

ATRIAL NATRIURETIC FACTOR AT HIGH ALTITUDE PULMONARY HYPERTENSION

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SUMMARY : To investigate the physiological role of atrial natriuretic factor in highlanders with pulmonary hypertension, we studied 61 residents of Tien-Shan living at 2040-2800 m above sea level. According to the initial pulmonary arterial pressure levels the subjects were divided into 2 groups; Group 1 with initial normal pulmonary pressures and Group 2 with initially high pulmonary pressures at Highlanders of 2nd group with high pulmonary pressure the concentration of atrial natriuretic factor in plasma turned out to be approximately twice higher, than at highlanders of 1st group with normal pulmonary pressure. Noteworthy in our data are the higher renin levels in subjects of 2nd group with normal initial plasma aldosterone concentrations. This could suggest dissociation of interaction in renin-angiotensin-aldosterone system.

Key Words : High altitude pulmonary hypertension, atrial natriuretic factor, plasma renin activity, aldosterone.

INTRODUCTION

Since the renin-angiotensin-aldosterone system (RAAS) and atrial natriuretic factor (ANF) are directly involved in the regulation of hemodynamics and structural alterations in the circulatory system, quite understandable is the interest of investigators in the observed changes at the RAAS and ANF and ANF at highlanders. The aim of this study was focused on changes in plasma renin, aldosterone and ANF in permanent moderate-altitude residents (2040-2800 m above sea level) with initially normal or elevated pulmonary arterial pressure (P_{PA}) levels.

MATERIALS AND METHODS

Sixty-one residents of Tien-Shan living at 2040-2800 m above sea level were studied. The subjects were apparently healthy male volunteers aged 16 to 50 years. According to the ini-

tial P_{PA} levels the subjects were divided into 2 groups. Group 1 consisted of 21 patients aged 25.0 ± 7.3 years. Their P_{PA} values were within the normal range. Forty subjects aged 29.4 ± 11.4 years (Group 2) had initially elevated P_{PA} values and were thus diagnosed as having stable High Altitude Pulmonary Hypertension (HAPH) (1). Causes other than the effect of altitude, which could be responsible for rises in P_{PA} were excluded in the subjects studied. Furthermore, none of the subjects had any ECG or EchoCG evidence of right ventricular hypertrophy. Pulmonary and cardiovascular diseases were also absent in them, with the exception of HAPH.

Methods of investigation were clinical investigations, ECG in 12 standard leads, EchoCG in B-mode, spirometry, chest X-ray, right heart catheterization, radioimmunoassay of ANF, plasma aldosterone and plasma renin activity (PRA). On days 4 to after descent from the mountains they underwent right-sided cardiac catheterization at the (700 m above sea level). PRA, ANF and aldosterone concentrations in venous (ulnar vein) blood were

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determined using the radioimmunologic method. The blood was drawn into test-tubes placed in an ice bath and was stored at 24-70°C before the radioimmunologic analysis was made.

Statistical analysis

Results are expressed as means ± SD. The distributions of single variables within 2 groups were compared by using 2-tailed unpaired Student's t test. All p values are 2-tailed, values <0.05 were considered to be significant.

RESULTS

In the clinical examination the 1st group of highlanders were practically healthy. X-ray and ECG studies revealed no changes of the right ventricle. In Group 1 patients, P_{PA syst}, P_{PA mean} and pulmonary vascular resistance (R_{pulm. tot.}) values were found to be 22.7±3.38 mmHg, 14.5±3.47 mmHg, and 220.7±40.8 din/sec/cm⁻⁵ respectively.

In Group 2 patients P_{PA syst}, P_{PA mean} and pulmonary vascular resistance (R_{pulm. tot.}) values as compared with previous group were significantly higher (34.7±7.30 mm Hg versus 22.7±3.38 mmHg, p<0.001; 254.1±30.5 din/sec/cm⁻⁵ versus 220.7±40.8 din/sec/cm⁻⁵ p<0.001).

Data on initial studies in the two groups (Table 1) differed significantly not only in pulmonary hemodynamics, but also in ANF and renin levels. The basal values of ANF in Group 1 averaged 12.3±0.60 pg/ml. (range; 6 to 16 pg/ml.)

At the same time the average meaning PRA and aldosterone concentrations at highlanders with normal pulmonary arterial pressure did not differ from the normal data.

In the second group of highlanders, who in resting conditions did not have increased pulmonary arterial pressure, the concentration of atrial natriuretic factor in plasma turned out to be approximately twice that of the 1st group. At systolic pulmonary arterial pressure 34.7±7.30 mmHg this atrial peptide was found to be 20 to 39 pg/ml and the mean being 25.2±5.34 pg/ml. The greatest concentrations of atrial natriuretic factor were encountered in those highlanders with significant pulmonary arterial hypertension.

Noteworthy in our data are the higher renin levels in subjects of Group 2 with normal initial plasma aldosterone concentrations.

DISCUSSION

Since the renin-angiotensin-aldosterone system (RAAS) and atrial natriuretic factor (ANF) are directly involved in the regulation of hemodynamics and structural alterations in the circulatory system, quite understandable is the interest of investigators in determinations of RAAS and ANF.

It is well known that the predominant stimulus for the secretion of the atrial hormone at the physiologic conditions are the changes of atrial and pulmonary pressures (2-4). In the studies reported here the close and direct correlations were observed between plasma ANF concentration and pulmonary arterial pressure (r=0.80, p<0.001). The presence of non-expressive positive correlation of interrelations with pulmonary vascular resistance (r=0.37, p<0.05) allows to suppose the presence of regulating influence of ANF on the formation of vascular state of pulmonary blood circulation.

The data reported here co-inside with the results obtained by other investigators (5-8), who examining the patients with secondary pulmonary arterial hypertension in patients with chronic obstructive pulmonary diseases found that the plasma concentration of ANF was significantly higher than those of normal resting individuals with normal pulmonary arterial pressure. Similar results were uncovered experiments performed in rats (9).

In the group of individuals presented here the concentrations of aldosterone was low, comparing with the data, obtained from the valley inhabitants (10). At the same time the average mean plasma renin activity was not different from the data obtained from healthy valley inhabitants.

It is well known that the levels of hormones levels in peripheral blood reflect quite closely the functional activity of endocrine system. One of the possible reasons of increasing plasma renin activity at highlanders with pulmonary arterial hypertension may be the formation of change in pulmonary blood circulation, leading to compensatory shifts in function of a number neuro-humoral regulation system.

The results of this study show that ANF in physiological conditions possibly functions as a 'countre-hormone' blocking the hyper-activation of vasoconstrictors, including RAAS (11-13). This may perhaps be one explanation of reduction of ANF in plasma of highlanders with pulmonary arterial hypertension.

Table 1: Certain indices in subjects with normal (GR 1) and elevated (GR 2) pulmonary arterial pressure levels.

Values	Group 1 n=21	Group 2 n=40	P
P _{PA} syst. (mm Hg)	22.7±3.38	34.7±7.30	p<0.001
P _{PA} mean (mm Hg)	14.5±3.47	22.9±7.50	p<0.001
R _{Pul. tot.} (dyn.sec.cem-5)	220.7±40.8	254.1±30.5	p<0.001
ANF (pg/ml)	12.3±2.79	25.2±5.34	P<0.05
PRA (ng/ml/h)	1.7±0.72	3.7±2.0	P<0.05
Aldosterone (pg/ml)	92.0±0.43	102.8±34.7	P<0.05

Thus, the presented data reflect the state of neuro-humoral regulation system at highlanders with stable PAH. Summing up it is necessary to note that the concentration of atrial natriuretic factor of highlanders plasma with stable High Altitude Pulmonary Arterial Hypertension is considerably above that of the native highlanders with normal pulmonary arterial pressure at rest.

Noteworthy in our data are the increased renin levels in highlanders with pulmonary hypertension and with normal initial plasma aldosterone concentrations. This suggests dissociation of interaction of renin-angiotensin-aldosterone system. Perhaps, significantly elevated atrial natriuretic factor levels at this group is related to such a dissociation.

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