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Effect of Eledoisin on the Systemic Venous Return in Dogs.* (29770)

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A few investigators have recently studied the effects of synthetic eledoisin on the cardiovascular system in dogs(1-4). They found that eledoisin decreases systemic arterial pressure and total peripheral resistance, whereas this peptide increases cardiac output, regional arterial blood flow, myocardial contractile force, left atrial pressure and pulmonary arterial pressure. From these observations, however, it is rather difficult to explain the hemodynamic mechanism responsible for the increases in left atrial pressure and pulmonary arterial pressure, since cardiac output and myocardial contractile force were found to increase at the same period(4). To elucidate this problem, the present study was undertaken to investigate the effect of eledoisin on the systemic venous return in anesthetized dogs.

Methods. Dogs (18-24 kg) were anesthetized with i.v. injection of sodium pentobarbital (30 mg/kg). The chest was opened under artificial respiration in all dogs. *Group A:* In 6 dogs, cardiac output (CO), mean systemic arterial pressure (MSAP), mean pulmonary arterial pressure (MPAP), left atrial pressure (LAP), myocardial contractile force (MCF) and heart rate (HR) were measured continuously using the technic described previously(4). *Group B:* In 6 dogs, systemic venous return (SVR), MPAP and LAP were measured continuously using a technic depicted in Fig. 1. In this arrangement, blood was directed from the severed ends of the superior and inferior venae cavae to a calibrated venous reservoir, then through a Sigmamotor pump (Model TM2) to the right atrium, thus allowing direct measurement of the SVR. During a control period, cardiac input was equalized to the SVR by adjusting the flow rate of the Sigmamotor pump and kept constant throughout a period of the experiment. The cardiovascular effects of i.v. administration of 200 ng/kg of synthetic eledoisin were studied in all 12 dogs.

Results. The results of all experiments in each group are summarized in Table I. The results of the effects of eledoisin on systemic and pulmonary circulations (Group A) were essentially similar to those observed previously in this laboratory(4). A tracing of a representative experiment is illustrated in Fig. 2. Eledoisin decreased MSAP from a control value of 142 mm Hg to 108 mm Hg, whereas MPAP and LAP rose by 6 mm Hg and 1.2 mm Hg, respectively (Fig. 2). At the same time, CO, MCF and HR increased by 39%, 31% and 22 beats/min, respectively, whereas total peripheral resistance decreased by 33% of control. All the hemodynamic parameters returned toward control values approximately 15 to 20 minutes after injection of eledoisin.

The results of a representative experiment in Group B in which SVR was measured are shown in Fig. 3. Eledoisin decreased MSAP more markedly in Group B dogs than in Group A, although the peptide increased HR by almost the same degree. As eledoisin decreased MSAP, the blood volume in the reservoir increased markedly, indicating an increase in the SVR (Table I). During this period, eledoisin caused a slight decrease or essentially no change in MPAP and LAP. All the hemodynamic parameters including the level of the reservoir returned to controls within about 15 to 20 minutes after injection of eledoisin. Not infrequently the level of the

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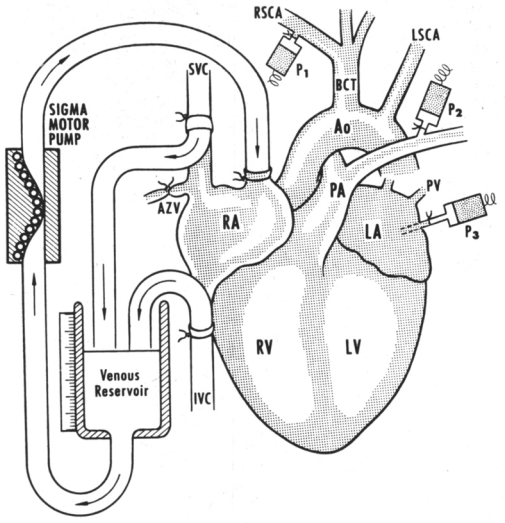

FIG. 1. Schematic representation of the technic used to measure systemic venous return. AZV: Azygos vein. SVC and IVC: superior and inferior vena cava. RA and LA: right and left atrium. RV and LV: right and left ventricle. PA and PV: pulmonary artery and vein. Ao: aorta. BCT: brachiocephalic trunk. RSCA and LSCA: right and left subclavian artery. P_1, P_2 and P_3: Statham pressure transducers.

reservoir reached below control before a complete recovery.

Discussion. It has been found that eledoisin is one of the most powerful vasodilators in dogs(1-4). The systemic hemodynamic changes observed following eledoisin are predominantly due to the primary vasodilator action of this polypeptide and also to the subsequent reflex sympathetic stimulation(4). Another vasodilator, nitroglycerin, decreases SVR, MPAP and LAP by possibly increasing the peripheral vascular capacitance(5,6). In contrast, from the present observations, eledoisin increases the SVR, MPAP and LAP by possibly decreasing the peripheral vascular capacitance. Recently, in this laboratory, it was found that eledoisin causes biphasic responses in arterial pressure in chickens, an initial slight decrease being followed by much greater increases in arterial pressure. The second pressor phase was usually abolished by the pretreatment of reserpine. Hence the question could be raised whether eledoisin may increase HR, MCF and SVR by increas-

TABLE I. Summary of Effects of Eledoisin on Heart Rate, Mean Systemic Arterial Pressure, Left Atrial Pressure, Mean Pulmonary Arterial Pressure and Cardiac Output (in Group A Dogs with Intact Circulation) or Systemic Venous Return (in Group B Dogs with Constant Cardiac Input). VR indicates maximal increase in systemic venous return derived from maximal increment in blood level of the venous reservoir after eledoisin. Figures represent maximal changes (Δ) of the parameters (mean ± S.E.).

Parameters	Group A (n = 6)	Group B (n = 6)
HR, Δ beats/min	+21 ± 3*	+19 ± 3*
MSAP, Δ mm Hg	−31 ± 4*	−51 ± 3*
MPAP, Δ mm Hg	+ 3 ± 1*	− 4 ± 2
LAP, Δ mm H_2O	+59 ± 3*	− 5 ± 1
CO, Δ %	+42 ± 2*	—
VR, Δ ml	—	+173 ±22*

* $p < 0.01$.

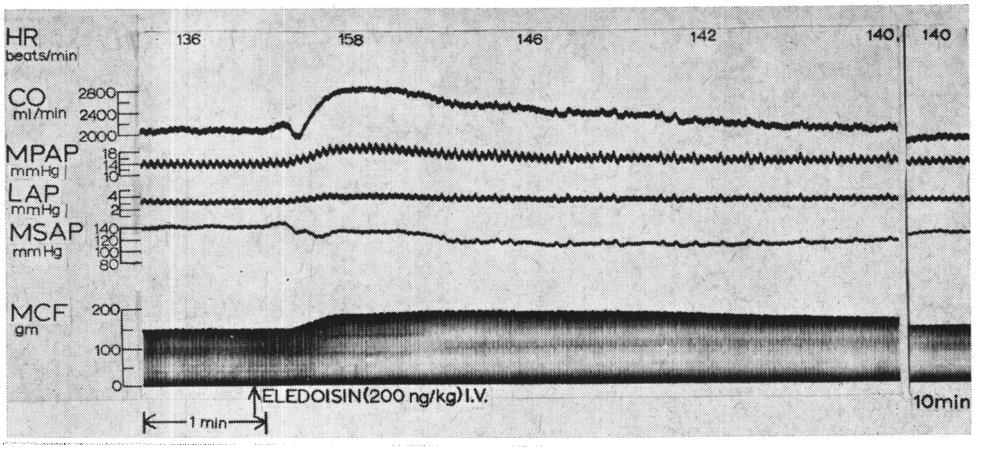

FIG. 2. Effects of eledoisin on heart rate (HR), cardiac output (CO), mean pulmonary arterial pressure (MPAP), left atrial pressure (LAP), mean systemic arterial pressure (MSAP) and myocardial contractile force (MCF) in a dog.

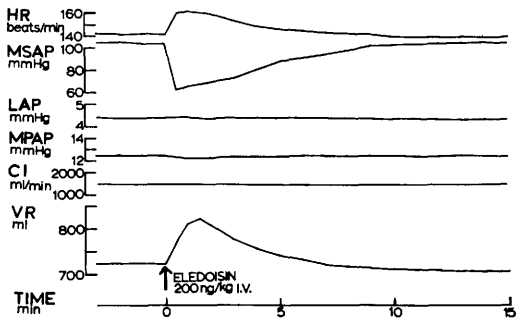

FIG. 3. Effects of eledoisin on heart rate (HR), mean systemic arterial pressure (MSAP), left atrial pressure (LAP), mean pulmonary arterial pressure (MPAP) and blood volume in venous reservoir (VR) in a dog. CI denotes cardiac input.

ing directly catecholamine secretion from the sympathetic post-ganglionic nerve endings and/or adrenals in dogs. Even if eledoisin would stimulate catecholamine secretion directly in dogs, the magnitude of this effect might be much smaller than in chickens or its effect might be overshadowed by the direct vasodilator action, since eledoisin decreases MSAP markedly and increases LAP and MPAP significantly(7). In contrast, it was found in this laboratory that electrical stimulation of cardiac sympathetic nerves or administration of norepinephrine usually increases MSAP and MPAP and decreases LAP. The present study indicates that the rises in LAP and MPAP are due to the increase in SVR by eledoisin. It remains uncertain, however, whether eledoisin decreases the peripheral vascular capacitance by the greater vasodilatation in the postcapillary arterioles(7), or whether eledoisin increases the arteriolovenular communications which exist physiologically in the peripheral vascular beds(8,9).

Summary. The effects of eledoisin on the cardiovascular system were studied in anesthetized dogs. It was found that eledoisin decreased MSAP and increased HR, CO, MPAP, and LAP. In addition, when cardiac input was kept constant by means of a Sigmamotor pump, eledoisin increased the blood level of the venous reservoir, indicating an increase in SVR. The increases in MPAP and LAP observed after eledoisin are most likely due to the increase in SVR.

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Effect of Prostaglandin E$_1$ on Blood Pressure, Heart Rate and Concentration of Free Fatty Acids of Plasma in Man.* (29771)

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The vasodepressor and smooth muscle stimulating activity discovered in extracts from seminal fluid and from male accessory glands(1,2,3,4,5) was named prostaglandin.

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