PULMONARY CIRCULATION AT HIGHLANDERS

GYLDYZ K. SODANBEKOVA*
AHMET BIRAND**
TALANTBEK A. BATYRALIEV*
ZAREMA A. NIYAZOVA**
FERIT AKGÜL**

SUMMARY: The high-altitude pulmonary arterial hypertension is discovered approximately at 45.7 percent of permanent inhabitants of Tien-Shan and Pamir and at 6.8 percent it is complicated by right heart failure. To investigate the especialities of pulmonary circulation at highlanders with normal and elevated pulmonary arterial pressure we studied 61 residents of Tien-Shan, living at 2800-3200 meters above sea level. The subjects were apparently healthy male volunteers aged 16 to 50 years, who underwent right-sided heart catheterization. Levels of systolic pulmonary arterial pressure (systolic P_{PA}) (22.7 ± 3.38 mmHg) and mean P_{PA} (14.5 ± 3.47 mmHg) at first group of highlanders were within the normal range, whereas the levels of pulmonary vascular resistance (PVR) were increased (220.7 ± 40.8 dyn/sec/cm-5, $p<0.05$). At highlanders of second group the levels of systolic P_{PA} (34.7 ± 7.30 mmHg) and mean P_{PA} (22.9 ± 7.50 mmHg) turned out to be higher than at highlanders of first group approximately of 53 and 58%. The levels of PVR were significantly higher ($p<0.001$) than at previous group. These findings suggest that among permanent high-altitude residents take place hidden form pulmonary arterial hypertension that consistent with our previous hypothesis that among highlanders there are individuals with normal and high sensitivity to exogenous hypoxia which reflect the changes of neurohumoral regulation of pulmonary circulation.

Key Words : High altitude pulmonary arterial hypertension, pulmonary circulation.

INTRODUCTION

It is well known that altitude 2000 meters above sea level is enough for developing of hypoxic pulmonary arterial hypertension (1,2,3). According to the literature data at 45.7% of native highlanders high altitude pulmonary arterial hypertension occurs and at 6.8% of them it's complicated with right sided heart failure (4).

It is shown that long-term living at mountains, especially at high altitude change the function of those system which are responsible for oxygenation of organism. It is especially important for pulmonary ventilation, circulation, blood system and others (5,6).

The aim of the present study was focused on the changes in pulmonary circulation at native highlanders in depend of presence pulmonary arterial hypertension.

*From Kirghiz Scientific Research Institute of Cardiology, Bishkek, Republic of Kyrgyzstan.
**From Department of Cardiology, Balcali Hospital, Çukurova University, Adana, Türkiye.

MATERIALS AND METHODS

61 residents of Tien-Shan, living at 2800-3200 meters above sea level were studied. The subjects were apparently

healthy male volunteers aged 16 to 50 years.

According to the initial pulmonary arterial pressure levels the subjects were divided into 2 groups. Group 1 consist of 21 subjects aged 25.0 ± 7.3 years. None of the subjects had any electrocardiographic or echocardiographic evidence of right ventricular hypertrophy. Their pulmonary arterial pressure values were within the normal range.

40 subjects aged 29.4 ± 11.4 years (group 2) had initially elevated pulmonary arterial pressure values, and, thus, were diagnosed as having high altitude pulmonary hypertension. Causes other than the effect of altitude, which could be responsible for rises in pulmonary arterial pressure were excluded from the subjects studied. At physical examination of the second group at 4 of them was revealed precordial pulsation, diameter of pulmonary artery at chest roentgenograms was over 14 mm at 28 subjects. Electrocardiographically at 5 subjects we found slight-moderated signs of right ventricular hypertrophy.

Compared groups do not different from each other at age, weight and height levels. Methods of investigation included clinical examination, electrocardiography in 12 standard leads, echocardiography in B-regimen, chest roentgenography and right heart catheterization.

2M-Echocardiography, ultrasound studies were performed on the 'Toshiba SSH-40A' according to the standard technique (7,8).

Right heart catheterization was performed according to the standard technique in an operating theatre under sterile conditions. A Swan-Ganz pulmonary artery catheter was introduced through a femoral vein. Placement of the catheter tip in the pulmonary artery was determined by monitoring the pressure trace during advancement by "Angioscope-D) (Siemens, FRG) catheter was clamped in the position at which pulmonary arterial pressure could be recorded.

Baseline hemodynamic measurements were obtained at least 30 minutes after insertion of the catheter while patients breathed room air.

Baseline hemodynamic parameters included systolic and mean pulmonary arterial pressures and heart rate. Arterial mixed venous blood gas analyses were performed using an OSM-2 hemoximeter (Radiometer) spectrophotometrically.

All measurements were performed on 4 to 6 days after descending from the mountains at standard conditions at morning and supine position.

All drugs, including diuretics and nitrates were excluded at least 48 hours prior to the study.

Table 1: Baseline echocardiographic data at native highlanders (2800-3200 m above sea level).

Values	Native Inhabitants					
	Valey	Highlanders		P		
		Group 1 (n=21)	Group 2 (n=40)			
	1	2	3	1-2	1-3	2-3
AOD, cm.	3.0 ± 0.006	3.0 ± 0.15	3.0 ± 0.32	>0.05	>0.05	>0.05
AP LAD, cm.	2.54 ± 0.11	2.6 ± 0.21	2.6 ± 0.26	>0.05	>0.05	>0.05
AP RVD, cm.	1.0±0.30	1.34±0.28	1.38±0.36	<0.05	<0.05	>0.05
AWT RV, cm.	0.3±0.08	0.30±0.04	0.30±0.06	<0.05	<0.05	>0.05
LVD_d, cm.	4.88±0.04	4.6±0.39	4.7±0.06	<0.05	<0.05	>0.05
VST, cm.	0.8±0.03	0.8±0.08	0.8±0.06	>0.05	>0.05	>0.05
PWT LV, cm.	0.91±0.02	0.8±0.07	0.8±0.07	<0.05	<0.05	>0.05
EFLV, %	65±1.50	74.8±5.88	75.4±5.83	<0.05	<0.05	>0.05
P_{PA} systolic, mmHg	23.4±0.70	27.1±4.71	33.3±7.07	<0.05	<0.05	<0.05
P_{PA} mean, mmHg	12.4±0.70	14.5±3.30	18.3±4.31	<0.05	<0.05	<0.05

AOD = aortic root dimension, AP= antero posterior. LAD= left atrium dimension, RVD= right ventricle dimension. AWT RV= anterior wall thickness of right ventricle, LVD_d= end-diastoic dimension of left ventricle. VST= ventricular septum thickness, PWT LV= posterior wall thickness of left ventricle, EF= ejection fraction. LV= left ventricle, P_{PA}= Pulmomary arterial pressure.

STATISTICAL ANALYSIS

All data are presented as mean ± SEM. The distribution of single variables within 2 groups were compared by using 2-tailed unpaired Students Test. All p values are 2-tailed, values < 0.05 were considered to be significant.

RESULTS

The data of noninvasive examination of left atrium dimension (2.6±0.21 cm) end-diastolic dimension of left ventricle (4.6±0.39 cm), interventricular septum thickness, left ventricle posterior wall thickness and ejection fraction of left ventricle at first group of highlanders do not differ from the same data obtained at native valley inhabitants (Table 1). The thickness of right ventricle anterior wall (0.3±0.04 cm) was within the normal range.

At the same time data of systolic (27.1±4.71 mmHg), mean pulmonary arterial pressure (14.5±3.30 mmHg) and right ventricle postero-anterior dimension (1.34±0.28 cm) were significantly increased in compare with the similar data at native valley inhabitants.

At the second observed group the levels of pulmonary arterial pressures (systolic P_{PA}=33.3±7.07 mmHg, mean P_{PA}=18.3±4.31 mmHg) were significantly higher than data of first group and valley inhabitants ($p<0.05$).Two groups do not differ from each other at right ventricle postero-anterior dimensions. Invasively measured systolic P_{PA}(22.7±3.38 mmHg), mean PPA (14.5±3.47 mmHg) and oxygen saturation at mixed venous blood from pulmonary artery (77.4±4.30) do not differ from data obtained at valley inhabitants (Table 2).

At the same time the levels of pulmonary vascular resistance at the first group of subjects (220.7±40.8 dyn/sec/cm^{-5}) were truly higher. It turned out that the functional state of pulmonary circulation at the second group of highlanders with stable form of high-altitude pulmonary arterial hypertension significantly differed in

Table 2: Index of pulmonary circulation on echocardiographic data and direct pulmonary artery tensometry at native highlanders (2800-3200 m above sea level).

Values	Native Inhabitants					
	Valey	Highlanders		P		
		Group 1 (n=21)	Group 2 (n=40)			
	1	2	3	1-2	1-3	2-3
Echocardiography						
Heart Rate	70.0 ± 8.6	73.7 ± 12.0	77.2 ± 10.0	>0.05	<0.05	>0.05
AP RV, cm	1.0 ± 0.3	1.34 ± 0.28	1.38 ± 0.36	<0.05	<0.05	>0.05
AWT RVD, cm	0.3 ± 0.08	0.3 ± 0.04	0.3 ± 0.06	>0.05	>0.05	>0.05
VST, cm	0.8 ± 0.03	0.8 ± 0.08	0.8 ± 0.06	>0.05	>0.05	>0.05
EF, LV, %	65 ± 1.5	74.8 ± 5.88	75.4 ± 5.83	<0.05	<0.05	>0.05
Direct tensometry						
P_{PA} systolic, mmHg	22.3 ± 2.1	22.7 ± 3.38	34.7 ± 7.30	>0.05	<0.05	<0.001
P_{PA} mean, mmHg	13.0 ± 1.2	14.5 ± 3.47	22.9 ± 7.50	>0.05	<0.05	<0.001
PVR dyn/sec/cm^{-5}	199 ± 27	220.7 ± 40.8	254.1 ± 30.5	<0.05	<0.05	<0.001
S_VO_2%	70-80	77.4 ± 4.30	76.2 ± 4.22	>0.05	>0.05	>0.05

AP= antero-posterior, RVD= right ventricle dimension. AWT RV=anterior wall thickness of right ventricle, VST= ventricular septum thickness, EF LV= Left ventricle ejection fraction, PPa= pulmonary vascular resistance, PVR= pulmonary vascular resistance, S_VO_2= Oxygen saturation in mixed venous blood.

compare with the previous group. At first, these differences were related to the levels of pulmonary arterial pressure. Mean PPA at rest was 22.9±7.5 mmHg (ranging from 15 to 30 mmHg) that was truly higher than the same data at the first group (14.5±3.4 mmHg).

Systolic pulmonary arterial pressure levels (34.7 ±7.30 mmHg) also significantly differs from the data of previous group.

The levels of pulmonary vascular resistance at rest were higher for 15% in compare with the data of first group of highlanders.

DISCUSSION

To investigate the changes in pulmonary circulation at native highlanders in depend of presence of pulmonary arterial hypertension was performed the present study.

Noninvasive data obtained at both groups of highlanders show that they have no signs of including in pathologic process of right and left ventricles.

Mean hemodynamic values of pulmonary artery blood circulation gained while direct tensometry of the right sides of the heart and pulmonary artery on 4-6 days after descending from the mountains to the altitude of 700 m above sea level were close to the data obtained from healthy valley inhabitants (9).

At the same time, according to obtained data, hemodynamic parameters of pulmonary vascular resistance in highlanders with normal at rest pulmonary arterial pressure in compare with data of other investigators of healthy valley inhabitants were higher (9,10).

Although the values of systolic and mean pulmonary arterial pressure were within the normal range, parameters of pulmonary vascular resistance confirm about the presence of hidden pulmonary arterial hypertension within the group. As it is known that descending of highlanders to lower altitude is accompanied with decrease of pulmonary arterial pressure, pulmonary vascular resistance and degree of arterial hypoxia, characterizing thus, the functional character of pulmonary arterial hypertension, that, at another turn, does not exclude the presence of increased pulmonary arterial hypertension at investigated people before their descent to low and (700 m above sea level) and its partial conversion (4,11,12).

Thus, the comparative analysis of noninvasive and invasive data show that the first group consists of highlanders with pulmonary arterial hypertension in the hidden form that perhaps reflect the changes of neurohumoral regulation of pulmonary circulation at highlanders (10,13,14).

Highlanders with stable pulmonary arterial hypertension were characterized with truly increased pulmonary arterial pressure, gained as noninvasive so invasive methods.

Pulmonary vascular resistance in compare with analogous data of the previous group was some more.

Revealed specialties of pulmonary circulation in native highlanders of Tien-Shan are close to the data obtained by other investigators who studied inhabitants of another mountain plateau by using right heart catheterization (1,3,5,6).

Summing up, our study indicate that among permanent high-altitude residents there are individuals with normal and elevated pulmonary arterial pressure, who, at our mind, have a different sensitivity to hypoxia. At highly sensitive individuals were revealed even at rest elevation of pulmonary arterial pressure and pulmonary vascular resistance, leading to the forming of stable form of high altitude pulmonary arterial hypertension. Highlanders with normal sensitivity and pulmonary arterial pressure have a hidden increase of pulmonary vascular resistance that during some period has a conversional character and reflect the changes of neurohumoral regulation of pulmonary circulation.

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Correspondence:
Talantbek A. Batyraliev
Department of Cardiology,
Çukurova University,
School of Medicine, Balcali Hospital,
Balcali, 01330 Adana, TÜRKIYE.