ORIGINAL RESEARCH

Electrocardiographic Evidence for Right Heart Strain in Asymptomatic Children Living in Tibet—A Comparative Study Between Han Chinese and Ethnic Tibetans

Charles W. Hulme, MB ChB; Thomas E. Ingram, MB ChB; David A. Lonsdale-Eccles, MB ChB

From the St James University Hospital, Leeds, UK (Drs Hulme and Ingram), and the Canterbury District Hospital, Christchurch, New Zealand (Dr Lonsdale-Eccles).

Objective.—To compare ethnic Tibetan children with Han Chinese migrants for signs of right ventricular strain using electrocardiography (ECG) that would suggest chronic hypoxia at altitudes of 3500 to 4500 m above sea level.

Methods.—One hundred thirty-five asymptomatic school children aged 7 to 12 years were assessed for height, weight, and blood pressure and underwent a single ECG at 2 centers at 3500 and 4500 m. A questionnaire was given to parents to provide demographic data with relevant medical history.

Results.—There was a high prevalence of right ventricular strain on ECG for both Tibetan and Han children (33%) with no significant difference between the 2 ethnic groups or sexes.

Conclusions.—Other studies showing higher observed rates of symptomatic chronic altitude sickness in Han Chinese children suggest that other extracardiologic factors play a role in the pathogenesis of the disease.

Key words: chronic mountain sickness, altitude sickness, electrocardiography, right ventricular strain, hypoxia

Introduction

It is well recognized that individuals who live at low altitudes (below 2000 m) require a period of adaptation to acclimatize to life at higher levels. The effect of rapid ascent to high altitudes causes acute mountain sickness with the potentially fatal complications of pulmonary and cerebral edema. It has only been more recently recognized that inhabitants at high altitudes for a period of years can develop a chronic form of the disease.^{1,2} Early manifestations of chronic mountain sickness (CMS or Monge disease) are headache, dizziness, and peripheral edema, which are followed by polycythemia and pulmonary hypertension with marked right ventricular strain. These symptoms, usually in children, can be fatal but are reversed on descent to lower altitudes; however, they can return on reascent.

A number of studies have examined this phenomenon and its prevalence in high-altitude communities, mainly in the Andes and Himalayas.^{3,4} The Tibetan plateau with

an average elevation of 4000 m is home to an estimated 5 million inhabitants, mainly either of Tibetan ethnic descent or of relatively recently immigrated and genetically dissimilar Han Chinese descent. This gives a vast population living at high altitude, where genetic change for thousands of years is met with a population influx of persons from lowlands who have had to adapt during a relatively short period. Observations in Tibet have suggested that the prevalence of chronic altitude sickness in children is higher in the Han population, suggesting a genetically protective mechanism among ethnic Tibetans.⁵

Studies have been conducted on the pathophysiology of CMS in subjects with established disease, where there is evidence of right ventricular enlargement, pulmonary hypertension, and pulmonary arteriolar hypertrophy.^{6,7} However, there has been little analysis of the asymptomatic population as a whole regarding subclinical evidence of right heart strain brought about by chronic hypoxia. The objective of this study was to examine the electrocardiographic (ECG) evidence for right heart strain in asymptomatic school children living in Tibet and to

Corresponding author: Charles Hulme, MB ChB, 36 Cragg Hill, Horsforth, Leeds, UK LS18 4NU (e-mail: billhulme@hotmail.com).

Table 1. Demographic data of 135 data sets

	<i>Tibetan</i>	<i>Han</i>	<i>Mixed</i>	<i>Other</i>	<i>Total</i>
Male	40	33	5	0	78
Female	31	21	5	0	57
Total	71	54	10	0	...

compare the prevalence of right heart strain between ethnic Tibetans and Han Chinese. This may give further clues as to the prevalence of and possible genetic protection from chronic altitude sickness.

Methods

During a 2-month period, school children in Lhasa (3500 m) and NaqCu (4500 m) aged 7 to 12 years were approached by the Pediatric Department of the Lhasa First Peoples Hospital and asked if they would be prepared to participate in the study. An anonymous numbered questionnaire translated into Chinese was handed to all participants to be filled in by the subjects' parents; this questionnaire covered date of birth, ethnic origin, length of time living in Tibet, and relevant medical history, including family history. Returned forms were then translated, and relevant details were entered in the database by an independent investigator. Children were measured for height, weight, blood pressure with a manual sphygmomanometer, and oxygen saturation with pulse oximetry; finally, children underwent a single-channel ECG to record leads I, II, III, aVR, aVL, aVF, V1, V3, and V5. Classes were randomly selected by school principals and contained mixed sexes and ethnic origins, thus removing any obvious pattern from the subject groupings. Returned completed questionnaires and ECGs were then kept separately, with only the relevant age of the subject written in the top left-hand corner of the ECG to aid interpretation. Investigators then blindly analyzed each ECG, looking only for evidence of right heart strain using the criteria outlined in the Appendix. Finally, data were combined in a database and analyzed for evidence of significant sex and ethnic differences regarding the prevalence of right heart strain.

Results

Of the 246 questionnaires and ECGs conducted, 111 subjects failed to produce a complete set of data, almost all (109) because of incorrectly filled-in or nonreturned forms. The subjects from the group that failed to produce a complete set of data had ECG tracings that were judged to be of too poor a quality to interpret accurately.

Table 2. ECG evidence of right heart strain

	<i>Tibetan</i>	<i>Han</i>	<i>Mixed</i>	<i>Total</i>
Male	13 of 40	12 of 33	2 of 5	27 (35%)
Female	12 of 31	6 of 21	1 of 5	19 (33%)
Total	25 (35%)	18 (33%)	3 (30%)	

* ECG indicates electrocardiographic.

Of the 135 remaining complete sets, the demographic data were split as shown in Table 1.

All of the children of mixed ethnicity were from parents of Han and Tibetan origin only.

ECG evidence of right heart strain using the criteria listed was found in subjects as shown in Table 2.

Analysis

Using the χ^2 test (chi-square test) to compare the prevalence of right heart strain between Han Chinese and Tibetans, no significant difference was found ($P = .904$). There was also no significant difference between Tibetans and children of mixed ethnicity ($P = .731$). Analysis for sex differences, regardless of race, was also not significant ($P = .839$). The overall prevalence of right heart strain shown by ECG for children living in Tibet when compared with that of low-altitude residents, however, seems much greater. An estimate of the prevalence of right ventricular strain at sea level, as evidenced by ECG, can be estimated by accumulating the prevalences for the conditions from causes other than chronic altitude-related hypoxia. These include congenital conditions, such as Fallot tetrad, tricuspid atresia, and pulmonary valvular dysplasia, in addition to normal variants who have, for example, right bundle branch block morphology. This total adds up to around 1% to 2%.^{8,9} It would also be expected that most of these children would show signs of their disease, making the proportion of asymptomatic children far lower.

Discussion

This study has found that ECG abnormalities suggestive of right heart strain are common in people living in Tibet when compared with a prevalence of around 1% to 2% at sea level, where congenital causes predominate.^{8,9} However, there was no significant difference between recently immigrated children from lowlands and long-term residents. Indeed, the incidences in both Tibetan vs Han and male vs female were remarkably similar. The components of our study did not allow us to determine whether these data are reflected in subsequent clinical

manifestations of CMS, because all the subjects of our study were asymptomatic and because there has been no long-term follow-up of the children.

Previously, in a study using a similar number of subjects, Rotta and Lopez³ analyzed Peruvian Indians living at 4500 m and found a higher prevalence of ECG abnormalities in recent immigrants than in lifelong residents. Differences between Andean and Tibetan populations have long been discussed, but little has come to light to explain differing rates of altitude sickness in terms of geography or population migration alone.⁵ A study in Lhasa by Halperin et al¹⁰ using a smaller number of subjects that compared Tibetan and Han adults, some with clinical manifestations of CMS, also showed a higher proportion of right heart strain among recent (Han) immigrants (17% vs 29%). This study supports the use of ECG in diagnosing CMS, because higher prevalences of ECG abnormalities were seen in symptomatic CMS patients (50%).

Suggested mechanisms of theoretical genetic adaptation in long-term high-altitude residents point toward the extent of pulmonary arterial constriction in response to hypoxia. It is thought that Yaks cannot survive permanently at low altitudes because of their inability to adjust to pulmonary circulatory pressures,¹¹ and postmortem examinations of infants who have died of CMS in Tibet show extreme hypertrophy of the pulmonary arterioles with right ventricular hypertrophy. In addition, Sen-Gupta et al⁴ reported minimal hypoxic vasoconstriction responses when testing an ethnic group similar to Tibetans. What needs to be studied now is whether our findings in asymptomatic children, in whom there appears to be an equal prevalence of right heart strain between Tibetan and Han children as detected by ECG, are reflected in clinical manifestations later in life. It is quite possible that, despite ECG evidence of right heart strain, there are other factors that are important in subjects developing CMS later in life.

Study limitations

This study was conducted using limited resources for only a short time available. Reliance on local schools for child selection for the study was largely out of the researchers' control but represented the spread of race and sex found in the population as a whole. The questionnaire sent to all participants was only translated into Chinese, despite many families using Tibetan as their first language. However, all schoolteachers and children were able to speak Mandarin, and the nonreturned and incorrectly filled-in forms were from both Han and Tibetan families. If a larger study could be performed, then sample groups could be analyzed to look for significant dif-

ferences between CMS evidence and length of stay in Tibet. In this study, subjects were included if they had spent most of their life in Tibet.

In our study, the assessment for right heart strain takes into account the varying sensitivities and specificities of all the ECG criteria used.¹²⁻¹⁴ Despite this, the study by Halperin et al¹⁰ had a sensitivity of only 50% for ECG evidence of right heart strain in patients with clinical manifestations of CMS. This suggests that, despite postmortem evidence of right heart strain in CMS victims, either the ECG tracings were not sensitive enough or other physiologic factors play a role in clinical CMS. It is also presumed that ECG evidence of right heart strain in healthy children is purely attributable to chronic exposure to high altitude and not other factors. The few questionnaires that had any medical history volunteered were not relevant to the ECG findings.

Conclusions

The study findings show that there is a high prevalence of ECG abnormalities consistent with right heart strain in healthy Tibetan and Han children living at altitude. It appears that there is a very similar level of abnormalities between the 2 ethnic backgrounds and sexes. This would not be expected when compared with previous studies, which show a higher occurrence of right heart strain evidence in symptomatic immigrant residents from low-altitude regions. This suggests that for the higher incidence of CMS found in Han children at altitude, other physiologic factors also play a role.

Acknowledgments

We would like to thank Dr Giorgio Cortassa of Comitato Internazionale per lo Sviluppo dei Popoli (CISP) and Dr Yunden Droma of the Tibetan First Peoples Hospital for their help in the concept and design of this study. This project was partly funded by the authors, with financial assistance from the Leeds University Medical School Dora Ratcliffe Fund. Equipment was provided by the Tibetan First Peoples Hospital Cardiology Department in Lhasa, Tibetan Autonomous Region, China.

References

1. De Meer K, Heymans HS, Zijlstra WG. Physical adaption of children to life at high altitude. *Eur J Pediatr.* 1995; 154:263-272.
2. Pei SX, Chen XJ, Si Ren BZ, et al. Chronic mountain sickness in Tibet. *Q J Med.* 1989;71:555-574.
3. Rotta A, Lopez A. Electrocardiographic patterns in men at high altitudes. *Circulation.* 1959;19:719.

4. SenGupta A, Auto J, Pawape G. Unexplained pulmonary hypertension in children in the highlands of Papua New Guinea. *P N G Med J*. 1995;38:45–51.
5. Wu T. The Qinghai-Tibetan plateau: how high do Tibetans live? *High Alt Med Biol*. 2001;2:489–499.
6. Ge RL, Helun G. Current concept of chronic mountain sickness: pulmonary hypertension-related high-altitude heart disease. *Wilderness Environ Med*. 2001;12:190–194.
7. Sui GJ, Liu YH, Cheng XS, et al. Subacute infantile mountain sickness. *J Pathol*. 1988;155:161–170.
8. Keith JD, Rowe RD, Vlad P. Electrocardiography. 3rd ed. In: Iceith JD, ed. *Heart Disease in Infancy and Childhood*. 1978:51–64.
9. Mart C, Zachay C, Rosen K. Right bundle branch block. Available at: <http://www.emedicine.com/ped/topic2500.htm>. Accessed March 14, 2003.
10. Halperin BD, Shinfu Sun, Jianguo Zhuang, Tarshi Droma, Moore LG. ECG observations in Tibetan and Han residents of Lhasa. *J Electrocardiol*. 1998;31:237–243.
11. Heath D, Williams D, Dickinson J. The pulmonary arteries of the Yak. *Cardiovasc Res*. 1994;18:133–139.
12. Fretz EB, Rosenberg HC. Diagnostic value of ECG patterns of right ventricular hypertrophy in children. *Can J Cardiol*. 1993;9:829–832.
13. Medvegy M, Antaloczy Z, Preda I. Connection between right ventricular pressure and the ECG. *J Electrocardiol*. 1988;27:23–27.
14. Kaushal SS, DasGupta DJ, Prashar BS, Bhardwaj AK. Electrocardiographic manifestations of healthy residents of a tribal Himalayan village. *J Assoc Physicians India*. 1995; 43:15–16.

Appendix I. Criteria used for assessing electrophysiological evidence of right heart strain

A subject was considered to have ECG evidence of right heart strain if any of the following points were seen:

- QR pattern in V_1 ($Q > 3\text{mm}$ and $R > 10\text{mm}$)
- Asymmetrical T wave inversion or ST depression in V_1 to V_3
- R wave in V_1 :

$>14\text{ mm}$	5 to 7 years
$>12\text{ mm}$	8 to 11 years
$>10\text{ mm}$	12 to 15 years
- R:S ratio in V_1 :

>2	5 to 7 years
>1.8	8 to 11 years
>1.7	12 to 15 years
- rSR' pattern in V_1 (S is smaller than R' and $R' > 10\text{mm}$)
- 1) Right axis deviation:

$+11^\circ$ to $+143^\circ$	5 to 7 years
$+9^\circ$ to $+114^\circ$	8 to 11 years
$+11^\circ$ to $+130^\circ$	12 to 15 years

Plus any of the following:

- 2) Pulmonary P waves ($>2.5\text{ mm}$ amplitude)
- 3) R wave in a VR $> 5\text{ mm}$
- 4) R wave $< S$ wave in V_5
- 5) S wave $> 4\text{ mm}$ in V_5