CARDIOVASCULAR AND ADRENAL MEDULLARY CATECHOLAMINE RESPONSES OF "NEW PRESSOR PROTEIN" IN BILATERALLY NEPHRECTOMIZED (2NX) RATS TREATED WITH CAPTOPRIL

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"New Pressor Protein" (NPP) observed in human and rat plasmas has strong N-terminal sequence homology with the βFXIIa fragment of coagulation FXII. Intravenous (i.v.) injection of NPP exerts potent cardiovascular effects i.e., increase in systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg) and heart rate (HR, beats per minute, bpm) with the release of adrenal medullary catecholamine. The administration of Angiotensin Converting Enzyme Inhibitor (ACEI), Captopril further potentiates these effects of NPP. Since it is known that the kidneys are rich in ACE, the removal of kidneys (2NX) should duplicate the effect of Captopril on NPP responses. The objectives of this study were to determine the extent to which the kidneys (i) mediate the specific cardiovascular effects of NPP (ii) influence the observed potentiation of NPP's effects by the ACE inhibitor Captopril (iii) influence the NPP induced catecholamine release from the adrenal medulla.

Direct pressor (SBP, DBP) and HR responses to NPP were recorded in 2NX rats and sham-2NX control rats before and after Captopril using a MacLab8/system. Plasma catecholamines were determined by HPLC with fluorimetric detection.

After 2NX, the cardiovascular responses to NPP were as follows: (i) 2NX itself had fully duplicated SBP potentiation of Captopril seen in control rats (ii) the peak DBP increment after NPP was significantly higher than that in the control rats, before or after Captopril ($p< 0.0001$ and $p< 0.01$, respectively). (iii) Captopril on top of 2NX produced no added potentiation of peak SBP or DBP responses to NPP beyond the effect of 2NX alone in contrast to what was observed in sham-2NX control rats. However, the DBP response in 2NX rats after Captopril was significantly higher than that in control rats before or after Captopril ($p< 0.01$ and $p< 0.05$, respectively). (iv) In 2NX rats, before Captopril, the HR response to NPP was significantly higher than that in sham-2NX rats ($p< 0.$ 0.0001). This effect was further potentiated by Captopril ($p< 0.05$). However, the HR response after Captopril in 2NX rats was significantly lower than in the sham-2NX rats ($p< 0.05$).
After 2NX, plasma catecholamine levels in response to NPP are as follows. (i) Without Captopril, NPP in 2NX rats increased peak plasma adrenaline from baseline value 199 to 4602 pg/ml, rising to 6598 after Captopril. (ii) In sham-2NX, NPP increased adrenaline from 16 to 960 pg/ml and Captopril raised this to 6364 pg/ml.

Thus, the present study suggests that the kidneys are required for the most of the potentiation of NPP's effects by Captopril and it is mediated via adrenal medullary catecholamines.

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