CORONARY VASOMOTOR RESPONSES TO CARDIAC SYMPATHETIC NERVE STIMULATION IN THE DOG TREATED WITH BETA ADRENOCEPTOR BLOCKING AGENTS

Fumio TAKENAKA and Takafumi ISHIHARA

Department of Pharmacology, Kumamoto University Medical School, Kumamoto, Japan

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It has been demonstrated that in anesthetized open-chest dogs pretreated with beta adrenoceptor blocking agents the cardiac sympathetic nerve stimulation produces a decrease in coronary blood flow which is abolished by alpha blockade (1-3). In the same condition a phenomenon of "rebound" increase in coronary blood flow was noticed after cessation of the stimulation (1, 2). The purpose of this communication is to elucidate the mechanism involved in this rebound phenomenon.

After thoracotomy under artificial respiration, the heart was exposed and a glass cannula was inserted into the left coronary circumflex artery via the left subclavian artery and perfused with blood led from the right common carotid artery. Coronary blood flow was recorded by means of an electromagnetic flowmeter, and blood pressure and left intraventricular pressure, with electronic manometers. The left ventral ansa subclavia, ventrolateral cervical cardiac nerve and right cervical vagosympathetic trunk were separated from surrounding tissue and the peripheral sites of the cut ends of each peripheral nerve were mounted on a pair of electrodes for stimulation. The parameters of the stimulation were 10 to 15 V in amplitude, 1 to 2 msec in duration and 2 to 20 sec in frequency. The left vagosympathetic trunk was kept intact so as not to impair vagus nerve supply to the heart.

When cardiac sympathetic nerves of the dogs pretreated with beta adrenoceptor blocking agents (propranolol and/or Kö 1366, 1-isopropylamino-3-(2-cyanophenox)-propanol, a newly developed beta adrenoceptor blocking agent) were stimulated a distinct decrease in coronary blood flow was obtained with little changes in blood pressure, left intraventricular pressure and heart rate. After cessation of the stimulation, an increase of coronary blood flow, appeared, that is a rebound phenomenon. Atropine, 0.5 to 1.0 mg/kg i.v. or hemicholinium, 1 to 2 mg/kg i.v. significantly reduced the poststimulatory increase in coronary blood flow while the initial decrease remained unaltered (Fig. 1). Phentolamine or benzylimidazoline, 2 to 5 mg given intracoronarily (i.c.) and 6-hydroxydopamine, 10 mg/kg i.v. completely abolished not only the initial decrease but also the following increase (Fig. 2). Physostigmine, 0.2 to 0.4 mg i.c. significantly potentiated the rebound and the associated bradycardia.

The initial decrease in coronary blood flow is likely due to stimulation of sympathetic vasoconstrictor nerves to the coronary vessels. The following poststimulatory
Fig. 1. Effect of atropine (0.5 mg kg, i.v.) on the poststimulatory increase in coronary blood flow (CBF) produced by stimulation of the left ventral ansa subclavia (AS) of the dog pretreated with propranolol 0.1 mg kg and Kø 1366 0.2 mg kg i.v. FBP: femoral blood pressure; LVP: left ventricular pressure; and HR: heart rate.

Fig. 2. Effect of phentolamine (2 mg, i.v.) on the decrease during stimulation and the poststimulatory rebound in coronary blood flow (CBF) induced by stimulation of the ventrolateral cervical cardiac nerve (VLCCN) of the dog pretreated with propranolol 0.1 mg kg i.v. Abbreviations, see Fig. 1.
increase is to be attributed to cholinergic vasodilator fibers (4, 5). Sympathetic nerve terminals are demonstrated in the vicinity of vagal ganglion cell bodies within the myocardium (6), and the terminals functionally liberate catecholamines which have an inhibitory effect on transmission through parasympathetic ganglia (7). It is considered that during sympathetic stimulation the transmission is inhibited via alpha adrenoceptors and on release a facilitation occurs which, in turn, produces a cholinergic dilatation of the coronary vessels.

REFERENCES

THE CONVERSION OF EXOGENTLY ADMINISTERED L-DOPA TO DOPAMINE IN THE STOMACH AND LIVER OF RATS

Yoshitsugu OSUMI, Ikuo WADA and Motohatsu FUJWARA
Department of Pharmacology, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto, Japan

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Dihydroxyphenylalanine(L-DOPA), a neurotransmitter precursor, is synthesized from tyrosine within chromaffin cells and adrenergic neurons (1). This amino acid has not, however, been detected in tissues and blood, probably due to the rapid conversion to dopamine. In 1966, Hakanson and Owman (2) discovered a large number of green fluorescent epithelial cells in the oxyntic gland area of rat stomach after treatment with L-DOPA and suggested that this green fluorescent material was dopamine converted from L-DOPA in the enterochromaffin-like cells.

The conversion of exogenously administered L-DOPA to dopamine in the stomach of rat has been chemically confirmed in the present studies. It was also shown that most of this amino acid was destroyed by the liver catechol-O-methyltransferase (COMT).

Methods and Materials: Male rats of Wistar strain weighing 180 to 250 g were used. Animals were fasted for approx. 16 hr prior to oral, intraperitoneal and intravenous administration of L-DOPA. Intravenous injection of L-DOPA to the femoral vein was done under pentobarbital sodium anesthesia. The intravenously and intraperitoneally

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