Role of Nitric Oxide(NO) in Augmented Constrictive Response to Endothelin-1(ET-1) in Coronary Artery of Hypertensive Heart.

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To determine the vasoconstrictive response to ET-1 in coronary artery of hypertensive heart whether NO release is involved in the isolated heart from normotensive and spontaneously hypertensive rats was perfused. Normotensive Wistar rats (NT), WKY and SHR (10 weeks old) were utilized. Half of WKY and SHR were treated by L-NAME (75mg/dl) in drinking water for one week. Hearts were isolated and fixed at Langendorff apparatus and perfused with modified Krebs-Henseleit solution at a constant pressure (75mmHg). Perfusion pressure and flow were measured by a small-volume transducer and drop counter respectively. Coronary perfusion resistance (CPR) was calculated by the pressure and flow. Minimum coronary perfusion resistance (MCPR) was obtained by adenosine (10⁻⁵M) infusion. LV weight was significantly larger in SHR than those of WKY. MCPR was significantly increased in SHR. ET-1 increased perfusion pressure dose dependently in both WKY and SHR. Increase of perfusion pressure was significantly larger in SHR than in WKY and NT.

Responses of increased perfusion pressure were significantly inhibited by the pre-treatment of ETA receptor antagonist (FR 139317) in both NT and SHR.

L-NAME administration elevated the blood pressure in WKY and SHR. Increased perfusion pressure response to ET-1 infusion was significantly larger in L-NAME administered WKY than those in WKY without administration of L-NAME. In SHR, however, increased perfusion pressure to ET-1 was not enhanced by L-NAME administration. After the treatment of L-NAME the differences of these responses to ET-1 between SHR and WKY were disappeared. These findings suggest that coronary constrictive responses to ET-1 were enhanced in hypertensive hearts and the decreased NO release in coronary artery of hypertensive hearts could contribute to this enhancement.