EFFECT OF NEUTRAL ENDOPEPTIDASE INHIBITION ON VASCULAR RESPONSE INDUCED BY EXOGENOUS ANGIOTENSIN I IN THE ISOLATED RAT LUNG

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It is suggested that vasoconstriction mediated by angiotensin II cleaved from angiotensin I by angiotensin converting enzyme (ACE) is counterbalanced by concomitant formation of vasodilator angiotensin (1–7) by neutral endopeptidase (NEP). Here, we tested this hypothesis using as a bioassay the isolated rat lung perfused with Krebs-Henseleit (KH) solution and ventilated with negative pressures.

Addition of angiotensin I (100 nM) into the isolated lung resulted in an immediate increase in pulmonary arterial pressure ($\Delta PAP$) which was not accompanied by a significant change in respiratory lung function or weight of the lung. The $\Delta PAP$ response induced by angiotensin I was abolished by an inhibitor of ACE, perindoprilate (1 $\mu$M), or by angiotensin type 1 receptor antagonist (losartan, 1$\mu$M) but not by angiotensin type 2 receptor antagonist (PD 123.319, 10 $\mu$M) suggesting the involvement of ACE and AT1 (but not AT2) receptors in this response. On the other hand, antagonist of bradykinin receptor B2 (icatibant, 100 nM) or an inhibitor of neutral endopeptidase, thiorphan (1 $\mu$M and 10 $\mu$M) did not modify $\Delta PAP$ response induced by angiotensin I.

In summary, in the isolated rat lung perfused with KH solution, ACE has a dominant role in the pulmonary conversion of angiotensin I to angiotensin II, while NEP-derived angiotensin 1–7 does not seem to constitute a major counterbalancing mechanism in the pulmonary vasoconstriction induced by endogenously formed angiotensin II.

Key words: angiotensin I, angiotensin II, angiotensin converting enzyme, neutral endopeptidase, angiotensin 1–7, isolated lung

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