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Chronic Effects of Arotinolol (S-596) in Spontaneously Hypertensive Rats*

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Arotinolol (S-596, ARL) is a β-adrenoceptor blocking drug with weak α-adrenoceptor blocking activity, and may be classified into the fourth generation. Antihypertensive effects of ARL were studied for 12 weeks in spontaneously hypertensive (SHR) rats. Propranolol (PPL) was used as the reference drug. ARL (20 and 100 mg/kg per day, *p.o.*) and PPL (100 mg/kg per day, *p.o.*) treatments significantly decreased heart rate, within a week after the drug treatments had started and thereafter. Tail blood pressure (BP), determined by prewarming the rat at 50°C for 3 min, was slightly higher in the two ARL treated groups than in the control. Tail BP was slightly lower in the PPL treated group than in the control. Mean BP determined directly at the 12th week was lower in the two ARL and PPL groups than in the control by more than 20 mmHg. Both ARL (100 mg/kg per day) and PPL (100 mg/kg per day) treatments significantly reduced incidences of the vascular lesions, and also prevented the decrease of kidney weights usually associated with mild vascular lesions. Furthermore, these treatments showed a tendency to decrease plasma renin (PRC) and aldosterone (PAC) concentrations determined 20 h after the last administration. As mean BP must be more reliable than tail BP, it was concluded that ARL (20 and 100 mg/kg per day) showed almost the same chronic antihypertensive activity in SHR rats as PPL (100 mg/kg per day). Preventive effects of ARL on development of vascular lesions also supported the above view.

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