
We have previously reported that ɑ1-adrenoceptors play an important role in the pressor response to noradrenaline (NA) in the hindlimb blood vessels of male SHR and WKY. On the other hand, both ɑ1- and ɑ2-adrenoceptors play important roles in female SHR and WKY. Moreover, on the basis of the results obtained from gonadectomized rats, we also suggest that sex hormone participates at least in part in the regulation of blood pressure of SHR and WKY. The present study will discuss effect of ɑ2-selective agonists on the pressor response to methoxamine (MTX) or NA in the hindlimb blood vessels of SHR, WKY and Wistar rats.

Both sexes of SHR, WKY and Wistar rats, 12-18 weeks old, were used. Animals were anesthetized with urethane (1.5 g/kg, s.c.). The right jugular vein was canulated and used for administration of hexamethonium. Blood was introduced from proximal abdominal aorta to a sigma pump and returned to the distal portion of the same aorta. Thus, hindlimb was perfused with blood at a constant rate (2 ml/min, giving perfusion pressure of approximately 75 mmHg). The perfusion pressure was measured with a pressure transducer and recorded on a thermal pen-writing recorder. Animals were given hexamethonium (5 mg/kg, i.v.) to block autonomic ganglia and allowed 15 min before the start of the experiments. MTX (12.5 μg) or NA (1 μg) was administered intra-arterially. The rise in the perfusion pressure was used as a control and compared with the changes of the perfusion pressure in combination with ɑ2-agonist and MTX or NA.

The drugs used in the study were NA hydrochloride and clonidine hydrochloride (CL) from Sigma Chemical Co., UK14304 (UK) from Pfizer Co., and MTX from Nihon Shinyaku Co. All other chemicals were of analytical grade.

Statistical significance of differences in mean values was analyzed by using Student's t-test.

Administration of ɑ2-agonist (UK or CL) alone showed transiently slight depression of the perfusion pressure at higher doses than 10 μg/kg. When UK was administered 2 min before MTX injection, the pressor response to MTX was suppressed dose-dependently and this effect was more prominent in the female than in the male. CL also inhibited slightly, but significantly the pressor response to MTX in the female of SHR and Wistar rats, while there was no difference between the male and female in WKY. On the contrary, the pressor effect of NA on the perfusion pressure was suppressed only at higher doses than 10 μg/kg UK or CL in all animal groups.

These results suggest the possibility that ɑ2-adrenergic agonists antagonized with the pressor effect of ɑ1-adrenergic agonist on hindlimb blood vessels of the female rats, whereas this antagonistic effect of ɑ2-agonist on ɑ1-agonist did not observe in the male. This sex-dependent difference in sensitivity to adrenergic drugs might be an important factor of the elevation of blood pressure in the male SHR.