Thesis Title Adenosine and Local Regulation of Hindlimb Blood Flow in Renal Hypertensive Rat

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ABSTRACT

A phenomenon of local regulation of skeletal blood flow namely reactive hyperemia was studied in renal hypertensive rats (RHR) and age-matched normotensive controls (NR) by measurement of hindlimb blood flow (HBF), arterial blood pressure (ABP) and hindlimb vascular resistance (HVR) following complete aortic occlusion for 3 sec to 11 min. In both groups, release of arterial occlusion resulted in an immediate increase in HBF associated with a fall in ABP, with a gradual return to the respective resting levels. The differences of this phenomenon between RHR and NR were influenced by the duration of aortic occlusion. Peak reactive hyperemic HBF and the amount increment of HBF were significantly less in RHR than that in NR ($P<0.05$) over the short range of arterial occlusions (3-60 sec). In contrast, duration of reactive hyperemia (repay time) and total HBF repayment of RHR were significantly less than those of NR ($P<0.05$)

as the occlusion durations were 3 min and above. Minimum resistance to flow produced by long period of arterial occlusions (3 min and above) was significantly greater in RHR than in NR ($P<0.01$). At all occlusion times, however, the reduction of HVR during the peak reactive hyperemic flow was more pronounced in RHR than in NR ($P<0.025$). Since adenosine (Ado) is well recognized as an important local blood flow regulator, it was postulated to play a role in the alteration of reactive hyperemia in RHR. Vascular responsiveness to Ado (0.0001-1.0 mg/kg BW) was examined by determining on changes of HBF and HVR. The relaxing effect of Ado was first observed in both NR and RHR when Ado at the dose of 0.001 mg/kg BW was injected. Graded Ado injections showed identical Ado "ED_{50}", i.e. 32±8 μg/kg BW (n=9) and 35±16 μg/kg BW (N=7) in NR and RHR, respectively. In addition, the slope of the Ado dose-response curves was likely to be the same in both groups.

These results indicate that reactive hyperemia is altered in hypertensive animals. The hindlimb vascular responsiveness to Ado in RHR was the same as in NR, suggesting that the alteration in reactive hyperemia in RHR should not possibly be concerned with the responsiveness of arterial smooth muscle to Ado.