PHYSIOLOGY

Role of Relative Changes in Caval Flows for Evaluation of Right Atrial Pressure Shifts Induced by Nitroglycerin

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Experiments on cats treated with nitroglycerin showed dynamic relationship between changes in caval venous flows: blood flow increased in the superior vena cava and decreased in the inferior vena cava. Blood pressure in the right atrium either decreased, or increased. No significant changes in total venous return were observed during maximum shifts in right atrial pressure, while contractility of the right ventricular myocardium usually decreased. Our findings suggest that the direction of the right atrial pressure shifts induced by nitroglycerin does not depend on venous return, but is determined by the prevalence of flow changes in the superior vena cava or inferior vena cava.

Key Words: *superior and inferior caval vein flows; right-atrial pressure*; *right ventricular contractility*; *venous return*; *arterial blood pressure*; *nitroglycerin*

Nitroglycerin is used in clinical practice for more than 100 years. This drug is routinely prescribed to patients with coronary heart disease. According to accepted views, hemodynamic effects of this preparation are associated with its potent vasodilating effect leading to a decrease in venous return to the right ventricle, right atrial pressure, preload, and thereby reducing myocardial oxygen demand [4]. However, recent clinical studies showed that the positive hemodynamic and clinical effects of nitroglycerine can not be merely attributed to venous dilation and decreased preload to the heart [6,7]. There is evidence that nitroglycerin did not decrease left ventricular end-diastolic volume [8], but can increase left atrial pressure [7]. In the earlier studies [2] it was established that the value and direction of peak shifts in right atrial pressure induced by systemic catecholamines depends on the proportion between venous return and right ventricular contractility. It was also of interest to study the relationship between these parameters during injection of nitroglycerin.

MATERIALS AND METHODS

The study was performed on 13 artificially ventilated open-chest cats (3.5-5.0 kg) anesthetized with Nembutal (35-40 mg/kg, intramuscularly). Right atrial (RAP) and ventricular pressures were measured with a low-pressure transducers based on 6MD11S and 6MD1B mechanotrons [1,3] using catheters introduced into cardiac chambers via the right auricle. Systolic and diastolic RAP were continuously recorded and mean RAP was calculated from these peak and valley magnitudes using an integrator. Right ventricular contractility was evaluated by the first derivative of right ventricular pressure (dP/dt_{max}) using an analog differentiator [5]. Blood flows in the superior (cranial) and inferior (caudal) caval veins were measured with a T-230 Transonic dual-channel ultrasonic cuff gage flowmeter. Venous return was calculated as the sum of two caval flows. Cardiac output (CO) was measured in the ascending aorta with a MFV-2100 Nihon Koh-

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den electromagnetic cuff gage flowmeter. Arterial blood pressure (ABP) was measured in the left femoral artery using a 6MD1B mechanotron transducer [1]. Total peripheral vascular resistance was calculated by Poiseuille's formula: (ABP-RAP)/CO. Nitroglycerin was injected into the left femoral vein in a dose of 10 μg/kg. This dose of nitroglycerin decreased ABP by about 25-30%. The test parameters (ABP, RAP, right ventricular contractility, CO and flows in the superior and inferior vena cava) were recorded with a N-338-8P ink-pen recorder. The data were statistically analyzed with originally designed and standard Axum 5.0 and Math. Soft. Inc. software using Student's *t* test.

RESULTS

Intravenous injection of nitroglycerin produced a decrease in ABP and total peripheral vascular resistance in cats by about 30%, blood flow increased by 20-25% in the superior vena cava and decreased by 6-8% in the inferior vena cava. These shifts were accompanied by opposite changes in RAP: this parameter decreased by -10±2% in 4 cats (group 1) and increased by 26±5% in 7 cats (group 2). In 2 cats nitroglycerin did not affect RAP.

In both groups the shifts in RAP peaked 8-12 sec postinjection. On the 40th sec RAP and blood flow in the superior vena cava returned to initial values, while blood flow in the inferior vena cava and total venous return remained decreased. The latter parameters recovered only on 90-100 sec postinjection. Thus, the time course of RAP changes differed significantly from the dynamics of the superior and inferior vena cava flows. In order to clarify possible mechanisms of opposite changes in RAP the relationships between the superior and inferior vena cava flows and right ventricular contractility at the peak of RAP responses were analyzed.

Nitroglycerin induced similar increase in the superior vena caval flow in both groups of cats (by 10±2 and 11±2 ml/min, respectively; Table1). At the same time, blood flow in the inferior vena cava decreased by 11±2 and 7±2 ml/min in groups 1 and 2, respectively. Changes in the total venous during maximum shifts were insignificant (-1±2 and 4±3 ml/min, Table 1) and can not be responsible for the pronounced and opposite shifts in RAP (26±5 and -10±2% in groups 1 and 2, respectively). The correlation analysis also revealed no relationships between RAP and venous return in both groups (r=0.01 and r=0.08, respectively). Since the nitroglycerine-induced decreases in right ventricular contractility were similar in both groups (-13±4 and -9±3 mm Hg/sec), the observed shifts RAP did not depend on this parameter.

Thus, the direction of maximum shifts in RAP induced by nitroglycerin did not depend on changes in total venous return and right ventricular contractility. It should be noted that the term "venous return" has no physiological sense, because in the whole organism the blood enters the right atrium via two caval veins. Blood flows in these viens are opposite and differed in magnitude (superior vena cava flow is about half as great as inferior vena cava flow). Thus, the nitroglycerine-induced shifts in RAP are determined by interaction between the two counter flows from the superior and inferior venae cavae (taking into account their opposite directions and dynamic pressure components) rather than by the "formal" sum of two flows (total venous return). Our findings confirmed the absence of the sucking function of the right atrium with respect to the mean venous return [2,3]. It can be hypothesized that the amount of the blood pumped by the heart into

TABLE 1. Changes in RAP, caval venous flows, and right ventricular contractility in Response to Intravenous Injection of Nitroglycerin (10 μg/kg) in Cats (*M*±*m*)

Parameter	Group 1 (*n*=4)		Group 2 (*n*=7)	
	initial value	abs. changes	initial value	abs. changes
RAP, mm Hg	5.4±0.9	-0.40±0.02	4.1±0.5	0.90±0.05
SVCF, ml/min	56±11	10±2	57±4	11±2
IVCF, ml/min	121±21	-11±2	149±12	-7±1
Σ VR, ml/min	177±30	-1±2*	206±12	4±3*
RVC, mm Hg/sec	450±44	-13±4	454±22	-9±3
CO, ml/min	179±26	3±2*	210±16	5±3*
TPVR, arb. units	0.71±0.03	-0.26±0.02	0.46±0.02	-0.14±0.01
ABP, mm Hg	133±26	-43±5	101±7	-25±6

Note. SVCF: superior vena caval flow; IVCF: inferior vena caval flow; Σ VR — total venous return; RVC: right ventricular contractility (*dP/dt*); TPVR — total vascular resistance; *n* — number of animals. Changes in parameters were measured at the maximum of RAP shifts. *p>0.05 compared to the initial level.

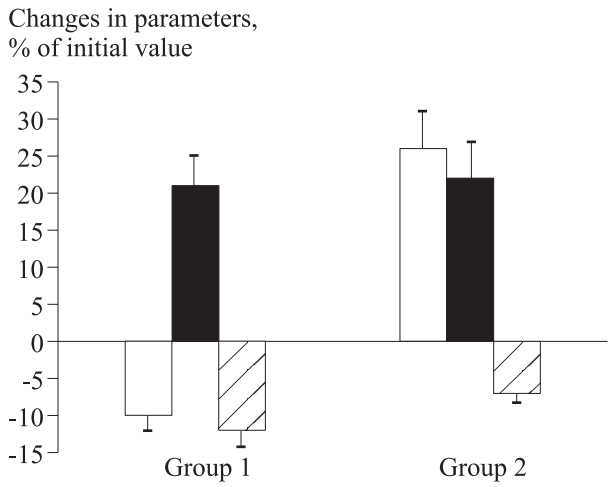

Fig. 1. The relationship between maximum shifts in right atrial pressure (RAP, light columns) and simultaneous flow changes in the superior (dark columns) and inferior vena cava (dashed columns) induced by nitroglycerin (10 μg/kg). Group 1: cats with a decrease in RAP. Group 2: cats with an increase in RAP.

the arterial bed corresponds to instant requirements under particular hemodynamic conditions. The function of the venous system is to provide enough blood supply to the heart. Regulation of venous supply is determined by counter flows from the two caval veins, one caval flow always increases under the effect of vasoactive substances. This is confirmed by the fact that despite the decrease in ABP and total peripheral resistance, intravenous nitroglycerine almost always increases blood flow in the superior vena cava and decreases it in the inferior vena cava, though the magnitude of these changes are different. The mechanisms underlying the increase in the superior vena caval flow caused by nitroglycerin or catecholamines require special investigations.

The maximum RAP responses (-10±2 and 26±5%) were associated with similar increase in the superior vena caval flow (21±4 and 22±5%) and similar reduction of right ventricular contractility in both groups (Fig. 1, Table 1). However, blood flow in the inferior vena cava decreased to a different extent. In group 1, this decrease (-12±2%) corresponded to the decrease in RAP, and approximately 2-fold surpassed that in group 2 (-7±1%; Fig. 1). These results suggest that the value and direction of peak shifts in RAP depend only on the relative contributions of the counter flows in the superior and inferior caval veins. If blood flow in the superior vena cava increased to a greater extent compared to slight decrease in the inferior vena caval flow, then RAP increased. Similar flow shifts in the superior vena cava led to a decrease in RAP, if the reduction of blood flow in the inferior vena cava was more pronounced than in the previous case.

In summary, our results indicate that the direction of RAP shifts at their maximum depends on the relative values of counter blood flows in the superior and inferior caval veins. Similar increases in the superior vena cava flow were usually accompanied by a decrease in right ventricular contractility in both groups of cats. The direction of RAP shifts did not depend on both the direction and value of changes in total venous return. In cats with a decrease in RAP in response to nitroglycerin a 2-fold greater reduction in the inferior vena caval flow was observed, compared to animal responding by an increase in RAP due increased superior vena caval flow.

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