Effects of endothelin-1 on the microcirculation of rat mesenteric vasculature. — Comparative studies of reactivities among WKY, SHRSR and SHRSP — Masao Masui, and Kazuki Matsunaga. Shionogi Research Laboratories, Futaba-cho, Toyonaka, 561 Osaka.

Endothelin(ET) is composed of 21 amino acids and is the most potent endogenous vasoconstrictive substance produced in the endothelium et al. Its relationship with several pathological situations such as hypertension, renal failure and cerebral vasospasm has been suggested. Although many studies on the vasoreactivities by ET have already been reported, the effects of ET in the microcirculation where it plays the most important role in the circulatory regulation have hardly been examined especially in a hypertensive situation. We studied the effects of ET-1 mainly on the change of arteriole diameter in the mesenteric microvasculature of three different strains of rats by the use of a microscope-TV-video system.

Seven to 20 week old male WKY, SHRSR and SHRSP bred in Shionogi Abrahi Laboratories were used. Their mesenterium was drawn out and extended in an organ bath filled and superfused with 37 °C Krebs-Henseleit solution. The zone of mesenterium for observation was put into the 0.2 mm space between two sheets of cover glass connected with a stainless O-ring. The microcirculation in the zone was transmittedly illuminated, and video photographed and recorded at the rate of 30 pictures/sec. VIR was analyzed for determination of diameter change in individual microvessels after each experiment. Blood pressure and heart rate were also simultaneously monitored from the femoral artery. ET-1 at the dose of 0.3, 1 and 3 µg/kg was intravenously injected. All experimental procedures were done under urethane(1g/kg, s.c.) anesthesia.

Arteriole, venule, capillary and lymph vasculature were observed in the view field of our experiment. The arteriole was narrower and the stream in it was faster in comparison with those of the venule. The contractile responses to ET-1 3µg/kg i.v. on the arterioles of the SHRSR and SHRSP were stronger and longer lasting than those of WKY. The contractile responses to ET-1 in the SHRSP were enhanced considerably at an earlier age of 8 weeks old and the changes from 13 to 18 weeks old were slight, whereas those in the SHRSR were gradually developed from 8 weeks old to 18 weeks old. The contractile responses to ET-1 in the WKY and SHRSR were homogeneous along the arteriole wall. However, the responses to ET-1 in the SHRSP were often heterogeneous such as intermittent spasm like a sausage, wind spasm like a snake and transient flow stop and reflow. Blood pressure transiently dropped immediately after ET-1 administration and thereafter was reversed to the pressor response. The degree of pressor responses in the SHRSR and SHPSP were similarly stronger than those in the WKY. However the response was markedly faster in SHRSP than in SHRSR. The maximal pressor response to ET-1 in SHRSR was achieved at 18 weeks old and that in SHRSP at 13 weeks old. The heart rate in WKY was clearly increased in the early transient depressor phase and thereafter decreased slightly, that in the SHRSR and SHRSP was also slightly increased but was not decreased subsequently. The heart rate in SHRSP was slightly but triphasically changed.

The contractile responses to ET-1 in the arteriole of the SHRSR and SHRSP were stronger than those in the WKY. The figures of contractile responses in SHRSP were heterogeneous even on the young arterioles. These findings suggested that enhanced contractile responses in their arterioles promoted the development of hypertension and end-organ injury in the SHRSR and SHRSP and that the characteristic vasospasm in the SHRSP might be related to the severe hypertension, hemorrhage and thrombosis occurring during a stroke.

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