Inhibition of neutral endopeptidase by thiorphan does not modify coronary vascular responses to angiotensin I, angiotensin II and bradykinin in the isolated guinea pig heart

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Abstract:
Both angiotensin-converting enzyme (ACE) and neutral endopeptidase (NEP) are involved in the regulation of renin-angiotensin and kallikrein-kinin systems. The aim of the present study was to assess the role of NEP and ACE in the regulation of vascular responses to angiotensin I (Ang I), angiotensin II (Ang II) and bradykinin (Bk) in the coronary circulation. For this purpose we used typical inhibitors of ACE and NEP, perindoprilate (1 µM) and thiorphan (1 µM and 10 µM), respectively, and analyzed their effects on the coronary vasoconstrictor responses to Ang I and Ang II and coronary vasodilator responses to Bk in the isolated guinea pig heart. Perindoprilate abolished coronary vasoconstriction induced by Ang I and potentiated coronary vasodilation evoked by Bk. Thiorphan at a concentration of 1 µM slightly reduced response to Ang I without a significant effect on the responses to Ang II and Bk. However, thiorphan at a concentration of 10 µM abolished coronary vasoconstrictor response to Ang I and enhanced Bk-induced vasodilation. Importantly, in the presence of perindoprilate, addition of thiorphan (10 µM) did not modify further either responses to Ang I, Ang II or to Bk. In conclusion, vascular responses induced by Ang I, Ang II and Bk in the isolated guinea pig heart are regulated by ACE but not by NEP. Moreover, thiorphan is not a perfect tool to assess functional role of NEP as it displays ACE inhibitory activity.

Key words:
angiotensin, angiotensin-converting enzyme, neutral endopeptidase, coronary vessels, guinea pig heart