patient or his nearest relative. Half of the patients received captopril 3 mg/kg, p.o., with a sip of water just before being transported to the operating suite. The decision whether or not to administer captopril was made randomly by lot. Anesthesia was induced with thiopental, 3 mg/kg, and maintained with morphine, 0.5 mg/kg, and N_2O (70 per cent in O_2). Endotracheal intubation was facilitated with pancuronium, 0.1 mg/kg, and ventilation was controlled throughout the study period (mean $PaCO_2$ = 35.1 mmHg ± 2.6 SD). Radial arterial and thermistor-tipped Swan-Ganz catheters were placed using pressure waveform control. Blood samples were obtained and cardiovascular variables were determined at the following times: (1) After induction of anesthesia, (2) After surgical incision, (3) After SNP infusion rate was adjusted to maintain a stable arterial pressure between 50 and 65 mmHg, and (4) After SNP infusion was discontinued (mean duration of SNP infusion = 135 min ± 55 S.D.). Arterial blood samples were analyzed for converting enzyme activity (radioassay system, Ventrex Laboratories, Portland, Maine) and plasma renin activity (radioimmunoassay, New England Nuclear, N. Billerica, Massachusetts). Captopril versus control data were compared using Student's t-test for unpaired data. Within-group comparisons between initial values and those during hypotension were analyzed using Student's t-test for paired data. $P<0.05$ was regarded as significant.

Results. Captopril pretreatment resulted in a significantly reduced SNP dose-requirement to maintain stable arterial hypotension (1.9 µg/kg/min ± 0.3 SE versus 5.0 µg/kg/ min ± 1.0 SE, $p < .02$). As indicated from the results of the laboratory studies (Table 1), captopril produced significant inhibition of converting enzyme activity which was sustained throughout the period studied. Plasma renin activity was increased in patients receiving captopril as compared to controls. Significant increases in PRA were observed during SNP infusion in the control group whereas no significant change occurred in those receiving captopril. Hemodynamic responses to induction of anesthesia and surgical incision were virtually the same in both the captopril and control patient groups. During SNP infusion the only difference was a greater mean arterial pressure in the control group, despite the larger SNP dose administered. Rebound hypertension was not seen in either patient group when SNP was discontinued.

Discussion/Conclusions. Oral captopril pretreatment appears to offer a simple, safe and effective method for potentiating the effects of SNP by inhibiting the renin-mediated formation of angiotensin II. The higher PRA's observed in the captopril-treated group are thought to reflect the loss of feedback inhibition by angiotensin II. Inhibition of converting enzyme activity does not significantly alter the hemodynamic response to either induction of N_2O-morphine-pancuronium anesthesia or to surgical stimulation. It does, however, effectively reduce SNP dose requirement and the attendant risk of cyanide toxicity.

Table. Hemodynamic and laboratory variables during anesthesia and hypotension with and without Captopril pretreatment

		Before Incision	After Incision	During SNP	After SNP
Heart Rate (beats/min)	Captopril	95±7	93±10	97±10	88±5
	Control	94±2	93±5	99±5	74±6
Mean Arterial Pressure (torr)	Captopril	73±7	94±6	54±2*	90±5
	Control	81±4	98±6	60±2*†	96±7
Right Atrial Pressure (Torr)	Captopril	8±3	7±2	6±2	8±3
	Control	7±1	7±1	7±1	8±2
Pulmonary Capillary Wedge (torr)	Captopril	9±3	9±2	8±2	10±3
	Control	7±1	7±1	7±1	8±1
Cardiac Output (L/min)	Captopril	4.6±0.3	5.5±0.5	5.2±0.7	5.3±0.6
	Control	4.8±0.5	6.7±0.8	7.3±1.0	5.0±0.4
Systemic Vascular Resistance (dyne·sec·cm^{-5})	Captopril	1127±130	1327±157	751±104*	1195±111
	Control	1288±135	1200±178	703±164*	1520±287
CEA (Units)	Captopril	24±5	24±5	26±2	27±5
	Control	58±11†	64±12†	71±5†	71±4†
PRA (ng/ml/hr)	Captopril	11±4	12±3	15±3	14±3
	Control	3±1	4±1†	7±1*†	4±1

All values: Mean ± S.E.; * = $p < .05$ vs. values before incision; † = $p < .05$ vs Captopril

References.

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