

Cardiac Arrhythmias at High Altitude

DR Woods¹, C Boos², PR Roberts³

¹Consultant Physician, RAMC and Consultant Physician in Endocrinology and Diabetes Northumbria and Newcastle NHS Trusts, Honorary Clinical Senior Lecturer University of Newcastle, MDHU Northallerton; ²Consultant Cardiologist, Poole Hospital, RAMC; ³Consultant Electrophysiologist and Cardiologist, Southampton University Hospital, Southampton, United Kingdom.

Abstract

Palpitations at high altitude have been experienced, but seldom recorded, for centuries. The hypoxia, sympathetic activation and alkalosis of altitude predispose to cardiac ischaemia and arrhythmia. Indeed, sudden cardiac death is responsible for 30% of all deaths during mountain sports at altitude. This article reviews the literature to date on the evidence for cardiac arrhythmias at altitude.

Introduction

As discussed elsewhere in this edition of the journal, and briefly summarized here, a number of key physiological changes occur with increasing altitude. Hypoxia is the key physiological challenge at high altitude (HA). At around 3500m the resting oxygen saturation (SpO₂) may be 85% and at Everest base camp (5300m) the partial pressure of oxygen is half that at sea level. During exercise at altitude significant reductions in SpO₂ are observed due to limitations in maximal pulmonary diffusing capability. High pulmonary artery pressure is a feature of high altitude exposure, which is a direct result of alveolar hypoxia on the pulmonary circulation [1], with resultant arterial hypoxaemia. In addition, resting and exercise-induced arterial adrenaline levels are higher than at sea-level [2]. This, in addition to the respiratory alkalosis that occurs, may further predispose to palpitations, arrhythmias and ischaemia [3], especially in those with pre-existing cardiac disease. This review will therefore examine whether these physiological demands translate into cardiac arrhythmias at HA.

Historical perspective

Historically, the effect of HA as a cardiac stressor was utilized in the "Levy test" of the 1940s which simulated the hypoxic environment of 5500m as a diagnostic tool for coronary artery disease [4]. Palpitations at HA have been experienced for centuries. The explorer D'Orbigny, on the crest of the Peruvian Cordilleras between 1826 and 1834, is quoted as saying: "*at the least movement, I felt violent palpitations*" [5]. Despite this history the logistical challenges of recording a clear ECG at HA limited early investigators. Early pioneers attempted to record ECG changes at rest but were dogged by interference from the static electricity generated by flapping nylon tents in the high winds on Makalu [6]. Other obstacles include extreme altitude, extreme temperature and attempting to get a recording during exercise when myopotential interference is likely to be maximal.

In 1957 the resting ECGs of 10 subjects at sea level and after 12 months residency at 1,540m demonstrated an increased heart rate, sinus arrhythmia, right axis deviation and ventricular

repolarization changes [7]. Similar changes were described by Jackson and Davies [8] in a group of climbers and sherpas ascending to around 6800m in the Himalayas in 1960. In 1962 Milledge [6] also described similar ECG changes in 15 subjects examined monthly over nine months at an altitude of around 5800m. Exercise was noted to produce a number of ventricular extrasystoles in one subject. Most early ECG recordings were done at rest, or soon after exercise, which at HA may be more than several minutes before an effective ECG can be recorded.

Ambulatory monitoring

In 1966 a method of recording a dynamic ECG at altitude, using a 3.5 lb tape recorder, was reported [9]. These investigators did identify an increase in heart rate during exercise and sinus arrhythmia during sleep at altitude but few others replicated this work and a relative paucity of data regarding ambulatory ECG monitoring at altitude persisted for many years. Over 30 years later ambulatory ECG monitoring in healthy elderly males recorded an increase in both supraventricular and ventricular extrasystoles at moderate altitude [10]. One case report documented the presence of frequent ventricular ectopy and ventricular bigeminy in a 65 year old with the subsequent development of non-sustained ventricular tachycardia (VT) and a single 14 beat run of VT while climbing the same mountain (Kilimanjaro) with ambulatory recording at 75 years of age [11, 12]. A very recent investigation of heart rate variability and microvolt T-wave alternans (MTWA) as a predictor of malignant ventricular arrhythmias on eight subjects climbing Gasembrum II (8150m) found no evidence to suggest an increased risk [13].

Simulated Ascent

One way around some of the difficulties of recording the ECG in the field at HA is to carry out investigation in a hypobaric chamber. Until recently the most exhaustive evaluation to date of the effects of altitude on the ECG comes from "Operation Everest II"-a simulated ascent in a barometric chamber. This concluded that exercise at 8848m was not associated with significant arrhythmias or ischaemia [14]. However, these conclusions were based on relatively sparse data. Two of the eight subjects were removed after acute hypoxic episodes without simultaneous ECG data despite the presence of altered consciousness or acute confusional state; resting ECGs were only recorded at five altitudes above sea level; exercise ECGs only recorded at two altitudes over eight minutes

**Corresponding Author: Lt Col David Woods RAMC,
Ward 31, Dept Medicine, Royal Victoria Infirmary,
Newcastle upon Tyne, NE1 4LP
Tel: 0191 2336161 Fax: 0191 2563212
E-mail: DoctorDRWoods@aol.com**

and only three of the subjects exercised at the simulated peak altitude. Occasional ventricular ectopics were observed during exercise and non-sustained runs of ventricular bigeminy were seen in two.

In a recent novel study 12 military pilots were exposed to an acute hypoxic protocol by supplementation with increasing oxygen concentrations during a simulated ascent to 8230m in a hypobaric chamber [15]. Hypoxia was associated with a significant alteration in heart rate variability in pattern similar to that noted in subjects undergoing heavy exercise or with ischemic heart disease at high risk for ventricular fibrillation [16].

Population perspective

These data seem a little incongruous with reported data: 10% of fatalities while trekking in Nepal are due to “heart attacks” [17]; 642 sudden cardiac deaths (SCDs) over an eight year period in the Austrian Alps [18] and the registry demonstrating 30% of all deaths during mountain sports at altitude are attributable to SCD [19], which from prospective studies at SL is due to arrhythmia in over 80% of cases [20]. In addition, syncope of unknown cause is a significant problem at altitude, accounting for 98% of all syncopal cases in lowlanders arriving at altitude in one series [21]. Finally, although other factors such as accessibility to emergency services may be involved, death rates have been noted to increase in line with altitude [18]: 2.3 deaths per 10⁶ days of exposure for hill-walking in England and Wales [22]; 5.7 for Austria [18], and 10.6 for Nepal [17, 23].

Implantable loop recorders

In view of the physiological stressors of HA and the epidemiological evidence regarding SCD at HA it is surprising that few arrhythmias have been recorded. It was this relative paucity of data that prompted the novel application of a relatively recent technology to both clarify the nature of frequently occurring palpitations at HA and to document if any arrhythmia occurred in a military HA expedition. The full experimental protocol has been published previously but is discussed briefly below [24].

Nine healthy male volunteers from the Army Training Regiment Lichfield, who had a normal cardiovascular examination, 12-lead ECG, 2-D cardiac echo and maximal exercise test had an implantable loop recorders (ILR, Reveal, Model 9525) inserted subcutaneously in the left pectoral region (Figure 1). Subjects flew to Kathmandu (1250m) and then Lukla (2800m) before immediately commencing an identical ascent and descent profile. All subjects reached intermediate camp at 5600m (Day 15), six members attained 5700m, four 6070m and two 6325m. The ILR has the great advantage over resting ECG in that it can be activated remotely using an electromagnetic induction unit that “freezes” the loop of ECG recording, which is then stored in the memory “bins” of the unit. Data can then be downloaded to diskette daily using a pacemaker programmer (Figure 2).

Two hundred and sixty three ECG recordings were made during the expedition, equating to just over 29 per subject. Analysis of R-R intervals at increasing altitudes demonstrated a progressive increase in mean heart rate both during exercise and rest and also mean maximum achieved heart rate during exercise (Table 1). All subjects experienced palpitations during exercise above 5000m with 2 symptomatic episodes at rest (5,600m and 6300m). Analysis of all symptomatic recordings was found to correlate with sinus tachycardia. The additional cardiac workload generated by hypoxic pulmonary vasoconstriction combined with



Figure 1: Insertion of the ILR under local anaesthetic in the left pre pectoral area



Figure 2: Downloading the recorded ECG data using a pacemaker programmer powered by an altitude-adapted domestic Honda generator.

neurohormonal mechanisms such as sympathetic stimulation resulting from hypoxia and exertion may well have produced the sensation of palpitations experienced by the subjects of this study during exercise and in two subjects at rest.

Altitude (m)	2-2999m	3-3999m	4-4999m	5-5999m
Mean HR during exercise (mean+/-sd)	98.6 +/-24.2	106.7 +/-27.8	144.1 +/-13.7	152 +/-23.8

Table 1: Analysis of R-R intervals at increasing altitudes demonstrated a progressive increase in mean maximum achieved heart rate during exercise.

Sleep recordings revealed sinus arrhythmia in all individuals with non-conducted ectopic p waves in one. Another subject demonstrated sinus arrhythmia during exercise (not previously reported at altitude).

In one subject an episode of asymptomatic atrial flutter with 2:1 conduction was observed (Figure 3) for 8.5 minutes immediately after a period of severe exertion at 4500 m (SpO₂ 76%). There was the possibility of asymptomatic polymorphic ventricular ectopy (5 beat duration) in a second subject during exercise at 4700m (SaO₂ 86%) but this may well have been artifact.

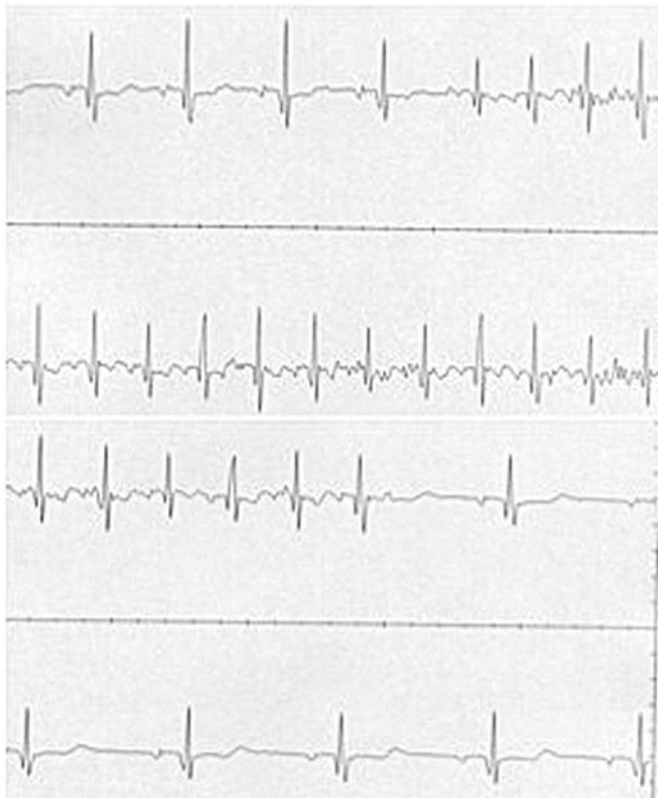


Figure 3: The onset and termination of an episode of atrial flutter (2:1 conduction) at a rate of 150 bpm at 4500m (SpO₂ 76%).

In general the quality of the electrocardiogram traces obtained was excellent with clear morphological discrimination of all components of the ECG. In two tracings from asymptomatic individuals during exercise it was not possible to clearly identify the underlying cardiac rhythm. In both cases analysis of the actual QRS complexes on recorded electrograms identified a frequency of 300 beats per minute consistent with a diagnosis of atrial flutter with 1:1 conduction. It is probable that these tracings represent artefact but extensive provocation during both rest and exercise post-expedition failed to reproduce such a pattern.

Discussion

The physiological stressors of HA should hypothetically make arrhythmias more likely. However the technical challenges of recording the ECG at HA particularly during exercise or symptomatic episodes has led to a paucity of data on which we can base no sound conclusion in the face of epidemiological data suggesting a significant increase in SCD at HA. While the study using ILRs suggests that palpitations at HA may frequently be associated with sinus tachycardia it also suggested that arrhythmias do occur even in young extremely fit people. While no malignant arrhythmias were seen it could be postulated that in subjects with underlying cardiac disease, such as coronary artery disease, there may be a significant risk of ventricular arrhythmias at altitude. Indeed, there is a recognised association between ventricular arrhythmias and sympathetic activation (known to be increased at altitude [2] especially in patients with known coronary artery disease [25]. In support of this, the risk factor profiles of 68 males who died from SCD during downhill skiing at altitude revealed prior myocardial infarction, hypertension and known coronary heart disease (CHD) as significant risk factors compared to controls [26].

The cohort studied using ILRs was very small but quite revealing. Although the all-cause mortality from HA exposure is small (around 0.015% in Nepal in the late 1980s) [17] further investigation is required particularly in the elderly who account for 15% of the 100 million visitors to HA annually [27, 28]. These figures are of genuine concern when SCD is the major cause of death in male hikers and downhill skiers over the age of 34 [29] and when up to 60% of elderly individuals in Western societies have significant coronary lesions at autopsy [28]. When counselling prospective visitors to HA we should be conversant with these facts and also aware that in hikers and downhill skiers who die from SCD a previous MI is a major risk factor (17% versus 0.9%) [29].

Conclusion

Thorough investigation of the effect of extreme environments on the risk of cardiac arrhythmias requires the innovative use of emerging technologies. In light of the epidemiological data regarding SCD at HA further research is warranted, particularly in an older population.

References

1. Bergofsky EH, Holtzman S. A study of the mechanisms involved in the pulmonary arterial pressor response to hypoxia. *Circ Res* 1967; **20**: 506-19.
2. Mazzeo RS, Bender PR, Brooks GA, et al. Arterial catecholamine responses during exercise with acute and chronic high-altitude exposure. *Am J Physiol* 1991; **261**: E419-24
3. Sutton JR, Reeves JT, Wagner PD, et al. Operation Everest II: oxygen transport during exercise at extreme simulated altitude. *J Appl Physiol* 1988; **64**:1309-1321.
4. Levy RL, Bruenn HG, Russell NG Jr. The use of electrocardiographic changes caused by induced anoxemia as a test for coronary insufficiency. *Am J Med Sci* 1939; **186**: 241-247.
5. Bert P. La Pression Barométrique, recherches de physiologie expérimentale. Masson, Paris (1878). English translation (1943) by Hitchcock MA and Hitchcock FA, College Book Co., Columbus, Ohio, p37.
6. Milledge JS. Electrocardiographic changes at high altitude. *Br Heart J* 1963; **25**: 291-8.
7. Penalzoa D, Echevarria M. Electrocardiographic observations on ten subjects at sea level and during one year of residence at high altitudes. *Am Heart J* 1957; **54**: 811-822.
8. Jackson F, Davies H. The electrocardiogram of the mountaineer at high altitude. *Br Heart J* 1960; **22**: 671-85.
9. Sanders JS, Martt JM. Dynamic electrocardiography at high altitude. *Arch Intern Med* 1966; **118**: 132-138.
10. Kujanik S, Snincak M, Vokal J, Podracky J, Koval J. Periodicity of arrhythmias in healthy elderly men at the moderate altitude. *Physiol Res* 2000; **49**: 285-287.
11. Alexander JK. Age, altitude, and arrhythmia. *Tex Heart Inst J* 1995; **22**: 308-316.
12. Alexander JK. Cardiac arrhythmia at high altitude: the progressive effect of aging. *Tex Heart Inst J* 1999; **26**: 258-263.
13. Gibelli G, Fantoni, C, Anzà C, Cattaneo P, et al. Arrhythmic Risk Evaluation during Exercise at High Altitude in Healthy Subjects: Role of Microvolt T-Wave Alternans. *Pacing and Clinical Electrophysiology* 2008; **31**: 1277-1283.
14. Malconian M, Rock P, Hultgren H, et al. The electrocardiogram at rest and exercise during a simulated ascent of Mt. Everest (Operation Everest II). *Am J Cardiol* 1990; **65**: 1475-1480.

15. Vigo DE, Pérez Lloret S, Videla AJ, et al. Heart rate nonlinear dynamics during sudden hypoxia at 8230 m simulated altitude. *Wilderness Environ Med* 2010; **21**:4-10.
16. Makikallio TH, Koistinen J, Jordaens L, et al. Heart rate dynamics before spontaneous onset of ventricular fibrillation in patients with healed myocardial infarcts. *Am J Cardiol* 1999; **83**: 880-884.
17. Shlim DR, Gallie J. The causes of death among trekkers in Nepal. *Int J Sports Med* 1992; **13**: S74-6.
18. Bartscher M, Mittleman MA. Time-dependent SCD risk during mountain sports changes with age. *Circulation* 1995; **92**: 3151-3152.
19. Bartscher M, Philadelphia M, Nachbauer W, Likar R. The risk of death to trekkers and hikers in the mountains. *JAMA* 1995; **273**: 460.
20. Albert CM, Chae CU, Grodstein F, et al. Prospective study of sudden cardiac death among women in the United States. *Circulation* 2003; **107**:2096-2101.
21. Nicholas R, O'Meara PD, Calonge N. Is syncope related to moderate altitude exposure? *JAMA* 1992; **268**: 904-906.
22. Avery JG, Harper P, Ackroyd S. Do we pay too dearly for our sport and leisure activities? *Public Health* 1990; **104**: 417-423.
23. Shlim DR, Houston R. Helicopter rescues and deaths among trekkers in Nepal. *J Am Med Ass* 1989; **261**: 1017-1019.
24. Woods DR, Allen S, Betts TR, et al. High Altitude Arrhythmias. *Cardiology* 2008; **111**:239-246.
25. Podrid PJ, Fuchs T, Cardinas R. Role of the sympathetic nervous system in the genesis of ventricular arrhythmias. *Circulation* 1990; **82**: I-103-I-113.
26. Bartscher M, Pachinger O, Mittleman MA, Ulmer H. Prior myocardial infarction is the major risk factor associated with sudden cardiac death during downhill skiing. *Int J Sports Med* 2000; **21**: 613-5.
27. Bartscher M, Bachmann O, Hatzl T, et al. Cardiopulmonary and metabolic responses in healthy elderly humans during a 1-week hiking programme at high altitude. *Eur J Appl Physiol* 2001; **84**: 379-86.
28. Levine BD, Zuckerman, JH, deFilippi CR. Effect of High-Altitude Exposure in the Elderly. *Circulation* 1997; **96**: 1224-1232.
29. Bartscher M. Risk of cardiovascular events during mountain activities. *Adv Exp Med Biol* 2007; **618**:1-11.