

EFFECT OF ACUTE HAEMODILUTION ON RIGHT ATRIAL TYPE-B RECEPTOR ACTIVITY IN ANAESTHETIZED CATS

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Abstract: In order to investigate whether the sensitivity of atrial type-B receptors to its natural stimulus is altered during acute haemodilution, experiments were conducted in nine anaesthetized, artificially ventilated and thoracotomized cats. Haemodilution was achieved by replacement of blood by the same volume of dextran (MW 150000). Atrial receptor activity, arterial blood pressure, right atrial pressure and ECG were recorded. Heart rate was calculated from ECG records. Arterial blood hematocrit was measured.

Mean arterial blood pressure and heart rate were not altered by haemodilution even at a hematocrit level of 12.17 ± 0.93 percent. Average activity of type-B atrial receptors, mean right atrial pressure, right atrial peak 'v' pressure, right atrial initial 'v' pressure and right atrial 'v' wave amplitude were changed significantly ($r < 0.05$) during acute haemodilution when the hematocrit was 12.17 ± 0.93 percent but the atrial type-B receptor activity per cycle did not show any significant change. Average activity of type-B receptors increased from 8.56 ± 1.02 spikes/sec to 9.56 ± 1.11 spikes/sec. Mean right atrial pressure, right atrial 'v' wave amplitude, right atrial peak 'v' pressure increased significantly ($P < 0.05$) from respective control values. Right atrial initial 'v' wave pressure decreased significantly. Heart rate changed from 168.11 ± 5.42 beats/min to 170.89 ± 5.65 beats/min. Mean arterial pressure changed from 134.33 ± 0.89 mmHg to 135.67 ± 1.46 mmHg. The data demonstrated that acute haemodilution caused increase in mean right atrial pressure, peak 'v' wave pressure, 'v' wave amplitude, average activity of type-B atrial receptor and decrease in initial 'v' wave pressure which could be attributed to increase in venous return. The increase in average activity following haemodilution could be attributed to a small increase in activity of atrial type-B receptors per cardiac cycle as there was no significant change in the heart rate.

Key words: atrial type-B receptor cardiac receptors haemodilution

INTRODUCTION

In acute haemodilution, the content of oxygen in arterial blood is reduced due to reduction in haemoglobin but the partial pressure of oxygen in the arterial blood could remain in the normal range (1, 2) and redistribution of blood volume may contribute to possible changes in certain haemodynamic responses. These responses include changes in flow characteristics (3), alteration in

catecholamines concentration (4, 5), increased oxygen extraction from the remaining haemoglobin (6), alteration of blood volume in different organs (7), decrease in blood viscosity (8), increase in both capillary RBC velocity and the ratio of H_{cap}/H_{sys} (9), increase in cardiac output (10), increase in end diastolic volume (EDV), decrease in end systolic volume (ESV), decrease in the ratio of $ESV:EDV$ (11) and increase in stroke volume (12).

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Some of the compensatory adjustments may involve altered reflex regulatory mechanisms through type-B atrial receptors localized in the atrial endocardium in the lateral wall of the atrial and in venoatrial junctions. Atrial type-B receptors discharge during the atrial filling phase of each cardiac cycle (13). The relationship of the discharge to peak pressure of the 'v' wave or mean atrial pressure while atrial pressure is rising, is different from the relationship when the pressure is falling (14). The activity of type-A receptors is not altered with the atrial dynamics in acute haemodilution (2). To examine whether atrial type-B receptors are involved in certain compensatory adjustments to dextran induced normovolaemic haemodilution, the present investigation was undertaken to determine the effect of acute haemodilution on the activity of atrial type-B receptors and atrial pressure parameters.

METHODS

Experiments were performed on nine adult cats of either sex weighing 2.5 to 4 kg. Cats anaesthetized with ip chloralose urethane mixture (Chloralose-60 mg/kg and Urethane 250 mg/kg). After induction of anaesthesia, the neck was incised in the midline and the trachea was cannulated. Polyethylene catheters were placed into the femoral vein for infusion, into the femoral artery for recording arterial pressure, into the other femoral artery for withdrawal of blood. A catheter was placed in the right atrium through the external jugular vein for recording the right atrial pressure. The animals were ventilated with a respiratory pump at a min volume of 300 ml/kg. The body temperature was monitored and was maintained between 37°C-38°C during the entire experiment.

The technique of exposing the vagus and the dissection of single fibres were as described earlier (15). Activity in these afferent fibres of vagus nerve was displayed on one channel of the oscilloscope (Tektronix type-422) with the help of a pair of chloride coated silver wire electrodes and a preamplifier (Tektronix type-122). The activity was also monitored by an

audio amplifier and a loud speaker. The electrocardiogram (Lead-III) was amplified by another preamplifier (Tektronix type-122) and displayed on one of the traces oscilloscope. Right atrial pressure was monitored with a P23Db pressure transducer connected to a strain gauge amplifier (Tektronix type-Q) whose output was displayed on one of the split traces (using Tektronix type-M unit) of the oscilloscope. Arterial pressure was monitored with another P23Db pressure transducer and strain gauge amplifier (Tektronix type-Q). The pressure recording systems were calibrated at the end of the experiment with a mercury/water manometer. Hematocrit was determined by the microcapillary method with centrifugation at 50000 r.p.m. for three min. Blood samples were withdrawn anaerobically from arterial catheter with heparinized syringes and arterial blood pO₂, pCO₂ and pH were measured (Radiometer) and ventilation pump adjustments were made to normalise the gas tensions and pH (1, 16).

Identification of atrial type-B receptor: An atrial type-B receptor was identified before opening the chest of the cat with the mean arterial blood pressure maintained within normal limits. Under normal conditions with the chest intact the characteristics of these endings are that they fire one main burst of impulses in cardiac cycle which begins most commonly a little after the beginning of the upstroke of the aortic pressure curve i.e. late systolic phase, the latency of the burst of impulses from the Q wave of the E.C.G. is about 70 to 210 msec in the cat (14). The first impulse of the burst in atrial type-B receptors varies markedly when each cycle is observed on the oscilloscope. It can be seen that the first impulse of each subsequent burst appears earlier as inspiration progresses. The pattern of discharge is closely related to the 'v' wave of the atrial pressure tracing. The location of the receptor in the right atrium was determined after opening the chest and probing the atrium externally with a glass rod.

Test procedure: After the dissection, 30-60 min were allowed for stabilization of all the

variables. Arterial blood pressure, right atrial pressure, atrial type-B receptor activity, hematocrit, arterial blood pO₂, pCO₂ and PH were recorded during control period.

Protocol for acute haemodilution: Acute haemodilution was induced by dextran (molecular weight 150000) for blood exchange. The dextran (Rallis), a 6% solution of dextran in 5% w/v dextrose was warmed to 37°C before infusion. Blood-dextran exchange was done in three steps of 15-20 percent of estimated total blood volume until the hematocrit fell to about 12-15%. In each step of haemodilution estimated volume of blood was withdrawn from the arterial catheter which was followed by rapid infusion of same volume of dextran through the femoral vein catheter.

The volume of blood to be withdrawn was calculated by conventional estimates based on age and lean body weight as 50 ml/kg in case of cat (17).

The average control hematocrit level was 43.56 ± 0.89 percent. It dropped to 33.22 ± 0.61 percent after 1st exchange, 22.11 ± 0.63 percent after 2nd exchange and 12.17 ± 0.31 percent after 3rd exchange. The atrial type-B receptor activity during control and after haemodilution was correlated with the amplitude of the 'v' wave of the atrial pressure wave, mean right atrial pressure and both peak and initial 'v' wave pressure.

In order to eliminate the influence of prolonged anaesthesia of 5 to 6 hrs on atrial type-B receptor activity, right atrial pressure, arterial pressure and heart rate observations were made on two separate cats in which saline infusions were given, through the femoral vein in steps of 10 to 20 ml, the atrial pressure and activity of atrial type-B receptors were recorded at different time intervals. In all the experiments punctate stimulation technique was used to confirm the location of the receptor.

Analysis of the atrial pressure curve: The initial pressure of the 'v' wave was taken as the pressure at the foot of the 'v' wave i.e., the point from where the 'v' wave begins soon after the 'c'

wave. The amplitude was taken as the difference between the pressure at the peak of the 'v' wave and the initial 'v' wave pressure, and mean atrial pressure as the average of the two (14). The statistical significance of the results was calculated by analysis of variance followed by students t test. Significant differences were those with $P < 0.05$.

RESULTS

Mean right atrial pressure, 'v' wave amplitude, initial and peak 'v' wave pressure, average activity (per sec) and activity per cardiac cycle of atrial type-B receptors, mean arterial pressure are given in Fig. 2. and Table I. After 1st, 2nd and 3rd exchanges, hematocrit fell

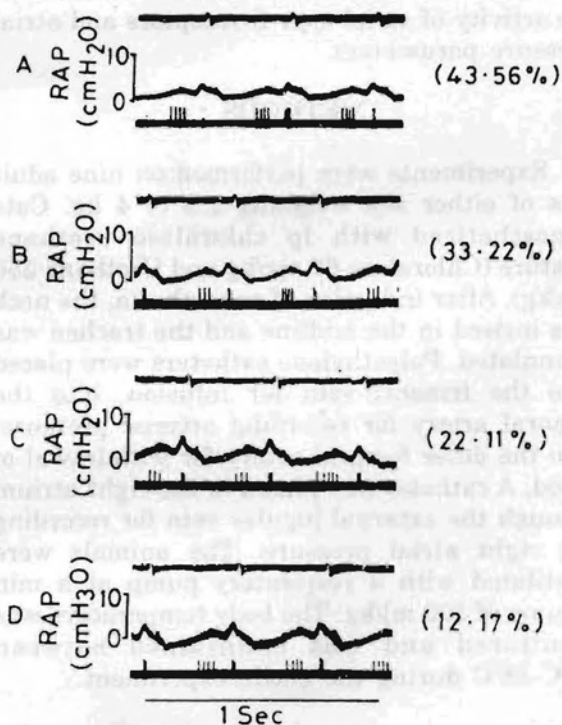


Fig. 1 : Original records from one of the experiments showing the effect of graded haemodilution on right atrial pressure (middle trace in each record), right atrial type-B receptor activity (bottom trace) and ECG (upper trace) in each record. A-control values and B, C and D following 1st, 2nd and 3rd exchanges of dextran for blood respectively. Hematocrit values are shown on the right hand side of each record.

from a control value of 43.56 ± 0.89 percent to 33.22 ± 0.61 , 22.11 ± 0.63 and 12.17 ± 0.93 percent respectively. Acute haemodilution produced a small increase in the number of spikes in the 'v' burst of the receptor activity which was not found to be significant. However, average activity per second showed significant ($P < 0.05$) increase following second and third exchanges of blood. A small increase in the heart rate was not found to be statistically significant ($P > 0.05$)

(Table I and Fig. 2) as observed by us also in our earlier study (2). There was no significant change ($P > 0.05$) in the mean arterial blood pressure. Mean atrial pressure, peak 'v' wave pressure and 'v' wave amplitude were increased significantly ($P < 0.05$) after 3rd exchange. Initial 'v' wave pressure was decreased significantly ($P < 0.01$) after 2nd and 3rd exchanges when compared with the control (Fig. 1 and 2).

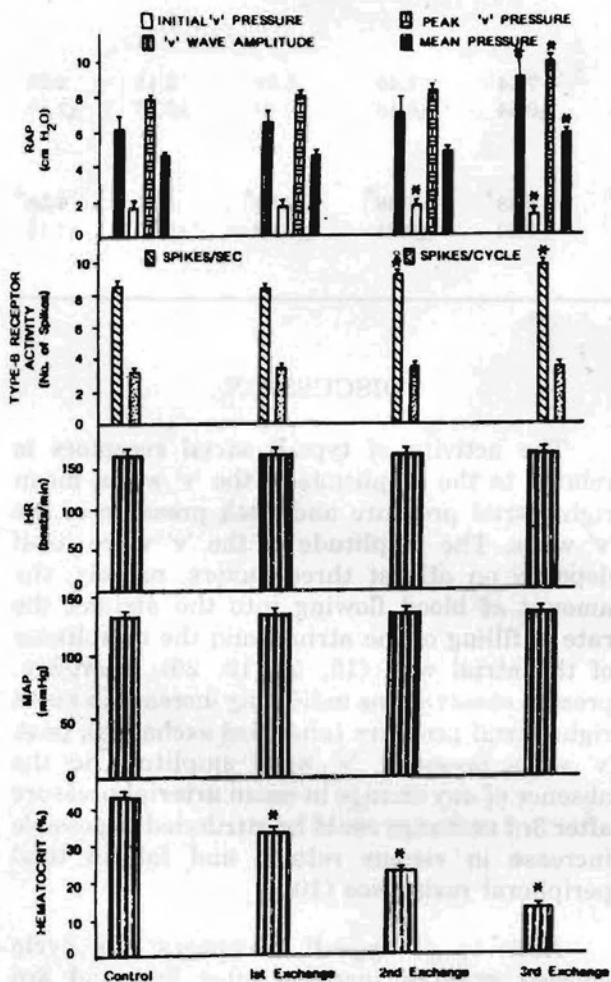


Fig. 2 : Effect of graded haemodilution on hematocrit, mean arterial pressure (MAP), heart rate (HR), type-B receptor activity and various parameters of right atrial pressure (RAP). Values are mean \pm SEM from data obtained on nine cats. * $P < 0.05$ compared to corresponding control (prehaemodilution) values.

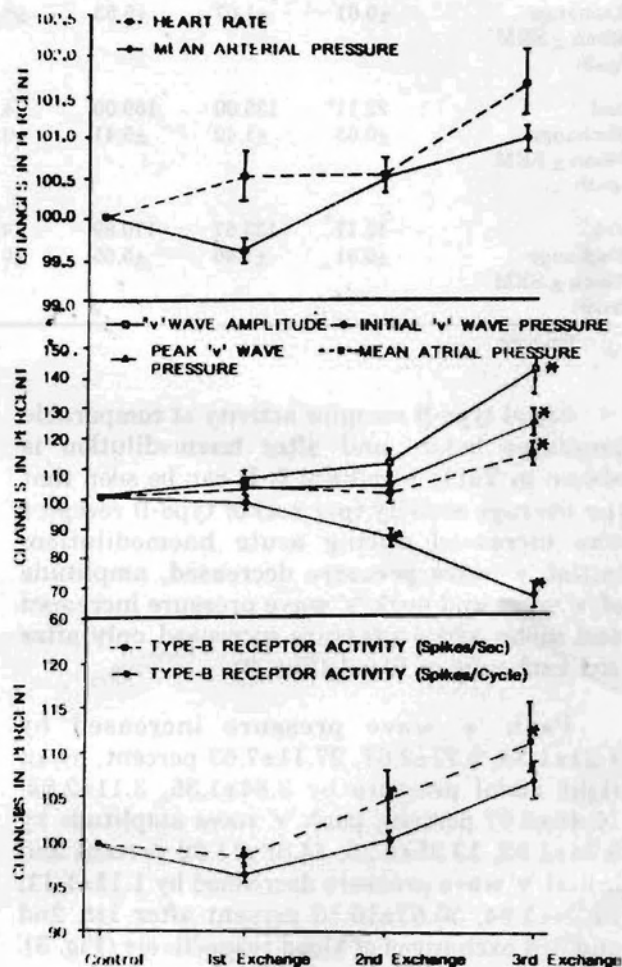


Fig. 3 : Effect of graded haemodilution on percentage change in heart rate, mean arterial pressure (top panel), various parameters of 'v' wave of right atrial pressure wave (middle panel) and type-B receptor activity (bottom panel). Each point represents mean \pm SEM from data obtained on nine cats. * $P < 0.05$ compared to corresponding control (prehaemodilution) values.

TABLE 1: Showing the effect of graded haemodilution on right atrial pressure, right atrial type-B receptor activity, arterial pressure, heart rate and arterial blood hematocrit.

	Hematocrit (HCT) %	Mean arterial pressure (mmHg)	Heart rate (beats/ min)	Right atrial pressure (cm H ₂ O)				Right atrial type-B receptor activity	
				Mean	Peak 'v' pressure	Initial 'v' wave amplitude	'v' wave amplitude	(spikes/ cycle)	(spikes/ sec)
Control	43.56	134.33	168.11	4.33	7.11	1.61	5.50	3.11	8.56
Mean ± SEM (n=9)	±0.89	±0.89	±5.42	±0.38	±0.60	±0.20	±0.40	±0.30	±1.02
1st Exchange	33.22*	133.78	169.00	4.49	7.39	1.59	5.80	3.00	8.44
Mean ± SEM (n=9)	±0.61	±1.07	±5.53	±0.38	±0.59	±0.20	±0.40	±0.37	±1.00
2nd Exchange	22.11*	135.00	169.00	4.42	7.44	1.40	6.04	3.11	9.00
Mean ± SEM (n=9)	±0.63	±1.42	±5.41	±0.34	±0.54	±0.18	±0.40	±0.35	±1.19
3rd Exchange	12.17*	135.67	170.89	4.97*	8.88*	1.08*	7.80*	3.33	9.56*
Mean ± SEM (n=9)	±0.31	±1.46	±5.65	±0.38	±0.60	±0.21	±0.60	±0.44	±1.11

*P<0.05

Atrial type-B receptor activity at comparable pressures before and after haemodilution is shown in Table 1 and Fig 1. It can be seen that the average activity (per sec) of type-B receptor was increased during acute haemodilution, initial 'v' wave pressure decreased, amplitude of 'v' wave and peak 'v' wave pressure increased and mean atrial pressure increased only after 3rd exchange of blood (Fig. 2).

Peak 'v' wave pressure increased by 4.21±1.38, 5.77±2.67, 27.11±7.63 percent, mean right atrial pressure by 3.84±1.35, 3.11±2.62, 16.48±5.87 percent, peak 'v' wave amplitude by 5.74±1.93, 13.25±5.26, 44.88±11.22 percent and initial 'v' wave pressure decreased by 1.11±1.11, 12.78±5.84, 36.67±10.10 percent after 1st, 2nd and 3rd exchanges of blood respectively (Fig. 3).

There was no significant. (P>0.05) increase in the average activity of type-B receptors after 1st exchange of blood, however, following 2nd and 3rd exchanges of blood, the average activity of type B receptors increased significantly (Table 1) There was no change in the heart rate after exchanges of blood.

DISCUSSION

The activity of type-B atrial receptors is related to the amplitude of the 'v' wave, mean right atrial pressure and peak pressure of the 'v' wave. The amplitude of the 'v' wave itself depends on atleast three factors, namely, the amount of blood flowing into the atrium, the rate of filling of the atrium and the compliance of the atrial wall (15, 18, 19, 20). Therefore, present observations indicating increase in mean right atrial pressure (after 3rd exchange), peak 'v' wave pressure, 'v' wave amplitude in the absence of any change in mean arterial pressure after 3rd exchange could be attributed to possible increase in venous return, and fall in total peripheral resistance (10).

Activity of type-B receptors per cycle showed a small increase after 2nd and 3rd exchanges of blood, amplitude of 'v' wave, peak 'v' wave pressure and mean 'v' wave pressure were also increased. One possible explanation could be the altered smooth muscle tone during haemodilution (21). Average activity of type-B receptors was increased after 2nd and

3rd exchanges of blood while there was no significant increase in the heart rate. Mean arterial pressure was also not changed after 1st and 2nd exchanges of blood as reported earlier (2, 22). It could be the result of local vasodilatation produced by tissue hypoxia (16), increased venomotor tone produced by the stimulation of aortic chemoreceptors (1, 23), increase in cardiac output as decrease in blood viscosity is expected to play some role in the increase in venous return as well as increase in stroke volume (12). However, the degree to which it contributes is considered to be small (16).

In conclusion, the activity of atrial type-B receptor per cycle was marginally increased by reduction in the hematocrit during acute

haemodilution and the average activity was increased with significant change in mean right atrial pressure, peak 'v' wave pressure and 'v' wave amplitude induced by acute haemodilution.

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