MECHANISM OF DECREASED VENOUS RETURN WITH NITROGLYCERIN

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It has been widely accepted that nitroglycerin (NG) causes a redistribution of the myocardial nutritional circulation and the mechanism could account for relief of angina pectoris by NG (1). In addition, some possible other extracoronary mechanism may be affected by a systemic administration of NG. Albad and Mellander (2) and Mason and Braunwald (3), showed that NG has a more pronounced dilator effect on the capacitance vessels than on the resistance vessels. They then inferred that this mechanism could be responsible for decreased venous return by NG administration (preload). Furthermore, it has been demonstrated by other investigators (4, 5, 6) that end-diastolic left ventricular volumes decrease and left ventricular filling pressure lowers resulting in decrease on the work load and oxygen requirement of the heart after NG administration. The studies mentioned above, however, failed to elucidate the primary site of action in which NG caused extracoronary decrease of preload or afterload.

In the present experiment, the effect of NG on systemic and pulmonary vascular bed was examined to study its mode of action under controlled cardiac output with a mechanical left ventricle devised by Rose et al (7). Eight mongrel dogs of both sexes weighing from 10.5 to 14.5 kg (average 12.0 kg) were anesthetized with 30 mg/kg of sodium pentobarbital injected intravenously. Chests were kept open under artificial respiration, and the left ventricule was replaced by a Sigmamotor pump (TM-5), which maintained constant cardiac output (60–70 ml/kg/min). With this pump, blood in a reservoir taken from another donor dog is pumped up and allowed to flow into the descending aorta. The blood then circulates through the whole body and returns to the reservoir passing through the cannula inserted into the left auricle. Systemic arterial pressure (FAP), femoral venous pressure (FVP), left auricular outflow (LAO), superior vena-caval flow (S-VCF), inferior vena-caval flow (I-VCF) were measured using a pressure transducer (Nihon Kohden MP-3A, RP-3) and a electromagnetic flowmeter (Nihon Kohden MF-2) and were recorded on a 8-channel, ink-writing oscillograph (Nihon Kohden WI-380). The drug was injected intra-aortically through the cannula inserted into the descending aorta. Since dogs were perfused at constant cardiac output, we could assume that changes in venous flow and blood pressure following injection of drugs reflect phenomena caused by direct action of the venous system. Venous return to the left heart from lesser circulation was termed LAO, direct venous return from the upper half of the body, S-VCF, and direct venous return from the lower half body,
I-VCF. The total of the latter two parameters was considered as the total venous return to the right heart from the systemic circulation. The drug used was NG (Nippon Kayaku). Data were analyzed statistically using the Student’s t-test modified for paired replicates. Only P values below 0.05 were considered significant.

Changes by intra-aortic administration of NG (50 μg/kg) are shown in Fig. 1. The marked decrease in LAO (P<0.05) that occurred during the first three minutes after NG administration indicates the decrease in venous return to the left heart. Later LAO gradually increased to become stable at a level slightly above the control flow. Total venous return to the right heart, however, showed only an insignificant increase and was significantly different (P<0.05) from LAO during the first two minutes. NG caused a significant decrease in FAP (P<0.01), but in S-VCF and I-VCF it caused a slight and insignificant increase. FVP remained fairly constant during NG administration.

The flow rate of LAO can be determined by several factors: venous return to the right heart, functions of the right ventricle, and capacitance of the pulmonary vascular bed. In the lung, there are high capacitance vascular beds that can be regulated by several agents and physiological conditions. The lung may be regarded as a reservoir that can store or release large quantities of blood (8, 9). In the case of drugs that have no marked effects on the right ventricle and pulmonary vessels, for instance a small dose of Adr (10), changes in LAO could cor-

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**FIG. 1.** Effect of NG (50 μg/kg) on systemic and cardiopulmonary hemodynamics in dogs examined under controlled cardiac output with a mechanical left ventricle. Average change (±S.E.) of FAP, LAO, S-VCF, I-VCF, FVP and total of S-VCF and I-VCF following NG intra-aortically administration expressed as relative changes from the control values in eight experiments.

FAP: mean femoral arterial pressure
LAO: mean left auricular outflow
S-VCF: mean superior vena-caval flow
I-VCF: mean inferior vena-caval flow
FVP: mean femoral venous pressure
respond to changes in the venous return to the right heart. It is necessary, however, to analyze changes in LAO more extensively when drugs that have marked effects on the right ventricle and pulmonary vessels are administered. Therefore, it is imperative to distinguish the venous return to the right heart from that to the left (LAO) when discussing the relationship between the left ventricle loading and the systemic circulation. In our experiment, NG administration decreased LAO despite a slight increase of total venous return to the right heart, resulting from a pharmacological phlebotomy induced in the pulmonary circulation (11). Müller and Rørvik (12) showed that pulmonary capillary pressure, left auricular pressure and left ventricular enddiastolic pressure increased when anginal episodes were rapidly released by NG. Further, Ferrer, et al (13) confirmed the thesis that NG constricted the splanchnic vascular bed but induced vasodilatation of the pulmonary and peripheral areas.

The present study indicates that decrease in LAO has beneficial effects in cases of anginal attack as a result of a reduction in left ventricular loading. It is suggested that the decrease induced by pulmonary vasodilatation may be the primary mode of action of NG in the relief of angina pectoris.

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