Title : CAPTOPRIL ATTENUATES VASOACTIVE HORMONAL RELEASE DURING NITROPRUSSIDE-INDUCED HYPOTENSION

Authors : Hoshang J. Khambatta, M.D., J. Gilbert Stone, M.D., Emaduddin Khan, M.S.

Affiliation: Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, NY 10032

Introduction. Nitroprusside-induced hypotension causes an increase in plasma renin activity (PRA) and plasma vasopressin (ADH), epinephrine (E) and norepinephrine (NE) levels.[1,2,3] Propranolol attenuates the release of renin, E and NE during nitroprusside-induced hypotension.[1,2] The purpose of this study was to determine whether during nitroprusside-induced hypotension effective hormonal suppression could also be achieved with the use of captopril, an inhibitor of angiotensin converting enzyme.

Methods. Twelve mongrel dogs, average wt 10 kg, were anesthetized with pentobarbital 30 mg/kg IV and paralyzed with pancuronium 0.2 mg/kg IV and mechanically ventilated with air through an endotracheal tube. Arterial pH was maintained at approximately 7.4. Following a steady state period of 30 min, nitroprusside (NP) was administered by continuous IV infusion, the rate of which was adjusted to achieve a 40 percent reduction in mean arterial pressure (MAP). This degree of hypotension was maintained for 1 hr after which the infusion was discontinued. Following a recovery period of 1 hr, the dogs were given a bolus of captopril 0.5 mg/kg IV. Thirty minutes later, NP infusion was restarted and the same degree of hypotension was again induced for 1 hr and then followed by another hr of recovery. Arterial and central venous blood samples were obtained before and during induced hypotension and 30 and 60 min thereafter; both before and after captopril administration. PRA and ADH levels were determined in arterial blood by radioimmunoassay. Plasma E and NE levels were measured radioenzymatically in central venous samples. Statistical significance ($p<0.05$) was determined by analysis of variance.

Results. The results are displayed in the table. Values represent mean±SEM. Captopril pretreatment significantly reduced the required infusion rate of NP from 1.5±0.3 to 0.3±0.1 mg/kg/hr.

Discussion. PRA and plasma levels of vasoactive substances increased during NP induced hypotension. Captopril pretreatment significantly reduced the increase in plasma levels of ADH, E and NE during deliberate hypotension. In contrast, the increase in PRA during NP infusion was greater after captopril. This can be attributed to the fact that captopril inhibited the conversion of angiotensin I to angiotensin II, thus suppressing the negative feed-back loop and bringing about further renin release. Without captopril pretreatment, vasoactive hormone levels did not return to control until 60 min after NP was discontinued and rebound hypertension was noted at 30 min. After captopril rebound hypertension did not occur and hormone levels were back to normal at 30 min. Captopril per se, in the dose given, did not alter the arterial pressure or hormone levels. We conclude that during NP induced hypotension, the renin-angiotensin system can be beneficially modified not only by propranolol but also by captopril.

Untreated State

	Control	Hypo	Rec ½ hr	Rec 1 hr
MAP	135± 5	85± 5*	149± 6*	138± 6
PRA	3± 1	8± 2*	5± 1*	3± 1
ADH	7± 2	225± 87*	19± 7*	11± 5
E	151±35	641±196*	225±92*	187±79
NE	234±47	938±123*	520±89*	336±66

Captopril Treated

	Control	Hypo	Rec ½ hr	Rec 1 hr
MAP	127± 5	82± 5*	128± 7 †	128± 7
PRA	5± 1	33± 8*†	13± 2*†	9± 2*
ADH	7± 2	28± 10*†	7± 2 †	5± 1
E	115±41	324±110*†	92±28 †	100±27
NE	242±45	581± 72*†	214±36 †	168±32

Units of measurement: MAP torr, PRA ng/ml/hr, ADH pg/ml, E pg/ml, NE pg/ml

* $p<0.5$ Control vs hypo, control vs Rec ½ hr, control vs Rec 1 hr

† $p<0.05$ Untreated state vs captopril treated, same phase

References.

1. Khambatta HJ, Stone JG, Khan E: Propranolol alters renin release during nitroprusside-induced hypotension and prevents hypertension on discontinuation of nitroprusside. Anesth Analg 60:569-573, 1981.
2. Khambatta HJ, Stone JG, Khan E: Nitroprusside hypotension: Catecholamines, propranolol. Anesthesiology 53:A8, 1981.
3. Khambatta HJ, Stone JG, Khan E: The role of vasopressin during nitroprusside-induced hypotension and subsequent rebound hypertension. Fed Proc 41:1473, 1982.