PHYSIOLOGY

Role of Vascular System Adrenoceptors in Formation of Venous Return

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In experiments on cats electromagnetic flowmetry showed that contribution of the blood flow in the anterior and posterior cava venae to the formation of venous return during stimulation of adrenoceptors with catecholamines is determined by the dynamics of systemic pressor reactions. At the moment of maximum elevation of blood pressure, the major role is played by blood flow changes in the anterior vena cava, while the posterior vena cave plays the predominant role during the period of maximum venous return. Under the action of α- and β-adrenoceptor blockers, venous return is predominantly formed by the blood flow in the posterior vena cava independently on the dynamics of systemic depressor reactions. Adrenoceptor blockade modulates the structure of venous return formation in response to catecholamines: α-adrenoceptor blockade reduced the role of anterior vena cava blood flow and increased that of posterior vena blood flow in the formation of venous return, while β-adrenoceptor blockade induced opposite changes. It is concluded that α- and β-adrenoceptors predominantly control changes in the blood flow in the anterior and posterior cava venae, respectively.

Key Words: *venous return; blood flow; anterior vena cava; posterior vena cava; catecholamines; adrenoceptor blockers*

The mechanisms related to activation of α- and β-adrenoceptors in the cardiovascular system are important elements involved in the formation of venous return, one of the most important parameters of the circulatory system [4,5]. The action of stimuli of different modality associated with activation of α- and β-adrenoceptors on the circulatory system is usually followed by an unambiguous systemic pressor or depressor reaction [2]. However, the involvement of the adrenoceptor structures into the formation of venous return at the systemic level remains little studied.

Our aim was to study the adrenoceptor pathway of the regulation of venous return by evaluating quantitative parameters of contribution of the blood flow in the anterior and posterior cava venae into the formation of changes in venous return induced by α- and β-adrenoceptor activators and inhibitors on the circulatory system.

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MATERIALS AND METHODS

Experiments were carried out on cats (n=21) narcotized with urethane (1.00 g/kg) and chloralose (0.01 g/kg) under conditions of open thorax, artificial ventilation with a VITA-1 apparatus and heparin treatment (1000 U).

Systemic blood pressure was measured in the left subclavian artery with an EMT-34 electronic manometer (Elema-Siemens). Blood flow in anterior and posterior cava venae was measured with

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cuff-type transducers of a MFB-2100 electromagnetic flowmeter (Nihon Kohden). The total venous return was calculated using an AVK-31 computer system.

In group 1 cats, changes in hemodynamic parameters were measured after administration of adrenoceptor agonists epinephrine (20 μg/kg) and norepinephrine (10 μg/kg) inducing systemic pressor reactions, or nonselective adrenoceptor blockers (α-adrenoceptor blocker phentolamine (regitine), 0.2 and 0.3 mg/kg, and β-blocker propranolol, 0.3-0.5 mg/kg) inducing depressor changes. In group 2 cats, we compared parameters characterizing the contribution of each vena cava to venous return under the action of adrenomimetics before and after administration of α-and β-adrenoceptor blockers. The drugs were injected into the femoral artery. Changes in the blood flow in the cava venae and total venous return are given in absolute units (Δ, ml/min), because these values allow evaluation of individual role of each vena in the formation of venous return [2].

The data were processed statistically using Student's *t* test, taking into consideration the dynamics of systemic reactions in the most characteristic moments of their development in circulatory system: during the maximal changes in systemic arterial pressure and during the maximum change in venous return [1].

RESULTS

Catecholamines elevated systemic blood pressure by on average 25% relative to the initial value and produced an equal increase in venous return (Table 1). The structure of venous return formed by the blood flow changes in the anterior and posterior cava venae significantly differed during the development of systemic reaction. During the initial period of these reactions referred here as maximum blood pressure rise, the most pronounced changes in venous return were significantly determined by blood flow variations in the anterior vena cava (67.8 and 78.6% under the effect of epinephrine and norepinephrine, respectively, $p<0.001$) compared to those in the posterior cava vena (32.2 and 21.4%, respectively). To the moment of maximal elevation of venous return, the contribution of blood flow changes in the anterior vena cava into venous return significantly decreased (29.5 and 29.6% in response to epinephrine and norepinephrine, respectively), while the contribution of blood flow in the posterior vena increased (up to 70.5 and 70.4% in response to epinephrine and norepinephrine, respectively). Therefore, the maximum changes in venous return induced by catecholamines resulted

TABLE 1. Effect of Adrenomimetics and Adrenoceptor Blockers on Blood Flow in Cava Venae and on Their Contribution to Total Venous Return (*M*±*m*)

Pharmacological agent	Maximal shifts in arterial pressure (Δ, ml/min)			Time of maximum in arterial pressure, sec	Maximal shifts in venous return (Δ, ml/min)			Time of maximum in venous return, sec
	total venous return	blood flow in anterior vena cava	blood flow in posterior vena cava		total venous return	blood flow in anterior vena cava	blood flow in posterior vena cava	
Epinephrine (20 μg/kg, *n*=9)	23.6±7.4	16.0±3.1 (67.8%)	7.6±4.7 (32.2%)	51±2	49.1±7.0	14.5±3.0 (29.5%)	34.6±7.5 (70.5%)	90±7
Norepinephrine (10 μg/kg, *n*=14)	21.5±5.0	16.9±2.0 (78.6%)	4.6±4.0 (21.4%)	43±2	43.9±7.5	13.0±2.0 (29.6%)	30.9±5.0 (70.4%)	82±5
Phentolamine (0.2, 0.3 mg/kg, *n*=12)	-23.6±5.4	-1.4±2.2 (5.3%)	-24.9±3.1 (94.7%)	80±6	-31.4±3.6	-4.6±1.7 (14.6%)	-26.8±2.9 (85.4%)	105±9
Propranolol (0.3-0.5 mg/kg, *n*=9)	-40.8±9.2	-4.5±5.0 (11.0%)	-36.3±9.1 (89.0%)	117±21	-46.8±8.4	-8.3±5.2 (17.7%)	-38.5±8.2 (82.3%)	145±12

Note. The contribution to the changes in total venous return is shown in parenthesis.

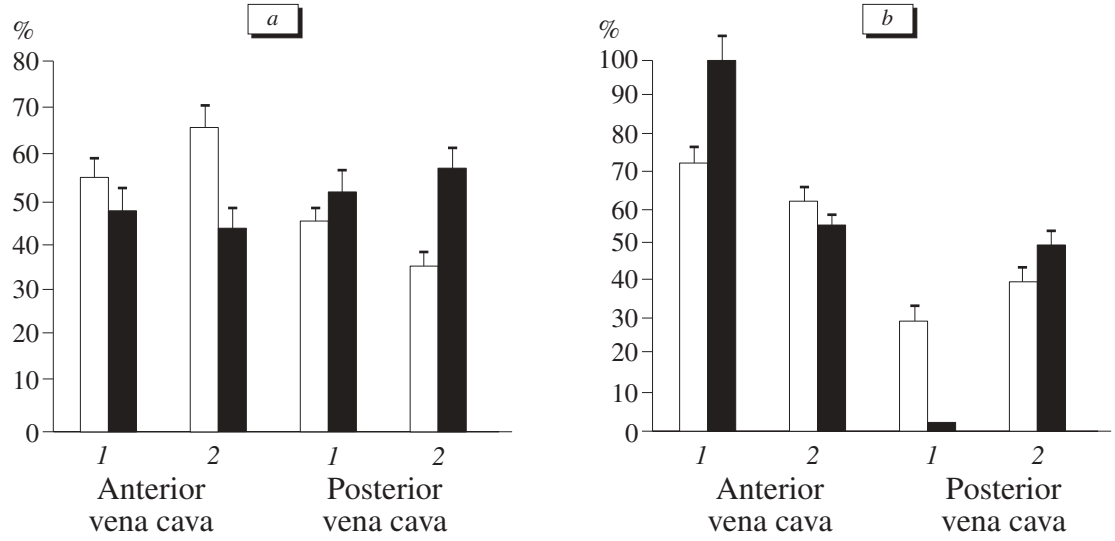

Fig. 1. Effect of blockade of α- (*a*) and β-adrenoceptors (*b*) on epinephrine-induced changes in contribution of cava venae into venous return. Open and solid bars show contribution of the venas into venous return during maximum rise of systemic arterial pressure (*1*) and maximal rise of venous return (*2*) before and after blockade of adrenoceptors, respectively.

predominantly from blood flow changes in the posterior vena cava.

Adrenoceptor blockers induced the systemic depressor reactions. Phentolamine and propranolol decreased blood pressure by 37.5±2.5% and 29.6± 9.0%, respectively. These changes were accompanied by blood flow decrease in both vena cavae and a decrease in total venous return; changes induced by β-adrenoceptor blocker were more pronounced (Table 1). The adrenoblocker-induced changes in venous return resulted from moderation of blood flow in each vena independently on the time course of system reactions (Table 1). The contribution of the anterior vena cave into venous return tended to increase to the moment of its maximum shift compared to the moment of maximum blood pressure drop. For example, changes in blood flow in the anterior vena cave induced by α-adrenoceptor blocker contributes 5.3% and 14.6% into the decrease of total venous return to the moment of maximal depressor reaction and the greatest drop in venous return, respectively. Similarly, the contribution of the anterior vena cava into β-blocker-induced changes in total venous return increased from 11.0 to 17.7%. The contribution of the posterior vena cave into the total venous return decreased proportionally.

Blockade of α-adrenoceptors produced different changes in the contribution of the cava venae into venous return at different moments of the development of the epinephrine-induced systemic reactions. The contribution of both vessels into the total venous return virtually did not change at the time of maximum blood pressure rise; at the moment of maximal increase of venous return, the contribution of the posterior vena cava into venous return tended to decrease (by 4.3%), while the contribution of anterior vena cava proportionally increased. Norepinephrine (Fig. 1, *a*) decreased the contribution of blood flow in the anterior vena cava into the total venous return by 6.4% during maximum blood pressure (the contribution of posterior vena cava increased proportionally), although significant changes (by 21.5%, $p<0.02$) were observed only at the moment of maximum increase in venous return.

Under conditions of β-adrenoceptor blockade (*i.e.*, during relative growth of α-receptors activity) we observed more clear shifts in the contribution of the cava venas into changes in venous return induced by each catecholamine. Before adrenoceptor blockade changes in venous return induced by epinephrine at the moment of maximum blood pressure resulted from changes in blood flow in the anterior and posterior vena cava by 73.1% and 26.9%, respectively. However, during β-adrenoceptor blockade, similar changes in venous return resulted by 100% from the rise of blood flow in the anterior vena cava. The contribution of the posterior vena cava into venous return increased significantly by 17.3% to the moment of the greatest rise of venous return ($p<0.05$). Similar changes were induced by norepinephrine during blockade of β-adrenoceptors (Fig. 1, *b*). To the moment of maximum blood pressure, the contribution of the anterior vena cava into changes in total venous return increased from 71.1 to 100%, while to the time of maximum venous return, the contribution of the posterior vena cava increased by 87% (respectively, the contribution of anterior vena cava decreased by the same value).

Thus, the structure of venous return is different during stimulation or blockade of α- and β-adrenoceptors in the cardiovascular system. Our experiments demonstrated significant effect of the adrenoreceptor structures on the contribution of anterior and posterior vena cavae into venous return during application of adrenoceptor agonists: α-adrenoceptors primarily determine the contribution of the anterior vena cava, while β-adrenoceptors primarily affect the role of posterior vena cava in this process. In animals with intact or blocked vascular adrenoceptors, the quantitative peculiarities in the effects of epinephrine and norepinephrine depend probably on the specific action of each catecholamine on α- and β-adrenoceptors in individual tissues and organs [3].

The peculiarities of the contribution of each vena cava into the total venous return during the action of stimulators or blockers of the adrenoceptors, and the effect of α- and β-adrenoceptors on the structure of changes in venous return are probably determined by differences in the degree of changes in regional components of the total peripheral resistance in the brachiocephalic and thoracic aorta basins, which redistribute cardiac output between these regions and produce the shifts of the blood flow in the corresponding cava venae [2].

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