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Original Article

Evaluation of cardiac function in healthy children native to 1890 metres

Cenap Zeybek,[1] Vildan Tasyenen,[2] Elif Kazanci,[2] Aysun Boga[2]

[1]*Pediatric Cardiology;* [2]*Pediatrics, District Training and Research Hospital, Erzurum, Turkey*

Abstract *Objective:* The aim of the study is, by comparing cardiac parameters between children native to 1890 metres with children living at sea level, to find out whether there is any impairment in cardiac function related to that altitude. *Methods:* Electrocardiographic, conventional, and tissue Doppler echocardiographic parameters were compared in 42 healthy children native to 1890 metres, and in 21 healthy age and gender matched children living at sea level. Plasma haemoglobin level and oxygen saturation measured by pulse oxymeter were also obtained from all patients. *Results:* Haemoglobin levels were higher, and oxygen saturation levels were lower in children native to 1890 metres. Conventional echocardiographic parameters and mitral annular myocardial parameters were all similar between children native to 1890 metres and children living at sea level. Tricuspid lateral annular early diastolic velocity and the ratio of early-to-late diastolic velocity were significantly lower and tricuspid lateral annular izovolumetric relaxation time was significantly higher in children native to 1890 metres than children living at sea level. *Conclusion:* Children living at 1890 metres of altitude predispose to asymptomatic right ventricular diastolic dysfunction or otherwise they remain as healthy children.

Keywords: Altitude; children; right ventricle; tissue doppler

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People living at high altitude environments develop alveolar hypoxia and hypoxaemia.[1] Hypoxaemia leads to the increase in myocardial work and the vasoconstriction in pulmonary arterial tree.[2,3] Cardiopulmonary effects become more pronounced with the increasing of altitude.[4]

Important cardiovascular changes have been shown in healthy children born and living at high altitudes.[5] Children native to high altitude have persistent right ventricular predominance, right ventricular hypertrophy, and mild pulmonary hypertension associated with increased pulmonary vascular resistance.[6,7] The pulmonary hypertension is principally related to structural changes seen in the pulmonary vessels. The increased amount of smooth muscle cells in the distal pulmonary arterial branches is the main element of this pulmonary remodelling.[8]

Although, it is clear that, living at high altitude causes early diastolic dysfunction in adults,[9] the real impact of altitude on ventricular diastolic function in children is not well established. We are assessing the effect of increasing altitude on ventricular diastolic function.

Methods

Patients

About 42 healthy childrens living in Erzurum city, Eastern Anatolia, Turkey with an altitude of 1890 metres for at least 10 years are studied. The control group was recruited from age, gender and body mass index matched children living in Istanbul, Turkey at the sea level for at least 10 years and have

Correspondence to: Dr C. Zeybek, MD, Bolge Egitim Arastirma Hastanesi, Cocuk Kardiyoloji Klinigi, Cat Yolu, Erzurum, Turkey. Tel: +90-442-2325357 and +90-505-7705873; Fax: +90-442-232; E-mails: cenapzeybek@yahoo.com and cenapzeybek@hotmail.com

recently come to Erzurum for vacation. The reason for admittance to the hospital was non-specific chest pain or innocent murmur in all of the children.

Patients with any congenital or acquired cardiac disease and any chronic non-cardiac disease were excluded from the study. Patients with any signs or symptoms of respiratory disease at the time of recruitment were also excluded. The protocol was approved by the local research ethics committee and all patients gave informed consent.

Clinical assessment

All of the children were examined by the same physician at the time of recruitment. Weight and height were measured and body mass index was calculated. Cardiac rate was measured twice in all patients and readings were averaged. Venous blood samples were collected and analysed to determine haemoglobin level in all of the children. Capillary oxygen saturation was measured by pulse oximeter (Nellcor N-560, Boulder, CO, USA).

Echocardiographic study

All patients were examined in a semisupine, left lateral position, by the same observer. Echocardiographic imaging was performed using Vivid-S5 and Vivid-3 machines (General Electric, Vingmed, Norway) equipped with 3.5 and 5 megahertz transducers, with continuous electrocardiographic monitoring. Routine echocardiographic examination was performed before conventional and tissue Doppler imaging to eliminate any congenital or acquired cardiac disease. In patients, where an adequate tricuspid regurgitation spectral Doppler profile was obtainable, pulmonary artery pressure was estimated from the sum of the modified Bernoulli equation and the estimated mean right atrial pressure of 5 millimetres of mercury.

Conventional and tissue doppler measurements

The dimensions of the left ventricle were measured at end-diastole and systole from M-mode traces and fractional shortening was calculated. Ejection fraction was calculated using the Teichholz et al formula. End-diastolic dimension and the anterior wall thickness of the right ventricle were measured in the parasternal long axis view. Right ventricular ejection fraction was calculated using the single plane area-length method, from end-systolic and end-diastolic frames of an apical four-chamber view of right ventricle. The mitral and tricuspid pulsed Doppler signals were recorded in the apical four-chamber view, with the Doppler sample volume placed at the tip of the mitral or tricuspid valve. Peak early filling velocity, peak atrial systolic velocity, early-to-late diastolic flow ratio, and isovolumetric relaxation time were measured for mitral and tricuspid valves, separately. Measurements were obtained during end-expiratory cardiac cycles averaged for each parameter.

Tissue Doppler imaging was performed from the apical four-chamber view and images were digitised. Myocardial velocity profiles of the mitral and tricuspid annuli were obtained by placing the sample volume at the junction of the mitral annulus and left ventricular free wall, and tricuspid annulus and right ventricular free wall, respectively. Images were chosen to minimise the angle of incidence between the scan lines and motion of the base of the heart. Peak systolic velocity, early and late diastolic velocities, and myocardial isovolumetric relaxation time were measured from three consecutive cardiac cycles and averaged. The ratio of early-to-late diastolic annular velocities was calculated. Isovolumetric relaxation time was normalised for heart rate.

Statistical analysis

Descriptive statistics are presented as mean and standard deviation. Independent samples t-test was used for comparison between groups. Probability values of $p < 0.05$ were considered significant.

Results

Healthy 42 childrens living at 1890 metres comprised of 22 males and 20 females and 21 age and sex-matched children living at sea level comprised of 11 males and 10 females were enrolled in the study. Age and body mass index were similar for all the childrens between groups. Cardiac rate and plasma haemoglobin level were found to be higher, oxygen saturation levels were found to be lower in children native to 1890 metres. Demographic and laboratory patient characteristics are summarised in Table 1.

Conventional echocardiographic parameters are summarised in Table 2. Left and right ventricular dimensions, volumes and ejection fractions, and mitral and tricuspid valves inflow parameters were all similar between the children living in Istanbul and in Erzurum.

Pulmonary artery systolic pressure could be estimated by using tricuspid regurgitation jet in 31 of children living in Erzurum and in 14 of children living in Istanbul. Mean pulmonary artery systolic pressure was 22.14 millimetres of mercury with a standard deviation of 5.66 in children living in Erzurum and 20.65 millimetres of mercury with a standard deviation of 6.05 in children living in Istanbul, with no statistically significant difference ($p > 0.05$).

The tissue Doppler echocardiographic parameters are summarised in Table 3. Tricuspid annular early diastolic velocity and ratio of early-to-late diastolic

Table 1. Demographic and laboratory data.

	Children native to 1890 m (n = 42)	Children living at sea level (n = 21)	p-value
Male/female	22/20	11/10	
Age (years)	12.35 (3.78)	12.9 (3.99)	NS
Body mass index (kg/m^2)	20.7 (2.8)	21.1 (2.1)	NS
Heart rate (per min)	90.4 (9.9)	82.8 (12.3)	$<$0.05
Oxygen saturation (%)	91.8 (7.4)	95.7 (4.5)	$<$0.05
Haemoglobin (gr/dl)	14.7 (3.6)	13.1 (3.9)	$<$0.05

NS, not significant

Table 2. Conventional echocardiographic parameters.

	Children living at 1890 m (n = 42)	Children living at sea level (n = 21)	p-value
Left ventricular diastolic dimension (millimetre)	38.81 (4.20)	37.53 (3.99)	NS
Left ventricular systolic dimension (millimetre)	25.35 (2.03)	24.61 (2.29)	NS
Right ventricular diastolic dimension (millimetre)	18.64 (0.90)	18.49 (0.90)	NS
Interventricular septum diastolic dimension (millimetre)	7.60 (0.93)	7.49 (0.98)	NS
Left ventricular posterior wall diastolic dimension (millimetre)	7.39 (1.00)	7.36 (0.93)	NS
Right ventricular anterior wall diastolic dimension (millimetre)	4.23 (1.21)	4.15 (1.05)	NS
Left ventricular mass (gram)	84.38 (25.88)	80.28 (25.71)	NS
Left ventricular fractional shortening (percent)	36.25 (5.10)	35.88 (4.89)	NS
Left ventricular ejection fraction (percent)	71.54 (5.57)	71.61 (3.38)	NS
Right ventricular ejection fraction (percent)	54.38 (4.42)	55.06 (4.59)	NS
Mitral inflow velocities			
Early diastolic velocity (centimetre/second)	101.13 (9.30)	103.81 (9.41)	NS
Late diastolic velocity (centimetre/second)	75.86 (6.62)	75.03 (8.18)	NS
Ratio of early-to-late diastolic velocity	1.35 (0.11)	1.38 (0.16)	NS
Isovolumetric relaxation time (millisecond)	72.07 (11.61)	69.38 (10.03)	NS
Tricuspid inflow velocities			
Early diastolic velocity (centimetre/second)	72.34 (7.13)	73.98 (7.11)	NS
Late diastolic velocity (centimetre/second)	52.28 (10.25)	53.47 (7.49)	NS
Ratio of early-to-late diastolic velocity	1.38 (0.26)	1.38 (0.27)	NS
Isovolumetric relaxation time (millisecond)	78.57 (10.78)	74.48 (10.45)	NS

NS, not significant; $p < 0.05$ was considered as statistically significant

velocities were significantly lower and isovolumetric relaxation time was significantly higher in children living at 1890 metres than children living at sea level, whereas tricuspid annular systolic velocity and annular late diastolic velocity were similar. Mitral annular myocardial parameters were found similar in groups.

Discussion

Acute hypoxia at high altitude constricts the pulmonary vessels and causes an acute increase in pulmonary vascular resistance.[10] In contrast, chronic hypoxic pulmonary hypertension related to altitude is due to postnatal delayed remodelling of the distal pulmonary arterial branches and consequently increased amounts of smooth muscle cells which increases the pulmonary vascular resistance.[1,6,8] Increased pulmonary vascular tone is a secondary factor in chronic hypoxia. Increased pulmonary vascular resistance, whether from increased vascular tone or from pulmonary arterial remodelling, leads to right ventricular pressure overload. This may impair right ventricular function and reduce stroke volume and venous return to the left atrium. Interaction between the right and left ventricles may impair diastolic left ventricular filling as a consequence of right ventricular pressure overload and reduce the stroke volume.[11]

A study examining healthy children native to 2200–2400 metres did not demonstrate any increase in pulmonary artery pressure or in right ventricular wall thickness.[4] In contrast, healthy children native to more than 3000 metres showed definite pulmonary hypertension and right ventricular hypertrophy.[7,8,12]

Table 3. Tissue Doppler echocardiographic parameters.

	Children living at 1890 m (n = 42)	Children living at sea level (n = 21)	p-value
Mitral annular velocities			
Systolic velocity (centimetre/second)	10.39 (1.33)	10.96 (1.51)	NS
Early diastolic velocity (centimetre/second)	17.15 (1.62)	16.86 (2.85)	NS
Late diastolic velocity (centimetre/second)	10.09 (1.81)	9.91 (1.87)	NS
Ratio of early-to-late diastolic velocity	1.69 (0.41)	1.70 (0.34)	NS
Isovolumetric relaxation time (millisecond)	72.76 (10.46)	71.07 (9.06)	NS
Tricuspid annular velocities			
Systolic velocity (centimetre/second)	10.46 (1.66)	10.78 (1.77)	NS
Early diastolic velocity (centimetre/second)	9.17 (1.43)	12.08 (1.51)	<0.05
Late diastolic velocity (centimetre/second)	10.30 (1.31)	9.61 (1.24)	NS
Ratio of early-to-late diastolic velocity	0.89 (0.16)	1.26 (0.26)	<0.05
Isovolumetric relaxation time (millisecond)	77.81 (13.13)	71.26 (13.46)	<0.05

NS, not significant; $p < 0.05$ was considered as statistically significant

Our results resemble the data of healthy children living at 2200–2400 metres,[4] except diastolic dysfunction that we found in our study group. A study on adult population described early diastolic dysfunction and normal systolic function in patients with acute and chronic hypoxia.[13] In a very recent study on adults,[9] in spite of relatively lower pulmonary arterial pressures, more pronounced alterations in diastolic function was found in the native highlanders compared with the acclimatised people.

To our opinion, impairment in right ventricular diastolic function is one of the early changes in the cardiopulmonary system related to the high altitude. Chronic hypoxia leading to postnatal delayed remodelling at pulmonary arterial tree also causesome adverse changes in ventricular myocardium as we consider. These changes leading to ventricular diastolic dysfunction go parallel with the increase in pulmonary vascular resistance. Developing of diastolic dysfunction in right ventricle but not in left ventricle in our study can be explained by these theories: the pulmonary arterial system is in direct continuity with right ventricle and right ventricle may be more vulnerable than left ventricle.

Our study showed that, tissue Doppler imaging, but not conventional imaging, can detect subclinical right ventricle dysfunction found in children living at 1890 metres. Hence, tissue Doppler imaging is superior to conventional imaging for detecting minute changes in ventricular diastolic function related to high altitude.

As the direct measurement of pulmonary artery pressure is invasive, transthoracic Doppler echocardiography is recommended for non-invasive evaluation of pulmonary hypertension. However, some recent studies have suggested that non-invasive pulmonary artery pressure estimation may frequently be inaccurate.[14] Recently, some novel methods have emerged for the estimation of pulmonary artery pressure by using Doppler indices.[15,16] Fahmy Elnoamany et al[15] found that tricuspid annular tissue Doppler-derived isovolumetric relaxation time correlates very strongly with both invasively measured pulmonary artery systolic pressure and endothelin-1 levels. According to this statement, increased tricuspid annular isovolumetric relaxation time in children native to 1890 metres seems to be related to some increase in pulmonary artery pressure. Pulmonary artery systolic pressure, estimated from measurable tricuspid regurgitation, was found similar between children living in Erzurum and in Istanbul. Perhaps, there might be a significant difference if we could estimate pulmonary artery pressure in all of the children.

In conclusion, children living at 1890 metres predisposes to some early changes in right ventricular diastolic function. The tissue Doppler imaging is superior to conventional imaging in detecting these early changes in diastolic function. The prolonged tricuspid lateral annular isovolumetric relaxation time in children native to 1890 metres seems to be related to some increase in pulmonary artery pressure at that altitude.

References

1. Penaloza D, Arias-Stella J. The heart and pulmonary circulation at high altitudes: healthy highlanders and chronic mountain sickness. Circulation 2007; 9: 1132–1146.
2. Maggiorini M. Cardio-pulmonary interactions at high altitude. Pulmonary hypertension as a common denominator. Adv Exp Med Biol 2003; 543: 177–189.
3. Gibbs JS. Biventricular function at high altitude: implications for regulation of stroke volume in chronic hypoxia. Adv Exp Med Biol 2007; 618: 13–24.
4. Ma RY, Pang Y, Qi HY, Sun K. Comparative study of pulmonary arterial pressure in healthy children at different altitude by Doppler echocardiography. High Alt Med Biol 2004; 5: 259.
5. Niermeyer S, Andrade MP, Huicho L. Child health and living at high altitude. Arch Dis Child 2009; 10: 806–811.

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6. Huicho L. Postnatal cardiopulmonary adaptations to high altitude. Respir Physiol Neurobiol 2007; 158: 190–203.
7. Penaloza D, Sime F, Ruiz L. Pulmonary hemodynamics in children living at high altitudes. High Alt Med Biol 2008; 9: 199–207.
8. Huicho L, Niermeyer S. Cardiopulmonary pathology among children resident at high altitude in Tintaya, Peru: a cross-sectional study. High Alt Med Biol 2006; 2: 168–179.
9. Huez S, Faoro V, Guénard H, Martinot JB, Naeije R. Echocardiographic and tissue Doppler imaging of cardiac adaptation to high altitude in native highlanders versus acclimatized lowlanders. Am J Cardiol 2009; 11: 1605–1609.
10. Naeije R. Pulmonary circulation at high altitude. Respiration 1997; 6: 429–434.
11. Alexander JK, Grover RF. Mechanism of reduced cardiac stroke volume at high altitude. Clin Cardiol 1983; 6: 301–303.
12. Huicho L, Muro M, Pacheco A, et al. Cross-sectional study of echocardiographic characteristics in healthy children living at high altitude. Am J Hum Biol 2005; 6: 704–717.
13. Huez S, Retailleau K, Unger P, et al. Right and left ventricular adaptation to hypoxia: a tissue Doppler imaging study. Am J Physiol Heart Circ Physiol 2005; 289: H1391–H1398.
14. Fisher MR, Forfia PR, Chamera E, et al. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. Am J Respir Crit Care Med 2009; 7: 615–621.
15. Fahmy EM, Abdelraouf DA. Right ventricular myocardial isovolumic relaxation time as novel method for evaluation of pulmonary hypertension: correlation with endothelin-1 levels. J Am Soc Echocardiogr 2007; 5: 462–469.
16. Friedberg MK, Feinstein JA, Rosenthal DN. A novel echocardiographic doppler method for estimation of pulmonary arterial pressures. J Am Soc Echocardiogr 2006; 5: 559–562.