Assessment of Cardiac Arrhythmias at Extreme High Altitude Using an Implantable Cardiac Monitor: REVEAL HA Study

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It has been suggested, though still unproven, that high altitude (HA) exposure is proarrhythmic and could potentially contribute to an increased risk of sudden cardiac death (SCD).[1,2] However, there are very limited data, particularly above 5000m to substantiate this claim. We hypothesised that extreme HA leads to an increased risk of pathological cardiac tachyarrhythmias, detected using an implantable cardiac monitor (ICM).

Sixteen healthy adult Caucasian male British Military servicemen underwent continuous ECG monitoring, using a Reveal LINQ ICM (Medtronic Ltd), for ≥7 weeks before, during and >8 weeks after an attempted summit of Mount Dhaulagiri (8,167 m). They were required to have a normal 12-lead ECG and transthoracic echocardiogram at recruitment and were excluded if they had a history of cardiac arrhythmia. They underwent written informed consent and the study was approved by the Ministry of Defence Research and Medical Ethics Committee. The participants flew from the UK to Kathmandu, Nepal (1400m, days 1-2), then by road (day 3-4) to 2679m. Thereafter, they trekked carrying moderate loads to 3720m (day 5), 4150m (day 7) and 5140m where they remained (days 11-24) for attempts on 6035m and 6800m peaks. One subject aborted at 4100m, due to severe gastrointestinal symptoms. On day 25, five subjects descended and 10 climbers remained at 4800m for an attempted summit of Mount Dhaulagiri over days 26-51(days 26-51). The subjects were monitored wirelessly pre and post-departure (Medtronic MyCareLink™ Monitor) and during trekking using a portable Medtronic Programmer every 2-5 days, depending on environmental conditions.

The subjects were 35.1±6.6 (24-48) years. Fifteen (93.8%) achieved an altitude of ≥6035m, six to 6800m, one to 7100m and three to 7500m. Unfortunately, an attempted summit of Mount Dhaulagiri became impossible, due to adverse weather

conditions. SpO_2 significantly fell at increasing HA from 96.4±1.6% at 1400m to 93.2±2.8% at 2650m, 88.8±3.5% at 4100m, 80.6±5.0% at 5140m and 78.1±4.5% at 5340 (Ordinary ANOVA P<0.0001). The ICM rhythm-detection settings are shown in table 1 (footnote). Significant rhythm abnormalities were observed in 9 out of 16 subjects (56.3%) at HA and only at ≥4100m. Symptom-related device activation was triggered on 18 occasions in 8/16 subjects at HA and related to extreme breathlessness and palpitations. Subject five developed an episode of nocturnal symptomatic rapid atrial fibrillation (AF) at 4100m, during the initial ascent phase, which occurred immediately after drinking cold water. It lasted for 282 minutes at a mean ventricular rate 133/minute. Subject four, developed an episode of supraventricular tachycardia (SVT) lasting for 30.8 seconds (mean rate 207/ minute). It occurred immediately on attempting to lift a 30kg load, at 5200m and was associated with sudden and transient light-headedness and breathlessness.

Significant pauses (>3 seconds) were identified at HA in 8 out of 15 (53.3%) subjects at HA at ≥4800m only, with none detected in any subjects below this altitude (Fisher's Exact Test p=0.0008). There were 82 pauses (3.0-7.0s) in total, which were sinus in 80 with evidence of high grade heart block in two cases (mean number10.3±14.1; range 1-41) (table 1). The number of pauses increased with altitude gain from 0 at <4800m to 4.2 at 4800m and 14.3 at >6000m (Kruskal-Wallis Test P<0.0001) with 19.3±20.6 pauses at 7550m (n=3) versus 1.9±4.2 among the rest of the subjects (n=13; Chi-squared Test p=0.007). The number of pauses increased with duration of HA exposure: 6 during first 17 days (tercile, 15-16 subjects), 29 during days 18-34 (10-15 subjects) and 47 (10 subjects) during days 35-51. The pauses typically occurred following cyclical periods of heart rate acceleration then deceleration preceding it.

This is the first study to convincingly demonstrate the pro-arrhythmic risks of significant HA and to the author's knowledge the first to continuously monitor healthy subjects above 6325m at terrestrial HA. In the only previous ICM study at HA nine subjects were studied using first generation Reveal ICM, which lacked auto-detection capabilities and only two subjects were assessed at 6325m.[1] They observed one short-lived episode of atrial flutter at 150/minute (8.5 minutes) immediately after a severe exertion at 4500 m. The episode of nocturnal AF detected in our study would suggest vagally-mediated AF. We would also postulate that the pauses observed in our study were likely physiological and also related to the effects of increased nocturnal vagal tone and sleep-disordered breathing which are well recognised at HA.[3,4] We believe the episode of SVT relates to the combination of sympathetic activation, hypoxia and sudden explosive exercise at HA. In addition to the factors outlined above the proarrhythmic effects of HA may be partly explained by other factors including acclimatization, changes in heart rate variability, sleep deprivation, dehydration and anxiety.[5]

In conclusion HA exposure to $\geq$4100m is associated with significant brady and tachy-arrhythmias in healthy adult men supporting a potential proarrhythmic risk. There was no link between HA and sustained ventricular arrhythmias linked to an increased risk of SCD.

DISCLOSURES

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References

1. Woods DR, Allen S, Betts TR, Gardiner D, Montgomery H, Morgan JM, Roberts PR. High altitude arrhythmias. Cardiology 2008; **111:** 239-46.

2. Burtscher M, Ponchia A. The risk of cardiovascular events during leisure time activities at altitude. *Prog Cardiovasc Dis* 2010; **52:** 507-11.

3. Lombardi C, Meriggi P, Agostoni P, Faini A, Bilo G, Revera M, Caldara G, Di Rienzo M, Castiglioni P, Maurizio B, Gregorini F, Mancia G, Parati G. HIGHCARE Investigators. High-altitude hypoxia and periodic breathing during sleep: gender-related differences. *J Sleep Res* 2013; **22:** 322-30.

4. Nemirovsky D, Hutter R, Gomes JA. The electrical substrate of vagal atrial fibrillation as assessed by the signal-averaged electrocardiogram of the P wave. *Pacing Clin Electrophysiol* 2008; **31:** 308-13.

5. Hansen J, Sander M. Sympathetic neural overactivity in healthy humans after prolonged exposure to hypobaric hypoxia. *J Physiol* 2003; **546:**921-9.

Table 1. ICM detection settings, key cardiac rhythm findings and altitudes achieved

Subject number	Age	Maximal altitude achieved	Significant Findings	Key Abnormalities	No of pause Episodes	Longest pause duration in seconds
1	30	6035m	No	None	-	-
2	40	6200m	No	None	-	-
3	41	7550m	Yes	Pauses	41	6.0
4	30	6800m	Yes	SVT and pauses	5	5.0
5	32	7550m	Yes	Atrial fibrillation	-	-
6	24	4100m	No	None*	-	-
7	38	6200m	Yes	Pauses	15	4.0
8	25	6800m	No	None	-	-
9	48	6800m	Yes	Pause	1	3.3
10	30	7550m	Yes	Pauses	17	7.0
11	33	6035m	Yes	Pause	1	4.4
12	41	7100m	No	None	-	-
13	38	6800m	No	None	-	-
14	38	6035m	No	None	-	-
15	32	6800m	Yes	Pause	1	3.4
16	41	6200m	Yes	Pause	1	5.0

SVT, supraventricular tachycardia; *descended due to gastrointestinal illness; Tachycardias were defined as a heart rate/minute >230-age in years for $\geq$16 beats; bradycardia as a heart rate <30/minute for $\geq$12 beats, pause R-R interval >3 seconds and atrial tachycardia/fibrillation/flutter as episodes fitting morphology detection criteria lasting >10minutes.