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# Down Syndrome in Moderate Altitude Residents: Are There Unique Features?

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Acute exposure to high altitude, which is defined as > 2500 m above sea level, is well-known to be associated with significant alterations to the cardiovascular system, with reductions in atmospheric pressure, oxygen pressure resulting in acute hypoxia, increased myocardial work, increased epinephrine release, and increased pulmonary artery pressures.[1] However, the effects of moderate altitude chronic hypoxia on the cardiovascular system have not been much studied. In general, clinically significant changes are difficult to demonstrate at elevations lower than 2500 m. High-altitude residents have successfully evolved adaptive regulatory mechanisms to survive in a chronic hypoxic environment.[2] Moreover, it has been suggested that exposure to mild to moderate chronic hypoxia may induce cardio-protective properties against various disease states such as hypertension or coronary heart disease and result in favorable outcomes.[2][3] In contrast, a few studies reported important physiological and anatomic features of pulmonary vasculature resulting in pulmonary hypertension even in healthy subjects living at moderate to high altitude.[4][5]

In this issue of the Journal, Espinola-Zavaleta et al.[6] report the results of their study of one-hundred twenty-seven patients with Down syndrome (DS) living in Mexico City to assess the prevalence of congenital heart disease and pulmonary hypertension. Mexico City is a capital of Mexico and located in the Valley of Mexico, a large valley in the high plateaus at the center of Mexico, at an altitude of 2240 m. Moderate altitude is defined as 1500–2500 m above sea level. Therefore, Halla Mountain (1950 m) in Korea is corresponding to moderate altitude but Paektu Mountain (2744 m) is at high altitude. In this study, the investigators demonstrated somewhat interesting features of DS in moderate altitude residents although this study could not provide conclusive causal relationship.

First, the most prevalent congenital anomaly in DS in this study was patent ductus arteriosus, probably related with the moderate altitude of Mexico City as interpreted by the authors. Since patent ductus arteriosus closes with high oxygen tension, it is possible that a hypoxic environment and postnatal persistence of pulmonary hypertension delay closure of ductus arteriosus resulting in the high prevalence of patent ductus arteriosus in this population. Białkowski et al.[7] also reported supportive evidences of this first unique feature in this study. Larger ductal diameter and higher pulmonary artery pressure were observed in patients living at moderate to high altitudes (1500–4200 m) than in those at low altitudes (340–700 m).[7]

Second, pulmonary hypertension is not rare (46%) even in DS patients without congenital heart defects. People native living in a chronic hypoxic environment develop alveolar hypoxia, hypoxemia, and polycythemia.[4] In the heart and pulmonary circulation, a delayed postnatal remodeling of the distal pulmonary arterial branches, increased amount of smooth muscle cells and increased pulmonary vascular resistance resulting in pulmonary hypertension, right ventricular hypertrophy have been reported.[4][5] The magnitude of pulmonary hypertension has been known to increase with the altitude level and the degree of exercise.[4] Interestingly, this structural change in the pulmonary vasculature becomes normal after 2 years of residence at sea level.[8]

In the interpretation of the present study, it is needed to understand the limitations of this study. In fact, this study was not a comparison study not only between DS patients living in moderate altitude and those living in sea level but also between DS patients and healthy subjects without DS. Therefore, further observation and comparison should be needed to confirm the higher prevalence of patent ductus arteriosus or pulmonary hypertension in DS patients at moderate altitude. In addition, the pathophysiology of pulmonary hypertension without congenital heart defects in DS or at moderate altitude should be studied in the future. Comprehensive cardiopulmonary hemodynamic evaluation using an exercise stress echocardiogram or


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cardiac magnetic resonance imaging is warranted in order to detect early changes of exercise-induced pulmonary hypertension or to clarify the clinical impact on exercise capacity, right ventricular function, or clinical outcomes.[9)10)]

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