Clinical Research

Does high altitude increase risks of the elderly patients with coronary artery disease?

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Objective To assess the effect of altitude hypoxia on the elderly patients with coronary artery disease (CAD). Methods Three subject groups were surveyed during their train trip on the highest railroad——the Qinghai-Tibet Railway: 22 elderly individuals with documented CAD, 20 healthy elderly controls, and 20 healthy young controls, all of whom from Beijing near the sea level (76 m). Survey questions addressed clinical features of their healthy conditions and aspects of their coronary disease. The baseline study was performed at Xining at an altitude of 2261m, and then during acute exposure to altitudes of 2808 m, 4768m, 5072 m and 4257 m by train for 24 hours. Resting pulse rate, blood pressure, oxygen saturation, electrocardiograph (ECG), and cardiac work estimated by the heart rate-blood pressure double product were obtained five times in each subject at different altitudes. Results On arrival to altitudes between 4768 m and 5072 m, the older passengers, especially those with preexisting coronary disease, had higher HR, higher BP, and lower SaO₂, as well as more frequent abnormalities on ECG, as compared to the younger healthy subjects. As compared with the healthy elderly controls, incomplete right bundle branch block, left ventricular hypertrophy, and ST segment depression were more frequently seen in the elderly coronary patients (P≤0.01). Cardiac work in group 1 was increased by 13% 12 hours after arrival to altitudes between 2808 m and 5072 m. Oxygen saturation decreased significantly with the altitude increasing by train ascent but improved after inhalation of oxygen. Most of the older subjects tolerated their sojourn at high altitude well except one who developed angina repeatedly with a significant ST segment depression. Conclusions Coronary events and ECG signs of myocardial ischemia are rare in elderly individuals with CAD who travel from sea level to moderate altitudes of 1500m to 2800 m. Patients with CAD who are well compensated at sea level generally tolerate this moderate altitude well. However, it would be prudent for patients with CAD going to altitude above 3000 m. The patients should consult their physician before undertaking a trip to such altitude (J Geriatr Cardiol 2009; 6:137-141).

Key words coronary artery disease; elderly; high altitude; hypoxia; angina

Introduction

Today, more and more people are going to altitude for adventure holidays and scientific or business activities. In China, after completion of the Qinghai-Tibetan railroad (QTR), more than 2.8 million passengers per year from lowlands take the train trip to the highlands-Tibetan plateau. Among the passengers, nearly 52% of individuals are over 40 years old, and about 12% are over 60. Coronary artery disease (CAD) is common in elderly Chinese, with more than 50% of elderly individuals having significant coronary arteriosclerosis as documented by autopsies. However, studies relating to the effect of altitude hypoxia on the elderly patients with CAD are limited. The Qinghai-Tibet railroad from Xining to Lhasa is 1956 km long and it takes about 24 hours for the train running on the Tibetan plateau at altitudes between 2261 m and 5072 m, of which, the distance from Golmud to Lhasa is over 1142 km long, with more than 85% of the distance above 4000 m, making it the highest railway in the world. In this study, we assessed the effect of altitude hypoxia on the elderly patients with CAD, and compared with the elderly and young healthy controls. In addition, we reported a case who had safely worked at high altitude after coronary stenting.

Methods

Three subject groups were surveyed. From 2006 to 2008, there were 1454 recorded older train passengers (age ≥ 60 years) taking the train trip from the near sea level at Beijing (76 m) to Qinghai-Tibet plateau by the QTR. Group 1 concerned 22 persons(17 males and 5 females, aged 60-73 years, with a mean age of 64.5 ± 4.5 years). All of them presented detailed clinical data. The initial physical examination suggested that they had a confirmed clinical diagnosis of CAD for 2 to 12 years, but the symptoms were ad-
equally controlled by medications, and there was no significant evidence of myocardial ischemia in ECGs at 2261 m, thus they were not prohibited from this railway travel. Group 2 included 20 healthy elder passengers (14 males and 6 females, aged 61 to 79 years with a mean age of 66.6 ± 5.5 years) without CAD randomly chosen from the above recorded older train passengers. In group 3, 20 healthy younger persons (10 males and 10 females, aged 22 to 38 with a mean age of 35.5 ± 4.2 years) was recruited from 1716 younger train registrants (< age 40), who boarded the QTR from Beijing and were absent of any preexisting cardiovascular disease. We observed all of the above three groups during the train journey first in Xining (an altitude of 2261 m) for physical and laboratory examinations for 24 hours, then from Xining to Golmud (2808 m) for 10 hours, subsequently from Golmud to Lhasa (3658 m) on the train for 14 hours. By the end of the train journey, 15 of 22 persons in group 1 had been continuously observed for 2-3 days during their stay in Lhasa.

Physical examination and laboratory studies

Xining is the main rail link to Golmud, thus the basal survey including an initial physical examination and laboratory studies were performed in all subjects in Xining before departure.

Initially, the passengers completed a Clinical Questionnaire including previous history of diseases, family history, previous exposure to altitude, exercise, and alcohol and cigarette consumption. Subsequently, the subjects underwent a physical examination before departure on a train journey. Co-synchronous resting pulse rate (PR) and arterial oxygen saturation (SaO₂) by finger oximetry (Detex Ohmeda, Louiseville, CO, USA), systemic blood pressure (BP) (by sphygmomanometer), a routine blood tests as well as a 12-lead electrocardiogram (ECG) were simultaneously determined. Cardiac work was evaluated by a previously reported formula with a heart rate-blood pressure double product [HRSBP product (× 10⁻⁵)].

During the train trip from Xining to Lhasa over a period of 24 hours, the subjects received four repeated measurements of ECG, BP, PR, and SaO₂. All the examinations were performed at a route section during the train in motion. First recording was made in the morning of the train starting site of Golmud at 2808 m, the second recording was 1.5 hours later when the train arrived at Kulum pass section at an altitude of 4768 m, the third recording was made in the afternoon of arrival at the railroad’s highest section “D” the Tanggula pass at 5072 m, and the fourth recording was made in the evening at Yanbajain section at 4257 m when the train will arrive in Lhasa. For subjects in group 1, we also obtained follow-up data for 2-3 days in Lhasa.

Statistical analysis

Results were reported with mean values ± standard deviation (SD). The Chi-square test was used to compare categorical variable and Student’s t test to compare continuous variables. Repeated measures of ANOVA was performed with statistical significance of P<0.05.

Results

Symptoms

After the train arrived at an altitude above 3500 m, most of the elderly patients with CAD (16/22, 73%) presented a slight headache, mild weakness, and anorexia. Two had a nausea but without vomiting. One person (case 1) developed an acute attack of angina and dyspnea.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>ECG changes in elderly subjects with and without CAD</th>
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<tbody>
<tr>
<td>ECG change</td>
<td>Elderly patients with CAD [n,%]</td>
</tr>
<tr>
<td>Sinus arrhythmia</td>
<td>6 (5.5)</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td>8 (7.3)</td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>24(21.8)</td>
</tr>
<tr>
<td>Atrial extrasos</td>
<td>11(10.0)</td>
</tr>
<tr>
<td>Ventricular extrasos</td>
<td>3(2.7)</td>
</tr>
<tr>
<td>Escape beat</td>
<td>5(4.5)</td>
</tr>
<tr>
<td>A-V heart block (first degree)</td>
<td>12(10.9)</td>
</tr>
<tr>
<td>Incomplete right BBB</td>
<td>20(18.0)</td>
</tr>
<tr>
<td>Left anterior hemiblock</td>
<td>5(4.5)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>25(22.7)</td>
</tr>
<tr>
<td>ST depression 0.5 mm</td>
<td>25(22.7)</td>
</tr>
<tr>
<td>ST depression 1.0 mm</td>
<td>5(4.5)</td>
</tr>
<tr>
<td>T wave changes</td>
<td>20(18.2)</td>
</tr>
</tbody>
</table>

BBB: incomplete right bundle branch block
ECGs

A total of 110 and 100 recorded ECGs in group 1 and group 2 were analyzed respectively. Abnormal resting ECGs were not uncommon when the train ascended to an altitude above 3500 m (Table 1). Sinus tachycardia was more common (64%) in the 14 patients with CAD. Incomplete right bundle branch block (BBB), left ventricular hypertrophy, and ST segment depression were more frequently seen in group 1 than in group 2 ($P<0.01$). Atrial extrasystoles occurred in 3 symptom-free individuals, and ventricular extrasystoles occurred only in one person after a physical activity when the train stopped at the station. During the trip, one subject aged 73 years (case 1) showed ST segment depression ($>1.0$ mm) with an angina, and he was advised to stop his altitude trip. Five persons, aged 62 to 68 years, developed a slight ST depression ($>0.5$ mm), but there was no complications or signs of myocardial ischemia. Two of whom used oxygen during the trip across Mt. Tanggula. They safely enjoyed such a train trip. During the first-day stay in Lhasa (3658 m), no subject showed new ST-T segment abnormality.

Pulse rate and blood pressure

Resting pulse rate (PR) was lowest in Xining and increased with altitude. At an altitude between 4768 m and 5072 m, mean PR was $96 \pm 22$ in group 1, $90 \pm 18$ in group 2, and $79 \pm 15$ in group 3 respectively, with a higher PR in the two elderly groups than in the younger group ($P<0.05$).

Before departure from Xining, systolic and diastolic blood pressures (SBP, DBP) were normal in most subjects. There was a moderate increase in SBP upon arrival in Golmud. When the train ascended to an altitude between 4768 m and 4905 m, BP increased by 18 of 22 (82%) subjects in group 1 and 13 of 20 (65%) subjects in group 2, respectively. There was no statistically significant difference in increased values of BP between the two elderly groups ($P>0.05$). Combining the two elderly groups, BP increased significantly, with the mean resting SBP rising from $120 \pm 18$ mmHg to $148 \pm 16$ mmHg ($P<0.001$) and mean diastolic pressure from $68 \pm 10$ mmHg to $94 \pm 15$ mmHg ($P<0.001$). Elderly passengers with or without CAD had remarkably higher BP than younger subjects (mean SBP $148 \pm 16$ mmHg vs $124 \pm 16$ mmHg, mean DBP $94 \pm 15$ mmHg vs $78 \pm 6$ mmHg ($P<0.001$).

Heart rate-blood pressure double product [HRSBP product ($\times 10^{-3}$)]

Cardiac work at rest as estimated by the HRSBP product was initially elevated by 13% in group 1 12 hours after arrival to an altitude of 4678 m, which reached its peak value (elevated by 14%) 15 hours after arrival to 5072 m. Mean value of HRSBP product in group 1 was higher at 5072 m than that at 2261 m ($16.5 \pm 1.2$ vs $9.2 \pm 0.6$), indicating significant increases in both heart rate and systemic blood pressure ($P<0.001$). At 5072 m, HRSBP product at rest increased by 14%, 12%, and 10% in group 1, group 2 and group 3 respectively, but with no statistical significance ($P>0.05$). Heart work in group 1 fell slightly (by 8.8%) after a two-day stay in Lhasa.

Arterial oxygen saturation

Arterial oxygen saturation (SaO$_2$) was measured four times daily using finger oxymetry in a sitting position. SaO$_2$ decreased with altitude increasing by train ascent, especially in the elderly subjects. The mean SaO$_2$ in group 1, group 2 and group 3 was $92 \pm 3.5\%$, $93 \pm 4.2\%$, and $95.5 \pm 6.6\%$ at Xining (2261 m), and $88 \pm 5.2\%$, $90 \pm 4.6\%$, and $91 \pm 5.5\%$ at Golmud (2801 m), respectively. There was no significant difference between the three groups at both altitudes ($P>0.05$). SaO$_2$ decreased significantly while the train ascended to an altitude between 4768 m and 5072 m. The mean SaO$_2$ in group 1, group 2 and group 3 was $78 \pm 4.5\%$, $81 \pm 6.2\%$, and $86 \pm 4.4\%$, respectively. The younger group had a higher SaO$_2$ than the elderly ($P<0.001$). The lowest SaO$_2$ in one older patient with CAD was 64%. Eleven elderly subjects (mean SaO$_2$ 77.5 ± 5.2%) received oxygen administration. There was a response to oxygen supplement within 30 minutes to 2 hours, with an increased mean SaO$_2$ of 84 ± 4.0%.

Clinical outcome

Despite the increased cardiac work and hypoxemia were presented in the elderly patients with CAD, most of the older subjects tolerated their sojourn at high altitude well during the train trip. One elderly patient with CAD was advised to stop his train traveling and return go sea level due to repeatedly episodes of angina with a significant cardiac ischemia occurrence at 3700 m. In spite of some mild symptoms consistent with altitude hypoxia during the first 2 days at altitude, but all other old subjects were well by the time after 4-5 days of acclimatization in Lhasa.

Case samples

Case 1. Patient with CAD had early development of angina and ST-segment abnormalities after ascent to altitude above 3000 m.

A 73-year-old engineer with known CAD for about 8 years had occasionally effort-related angina at sea level. His ECGs at Xining showed a significant ST depression with an incomplete right bundle branch block. He experienced chest pain with slightly physical effort when the train passed through the Guanje Tunnel (3698 m) and traversed the Halgan area at 3200 m 4 hours after leaving Xining. His BP was $142/86$ mmHg, PR 112 bpm, SaO$_2$, 78%. ECGs showed ST segment depression ($>1.0$ mm) with a complete right BBB. Sublingual administration of nitroglycerin tablet and oxygen inhalation performed in a medical aid room of the cars relieved his symptoms but the extrasystoles and ST depres-
sion still existed. He was advised stopping his altitude trip at Golmud and hospitalized.

**Case 2. Safe train traveling with cardiac pacemaker**
A 69-year-old doctor who had a history of CAD for 12 years received a pacemaker implantation for sinoatrial block 3 years before. After operation, he had good performance and was asymptomatic. He felt well during the whole travel on the train. His ECGs showed pacing rhythm with a heart rate of 74 bpm, a mean SaO₂ of 84 % and he passed the highest point at 5072 m without any symptoms.

**Case 3. The safety of working at high altitude after coronary stenting**
A 49-year-old male manager with a history of CAD was ever treated with two drug-eluting stents (Cypher Select, DES, Cordis company, USA) in the right and left coronary arteries in Beijing in 1999, and with aspirin (300 mg) and clopidogrel (75 mg) once daily. He was free of angina and an coronary angiography showed no re-stricture in his coronary arteries at six months post stenting. He was strongly advised not to go altitude. However, he went to altitude two years after the stenting procedure despite this advice. On May 1, 2001, he gradually ascended from Beijing (76 m) to Golmud (2808 m) by train for about 36 hours and then from Golmud to Fenghuoshan by car for 6 hours. He then worked at 4905 m and slept at 4600 m for about 10 days and declared that he felt better than pre-operation at sea level. Subsequently, from 2002 through 2005 (whilst he was aged 55), he spent 10 periods of 10-15 days of working and living at these altitudes without symptoms or signs of illness. Long-term follow-up during the altitude stay showed no new ST-T-segment abnormalities in ECGs. 2-D echocardiography indicated normal left ventricular function. Resting arterial oxygen saturation (SaO₂) varied between 78% and 89 %. Cardiac work at rest indicated by HRSSBp product (× 10⁻³) was elevated by 12% 12 hours after arrival at altitude. Mean value of HRSSBp product was 10.7 ± 1.2 at 4905 m, higher than 8.2 ± 0.6 at sea level, but the difference was not statistically significant (P>0.05). Since the tunnel was completed on June 30, 2006, he has stayed in Beijing (76 m) with no obvious healthy problem to date.

**Discussion**

How do CAD patients tolerate high altitude? What kind of patients with CAD should not go to altitude? Previous studies indicated that severe adverse effects of altitude hypoxia rarely occurred in patients with CAD at moderate altitude between 1500 m and 3000 m, even if in elderly subjects. During a visiting to an altitude of 2500 m, there was only low risk of myocardial ischemia in 97 elderly subjects including two with coronary angioplasty and 12 with coronary bypass. In this study, 22 elderly patients with CAD felt well generally and ECG showed no signs of significant cardiac ischemia at altitudes of 2261 m and 2808 m. Thus, it was probably safe for asymptomatic CAD patients to visit moderate altitude. However, it would be prudent for such patients to travel to a higher altitude above 3000 m. At an altitude of 3100 m, patients with CAD may probably complain early development of angina and abnormal ST depression (≥ 1.0 mm) during or immediately after exercise. In elderly subjects with CAD, altitude exposure may aggravate signs of cardiac stress and even lead to a new infarct. However, there was little information about patients with CAD at an altitude above 3500 m. In this study, the patients with mild CAD were symptoms free and displayed no evidence of cardiac ischemia, there was probably little risk in joining to altitude train trip. However, there was wide variation in individual responses to hypoxia. Many patients, especially the elderly ones with CAD, such as case 1 reported above, who were asymptomatic at sea level, may experience their first symptoms attack on going to altitude. Hultgren observed two elderly male cases (70 years old) with CAD, who went to high altitude and suffered an attack of angina.. We found that the older passengers, especially those with previous CAD, responded differently to altitude compared to the younger healthy subjects. They had higher HR, higher BP, and lower SaO₂, as well as more frequent abnormalities on ECG. Consequently, coronary patients with notable arterial desaturation, severe angina, a recent cardiac infarction, or heart failure should obviously be discouraged from going to high altitude, since they are at high risk of cardiac events during the first several days after ascent.

Whether altitude cause worsening of the patients who have coronary bypass surgery or angioplasty remains debated. Several authors suggested that, for asymptomatic patients with good exercise tolerance, high altitude exposure presented acceptable risk. In such patients, exercise testing or nuclear studies usually indicated a low-risk status allowing a visit to a moderate altitude area. The same consideration would apply to patients post coronary angioplasty. However, others believe that even after a successful bypass operation, the likely residual disease remains a contraindication for altitude exposure.

Heart work usually increase at high altitude. Our findings revealed that almost all of the subjects presented an elevated HRSSBp product 12 hours after arrival at altitudes between 4768 m and 5072 m, but it decreased during a 48 hours stay in Lhasa. Morgan et al have reported two CAD patients who had previous myocardial infarction and had subsequently undergone coronary artery bypass graft surgery showed a reduced oxygen saturation and an increased HRSSBp product during acute exposure to 3100 m altitude. This change was possibly due to an increased sympathetic nervous system activity, an early response to acute altitude hypoxia which would increase the heart rate, systemic blood pressure, the velocity of ventricular contraction, and car-
diac output, thus leading to increased cardiac work. After 5-10 days at altitude, sympathetic stimulation decreased, resulting in decreased heart rate, cardiac output and blood pressure.13

Is traveling or working at high altitude safe for patients after stenting? In the present study, we reported one patient (case 3) with CAD post coronary stenting, whose angiography showed no re-stricture at 6 months and who had an uneventful follow-up for two years, indicating that the risk can be low. The patient traveled repeatedly to about 5000 m, feeling well and remained free of angina. There was no evidence of myocardial ischemia or arrhythmia in spite of decreased oxygen saturation levels. Since CAD patients treated with coronary stents are common, readiness for travel to altitude traveling merits attention. This case would favor a flexible position for those CAD patients who are free of symptoms.

For patients who have received implantation of cardiac pacemaker, there is a concern that acute altitude exposure may influence the ventricular stimulation threshold,14 but it seems that they are not at increased risk, such as in case 2.

Taken together, it seems that, for patients with CAD post coronary bypass, coronary angioplasty, or coronary stenting, there is probably little risk in going to moderate altitude, and no particular disadvantage. However, the elderly patients with known or suspected CAD should consult their cardiologist before considering an altitude trip. The physician should evaluate the physical fitness of the patient, estimate the potential risks, and prescribe an appropriate preventive measures.15 An exercise test, perhaps incorporating a thallium or 99m Tc scan, which gives a picture of the blood flow to the heart muscle, may be helpful. If exercise is limited by chest pain or the exercise capacity is reduced, it is likely that symptoms will occur at altitude and the risk of cardiac irregularities and infarction may be increased. Clearly, such patients should avoid visiting to high altitude. If travel to high altitude or travel by the highest train is necessary, oxygen and an increase in medications may be necessary to control symptoms.

There are several limitations in the present study. The available data from the elderly and younger passengers are at high altitude only, there is no data at sea-level for comparison. Also, the observations were measured at rest only, without an exercise test for evaluations of cardiac workload and ischemia. The diagnosis of CAD was based on clinical studies whilst a nuclear study at sea level reflecting coronary circulation was scant. More complete data are needed to determine the effect of altitude hypoxia on the patients with CAD in future studies.

Acknowledgments

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References