ADRENERGIC AND CHOLINERGIC REGULATION OF CORONARY VASCULAR TONE IN OLD DOGS

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Disturbances of the coronary circulation arise most frequently in elderly and old people. Until recently, however, no special analysis has been undertaken of the character of regulation of coronary vascular tone during aging. Adrenergic and cholinergic influences, either of the direct nervous or mediator type, are known to lower coronary vascular tone and to increase the coronary blood flow [3-6, 9, 11, 12].

Age differences in the response of the coronary vessels to adrenergic and cholinergic nervous stimulation and to administration of the mediator of the corresponding systems (catecholamines, acetylcholine) were studied in the investigation described below.

EXPERIMENTAL METHOD

Experiments were carried out on adult (2-5 years) and old (12-17 years) mongrel dogs weighing 13-26 kg, under thiopental (30 mg/kg) anesthesia without thoracotomy and during natural breathing. Changes in the regional vascular resistance were judged from changes in perfusion pressure during perfusion of the hemodynamically isolated vascular region with a constant blood flow [8]. The left coronary artery was catheterized with a metal catheter [10]. Parallel recordings were made of the pressure in the left ventricle and its first derivative, the systemic arterial pressure, and the resistance of vessels of the hind limb by means of a polygraph (Nihon Kohden, Japan). Postganglionic fibers of the stellate ganglion and the peipheral end of the divided vagus nerve were stimulated with square pulses of current from an ISÉ-01 stimulator through an isolating transformer. Noradrenalin, adrenalin, and acetylcholine over a wide range of doses (from 0.00001 to 5.0 μg) were injected into the extracorporeal coronary blood flow.

EXPERIMENTAL RESULTS

In the experiments of series I, threshold values of stimulation of postganglionic fibers of the stellate ganglion and the trunk of the right vagus nerve causing changes in coronary vascular tone in the experimental animals were determined. In all experiments both on adult and on old dogs, stimulation of these nerve fibers with a sufficiently strong current evoked coronary vasodilation. Meanwhile the threshold strength of stimulation causing changes in coronary vascular tone was higher in the old dogs. For instance, dilation of the coronary vessels in response to stimulation of postganglionic fibers of the stellate ganglion occurred in adult dogs when current with a voltage of 0.55 ± 0.03 V was used, compared with 1.2 ± 0.02 V in old dogs. The threshold of the vagus nerve effect on the coronary vessels was also raised in old age. For instance, coronary vasodilation developed in adult dogs when a current with a voltage of 0.4 ± 0.02 V was used, compared with 0.9 ± 0.03 V in old dogs (Fig. 1). During stimulation of threshold strength a change in coronary vascular tone occurred without any change in the hemodynamics or cardiodynamics.

With an increase in the strength of stimulation of postganglionic fibers of the stellate ganglion (0.8 ± 0.01 V for adult animals, 1.5 ± 0.03 V for old animals) and of the vagus nerve (0.6 ± 0.02 and 1.2 ± 0.02 V respectively) the systemic arterial pressure and vascular tone in the hind limb decreased. The maximal rate of rise of the intraventricular pressure, the maxi-

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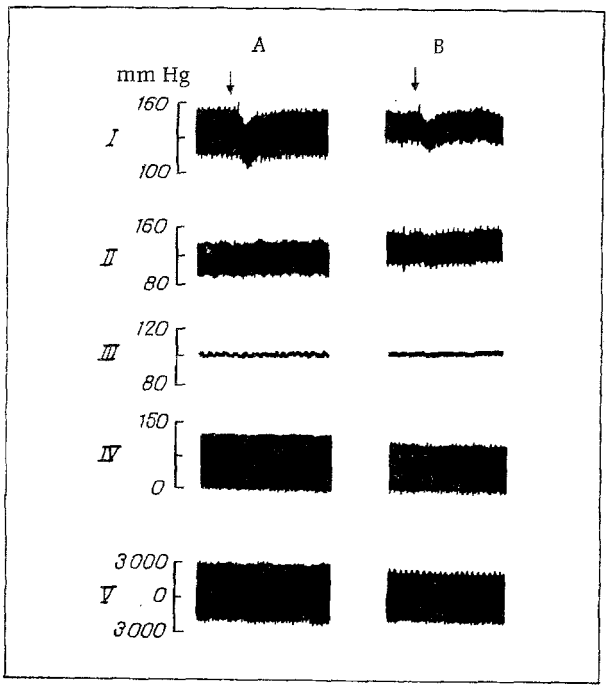

Fig. 1

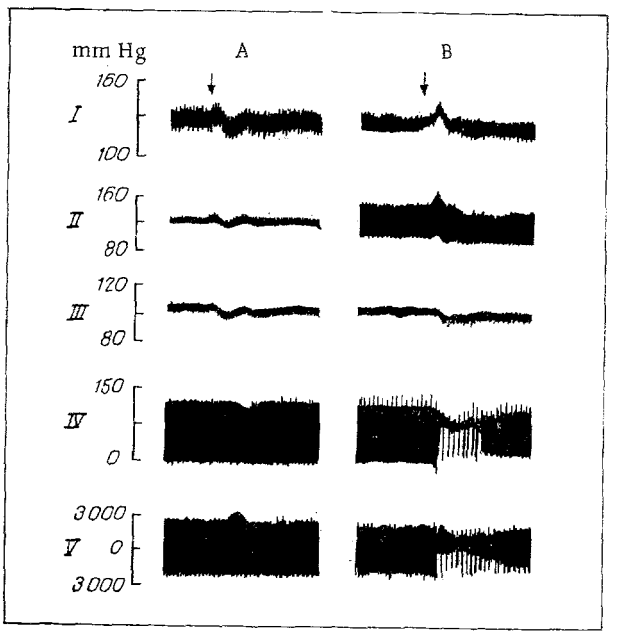

Fig. 2

Fig. 1. Effect of vagus nerve stimulation on coronary vascular tone in dogs of different ages. A) Adult dog (3 years), B) old dog (12 years). I) Perfusion pressure in left coronary artery, II) systemic arterial pressure, III) perfusion pressure in vessels of hind limb, IV) pressure in left ventricle, V) first derivative of intraventricular pressure.

Fig. 2. Effect of intracoronary injection of adrenalin on coronary vascular tone and on hemodynamics and cardiodynamics in dogs of different ages. A) Adult dogs (2.5 years), B) old dog (15 years). Remainder of legend as to Fig. 1.

mal rate of shortening of the myocardial fibers, and the index of contractility increased during stimulation of postganglionic fibers of the stellate ganglion, but decreased in response to vagus nerve stimulation.

Adrenergic and cholinergic effects are realized through the action of mediators — noradrenalin and acetylcholine. The response of the coronary vessels to catecholamines and acetylcholine was studied in a special series of experiments. They showed that the coronary vessels of old animals are more sensitive to the action of catecholamines and acetylcholine. For instance, the threshold dose of noradrenalin causing coronary vasodilation was 0.01 ± 0.002 µg in old dogs and 0.12 ± 0.02 µg in adult dogs. The threshold dose of adrenalin was 0.007 ± 0.001 and 0.015 ± 0.003 µg and of acetylcholine 0.005 ± 0.001 and 0.01 ± 0.002 µg respectively. With an increase in the doses of noradrenalin (0.4 ± 0.02 µg in old dogs and 0.5 ± 0.03 µg in adult dogs) and of acetylcholine (0.01 ± 0.002 and 0.035 ± 0.003 µg respectively) changes took place in the systemic arterial pressure, vascular tone in the hind limb, and the contractility of the myocardium.

During aging qualitative changes also arise in the response of the coronary vessels. In some of the old dogs (6 of 13) the coronary vessels constricted in response to 0.1 µg of adrenalin, and did not dilate. Meanwhile the myocardial contractility decreased (Fig. 2).

During aging, adrenergic and cholinergic nervous control of coronary vascular tone is thus weakened. The writers' previous investigations showed that this is connected with a decrease in the intensity of acetylcholine and noradrenalin synthesis in nerve endings [2, 7]. Even during prolonged and intensive stimulation of the vagus and sympathetic nerves in old animals, less mediator is secreted in the heart. Weakening of nervous influences on the heart and vessels also can be found in experiments without electrical stimulation of the vagus and sympathetic nerves (chemical and electrical stimulation of central nervous structures, reflex influences of the heart).

Coronary vasodilatation under conditions of strained function of the cardiovascular system plays an adaptive role, for it promotes an increase in the blood supply and an improvement in the metabolic provision for the intensively working myocardium. Weakening of nervous control over coronary vascular tone in old age limits this important adaptive reaction and may contribute to the development of the coronary insufficiency when the load on the myocardium is increased. The increase in sensitivity of the coronary vessels to catecholamines and acetylcholine in old age under conditions of weakening of adrenergic and cholinergic nervous control may also be adaptive in character.

Coronary vasoconstriction in old animals in response to certain doses of adrenalin is particularly important. Considerable release of adrenalin into the blood takes place during intensive activity, in stress situations, and during loads causing strengthening of the contractile function of the myocardium. Coronary vasoconstriction arising under these conditions under the influence of adrenalin may be a cause of the development of cardiac pathology in old age.

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