PHYSIOLOGY

Comparative Analysis of Direction, Value, and Duration Atrial Pressure of Shifts Caused by Depressor Agents

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Shifts in right- and left-atrial pressure after administration of acetylcholine, histamine, or isoproterenol to cats were oppositely directed in 69% cases; both parameters decreased in 11% cases (changes were more pronounced in the right atrium) and increased in 20% cases (similar shifts). Changes in the left-atrial pressure persisted for a longer time (compared to those in the right atrium) and their dynamics was similar to that of venous return and cardiac output.

Key Words: *right-atrial pressure; left-atrial pressure; venous return; cardiac output; depressor stimuli*

It is widely accepted that atrial pressure characterizes changes in preload caused by shifts in venous return to the right and left ventricles, which determines the cardiac output [3,5]. However, some clinical observations and experiments on cats and fishes treated with vasoactive agents showed the absence of interrelation between cardiac output and right- and left-atrial pressure [1,4,6]. We previously showed that changes in atrial pressure caused by intravenous injection of catecholamines to cats were co-directed and opposite in 70 and 30% cases, respectively, while shifts in venous return and cardiac output were always co-directed [2].

Our aim was to compare changes in direction, amplitude, and duration of shifts in atrial pressure in cats after intravenous injection of depressor agents acetylcholine, histamine, and isoproterenol.

MATERIALS AND METHODS

Experiments were carried out on 18 cats weighing 3.5-5.0 kg. The thorax was opened under nembutal narcosis (35-40 mg/kg intramuscularly) and artificial ventilation. Blood pressure was measured in the left femoral artery with a PDP-400-PA transducer. Atrial pressure was measured with Baxter transducers passed into the atria via the auricles. Instantaneous atrial pressure was recorded, and the mean atrial pressure was calculated from its maximum and minimum values. Venous return to the heart was calculated as the sum of blood flow in the anterior and posterior cava veins measured by cuff transducers of a T-206 (Transonic) ultrasonic flowmeter. Cardiac output was measured in the ascending aorta by a T-106 ultrasonic (Transonic) ultrasonic flowmeter. HR was calculated by *R—R* intervals obtained from standard ECG recorded in II standard lead. Depressor agents acetylcholine (0.001 μg/kg), histamine (0.001 μg/kg), and isoproterenol (2.5 μg/kg) were successively administered into the left femoral artery as bolus injections. First, acetylcholine was applied, after recovery of the examined parameters to the baseline and histamine and isoproterenol were tested. These agents decreased blood pressure by 40-50% relatively to the baseline.

The examined parameters (blood pressure, right- and left-atrial pressure, venous return, and cardiac

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output were recorded on an N-338-8P pen-ink plotter. Statistical analysis used the values measured in each experiment during maximum shift in the right-atrial pressure, because the differences between the time points corresponding to maximum changes in the atrial pressure values were insignificant. The data were analyzed statistically using Student's *t* test, standard Axum 5.0, and original software.

RESULTS

Intravenous injection of acetylcholine, histamine, or isoproterenol produced different shifts in atrial pressure: in 11% cases both parameters decreased (group 1); in 20% cases both parameters increased (group 2); in 22% cases the right-atrial pressure decreased and the left-atrial pressure increased (group 3), and in 47% cases the right-atrial pressure increased and the left-atrial pressure decreased (group 4). In other words, the used depressor agents produced opposite changes in atrial pressure in 69% cats and co-directed shifts in 31% cats.

In group 1 cats, the examined agents decreased the right- and left-atrial pressure by 14±8 and 7±2% (acetylcholine), by 15±5 and 12±2% (histamine), and by 20±4 and 9±4% (isoproterenol), respectively (Fig. 1). Therefore, the right-atrial pressure in this group was approximately the same irrespective of the chosen depressor agents. Similar regularity was observed for the left-atrial pressure. However, the pressure drop was more pronounced in the right atrium (Fig. 1). In cases of parallel increase in left- and right atrial pressure (observed in group 2 cats only with acetylcholine), these shifts were similar (14±4 and 12±3%, respectively). Thus, there was no general regularity in the changes of both atrial pressure values during their unilateral changes caused by the depressor agents.

In group 3 cats, the test substances decreased the right- and increased the left-atrial pressure by 17±5 and 9±4% (acetylcholine), by 11±3 and 9±5% (histamine), and by 11±3 and 28±9% (isoproterenol), respectively (Fig. 2). Thus, in this group the shift in right-atrial pressure was insignificant for all examined agents. Acetylcholine and histamine equally increased the left-atrial pressure, while isoproterenol produced a more pronounced pressure rise (Fig. 2). In group 4 cats, the test substances increased the right- and decreased the left-atrial pressure by 15±3 and 8±2% (acetylcholine), by 18±4 and 11±2% (histamine), and by 9±2 and 15±4% (isoproterenol), respectively (Fig. 3). In this group, acetylcholine and histamine equally shifted the right- and left-atrial pressure. By contrast, after injection of isoproterenol pressure rise in the right

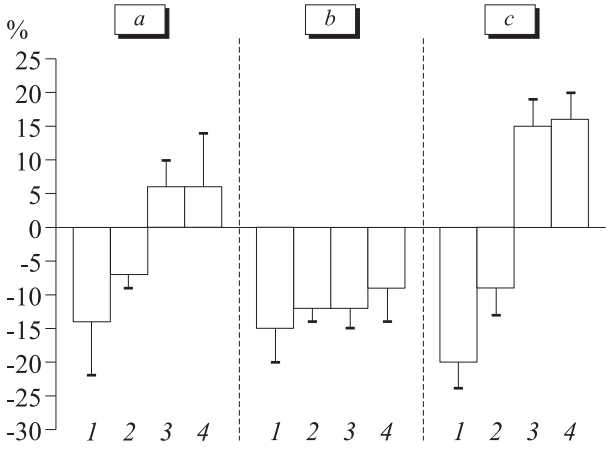

Fig. 1. Direction and degree of changes in atrial pressure, venous return, and cardiac output after injection of depressor agents in group 1 cats. Here and in figures 2-3: *a*) acetylcholine; *b*) histamine; *c*) isoproterenol. *1*) right-atrial pressure; *2*) left-atrial pressure; *3*) venous return; *4*) cardiac output.

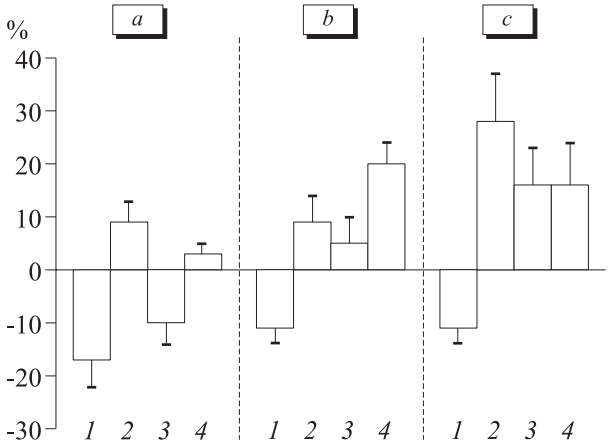

Fig. 2. Direction and degree of changes in atrial pressure, venous return, and cardiac output after injection of depressor agents in group 3 cats.

atrium was more pronounced, while pressure decrease in the left atrium was less pronounced than after injections of acetylcholine and histamine.

The experiments showed that in the group 1 cats (pressure decrease in the right atrium greater than in the left atrium) changes in venous return and cardiac output were practically identical, although the direction of these shifts caused by each depressor agent was opposite (Fig. 1). Therefore, the differences in atrial pressure in group 1 cats were not determined by different values of venous return or cardiac output. In a similar way, the linear dependence (similar to Frank-Starling relationship) between atrial pressure shifts and values of venous return and cardiac output was not observed in group 2 cats, where similar rise in the right and left-atrial pressure was accompanied by a 21±8% drop in venous return, while cardiac output did not change.

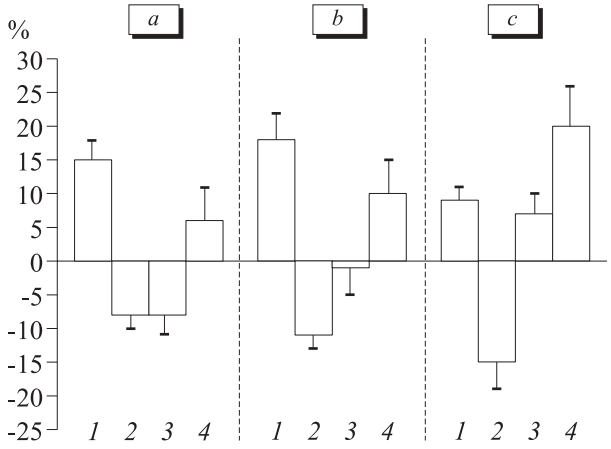

Fig. 3. Direction and degree of the changes in atrial pressure, venous return, and cardiac output after injection of depressor agents in group 4 cats.

In group 3 cats (pressure decreased in the right atrium and increased in the left one) acetylcholine decreased venous return and cardiac output by 10±4 and 3±2% (p>0.05), respectively. Histamine little changed venous return (5±5%), but significantly increased cardiac output by 20±4%. Isoproterenol almost equally increased both indices by 16±7 and 16±8%, respectively (Fig. 2). In group 4 cats (pressure increased in the right atrium and decreased in the left atrium) acetylcholine shifted venous return and cardiac output by 8±3 and 6±5%, respectively (p>0.05). The corresponding changes produced by histamine were 1±4% (p>0.05) and 10±5%. Isoproterenol increased both indices by 7±3 and 20±6%, respectively (Fig. 3). In comparison with acetylcholine and histamine, the pronounced increase of cardiac output and decrease of the left-atrial pressure by isoproterenol could result from direct positive chrono- and inotropic effect of this drug on the heart [5]. Probably, the differences in the direction of the shifts in atrial pressure in the group 3 and 4 cats induced by depressor vasoactive agents were not caused by different values and character of changes in venous return and cardiac output.

The time course of atrial pressure changes produced by the test depressor agents in various groups is shown in Table 1. The right-atrial pressure usually returned to baseline 30-55 sec postinjection. The left-atrial pressure returned to baseline during longer period (80-100 sec, Table 1). The only exceptions were group 1 cats treated with isoproterenol, in which the left and right-atrial pressure shifts were approximately equal (145±10 and 155±18 sec, respectively). This can be determined by a longer time of isoproterenol action on the heart in comparison with acetylcholine and histamine. The time course of the changes in left-atrial pressure produced by the test depressor agents was similar to that of venous return and cardiac output. Probably, in this case, like in those with injection of pressor

TABLE 1. Recovery Time to Baseline Atrial Pressure, Venous Return, and Cardiac Output after Injection of Depressor Agents (sec, M±m)*

Group, index		Acetylcholine	Histamine	Isoproterenol
Group 1	RAP	40±10	50±12	145±10
	LAP	80±15	160±20	155±18
	BB	200±30	150±18	150±20
	CO	200±40	150±20	150±25
Group 2	RAP	40±10	—	—
	LAP	160±12	—	—
	VR	80±15	—	—
	CO	80±12	—	—
Group 3	RAP	45±8	55±7	80±14
	LAP	90±10	110±12	140±22
	VR	100±25	160±30	260±35
	CO	110±15	160±24	260±40
Group 4	RAP	30±6	42±8	40±7
	LAP	120±15	140±25	135±16
	VR	80±14	130±12	200±28
	CO	80±15	145±15	175±20

Note. RAP: right-atrial pressure; LAP: left-atrial pressure; VR: venous return; CO: cardiac output. Dash sign (—) means the absence of data. *Time from the start of atrial pressure shift.

agents, the duration of left-atrial pressure changes depended on left-ventricular afterload [2].

Our experiments showed that intravenous injection of depressor agents acetylcholine, histamine, and isoproterenol producing similar decrease in blood pressure in cats induced different shifts in the right- and left-atrial pressure. In 69% cases, the atrial pressure shifts were oppositely directed. In these experiments, the right-atrial pressure increased in 47% cases and decreased in 22% cases. In 31% cases, the atrial pressure shifts were co-directed. In 20% cases these values increased, and in 11% cases they decreased. Irrespective of their direction, the duration of pressor changes in the left atrium was longer than in the right atrium and approximated to the duration of the changes in venous return and cardiac output.

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REFERENCES

1. B. I. Tkachenko, V. I. Evlakhov, and I. Z. Poyasov, *Fiziol. Zh. SSSR,* **90,** No. 6, 719-727 (2004).
2. B. I. Tkachenko, V. I. Evlakhov, and I. Z. Poyasov, *Byull. Eksp. Biol. Med.,* **139**, No. 1, 4-7 (2005).
3. O. Godje, M. Peyerl, T. Seebauer, *et al*., *Eur. J. Cardiothorac. Surg.*, **13**, No. 5, 533-539 (1998).
4. S. Gorgulu, A. Eksik, M. Eren, *et al*., *Int. J. Cardiol.*, **92,** No.2, 241-245 (2003).
5. S. Minatoguchi, H. Ito, K. Asano, *et al*., *Heart Vessels,* **12**, No. 1, 34-42 (1997).
6. E. Sandblom, A. P. Farrell, J. Altimiras, *et al., J. Exp. Biol*., **208**, No. 2, 1927-1935 (2005).