British Services Dhaulagiri Medical Research Expedition; A unique military/civilian research collaboration

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Abstract

Introduction: High altitude environments lead to a significant physiological challenge and disease processes which can be life threatening; operational effectiveness at high altitude can be severely compromised. The UK military research is investigating ways of mitigating the physiological effects of high altitude

Methods: The British Service Dhaulagiri Research Expedition took place from March to May 2016, and the military personnel were invited to consent to a variety of study protocols investigating adaptation to high altitudes and diagnosis of high altitude illness. The studies took place in remote and austere environments at altitudes of up to 7500m.

Results: This paper gives an overview of the individual research protocols investigated, the execution of the expedition and the challenges involved. 129 Servicemen and women were involved at altitudes of up to 7500m; 8 research protocols were investigated.

Conclusions: The outputs from these studies will help to individualise the acclimatisation process and inform strategies for pre-acclimatisation should troops ever need to deploy at high altitude at short notice.

Introduction

The UK military runs a programme of adventurous training (AT) with the aims of promoting, "*through the conduct of arduous outdoor activities with exposure to hardship and danger, the Army's core values, leadership, teamwork and other qualities necessary to enhance the Operational effectiveness of all military personnel*" [1] In a quadrennial cycle the Single Service mountaineering clubs, in rotation, lead a major expedition as an inspirational AT activity. This is usually, but not exclusively, a mountaineering expedition to one of the world's fourteen 8,000m peaks (located in the Himalayan range in Nepal and Pakistan). The 2016 expedition was a Royal Navy-led trip and the opportunity was taken to mount a significant medical research expedition to the Dhaulagiri region of Nepal - the British Services Dhaulagiri Medical Research Expedition (BSDMRE) 2016. The expedition had support of His Royal Highness the Duke of York and the Surgeon General.

This journal has previously published on the challenges and opportunities of research in high altitude environments and on the potential benefits of AT.[2, 3] This research expedition was part of ongoing UK military and civilian research with collaboration between the Royal Centre for Defence Medicine (RCDM), Leeds Beckett University and the University of Oxford. The studies focussed on the physiological response to high altitude (HA), the diagnosis of acute mountain sickness (AMS) and strategies to enable the rapid deployment of troops to a HA environment (pre-acclimatisation). This article describes the background to these studies and the research protocols used and acts as a foundation for subsequent publication of specific study results.

Methods

Funding

AT is formal, publicly funded military training. Participation in AT is "*an integral aspect of military training that supports the values and standards of the military thus enhances an individual's ability to withstand the rigours of operations*".[1] This direct public funding contributed around 50% of the costs for each subject which in turn facilitated the relatively large numbers for a research expedition. Research funding was supported by industry (Medtronic Reveal Linq devices provided free of charge), public funding through RCDM, funding from Leeds Beckett University, University of Oxford, the Mount Everest Foundation and a grant from the Royal Navy Royal Marines Charity (RNRMC). It is exceptional for the RNRMC to support research in this way but a large fundraising event with the support of the

Duke of York enabled the charity to raise sufficient funds to underwrite the research costs. Additional support with kit and equipment was provided by expedition sponsors notably Honda generators and Solarpod equipment to power the research kit described in the protocols.

Environment

For the initial part of the trek of the Dhaulagiri circuit the terrain was at low altitude (although daily ascent was considerable) and through hot, humid pasture and rainforest. From Italian Base camp (IBC) onwards the trek followed glaciated terrain around the western and northern aspects of Dhaulagiri. This terrain was dry and hot during the day and cold at night. Temperatures in the Hidden Valley (at 5140m) were frequently around -10ºC by night with considerable wind chill. By day temperatures in the direct sun or inside tents could be as high as +30ºC. Above IBC all precipitation fell as snow due to the low temperatures, whereas IBC itself experienced heavy afternoon rain storms during the latter part of the expedition. All research took place in tents as there is no hard accommodation on the circuit above IBC, and frequently early in the morning to take measurements in the starved state. This placed a great strain on the research teams who had to work in extreme temperatures, often clad in one piece down suits!

Research Protocols

The pathophysiology of HA illness remains ill-defined but the rate of AMS among military personnel ascending to HA as part of AT is significant, with 34% of those ascending Mount Kenya suffering severe AMS in one report. [4] AMS was also a significant cause of Disease Non-Battle Injury (DNBI) during the Battle of Taku Ghar in Afghanistan in 2002 with 18 cases of AMS requiring casevac from theatre of operations and treatment by 274th Field Surgical Team.[5] The programme of research on the expedition was aimed at enhancing our understanding of the pathophysiology of HA exposure and AMS and answering some of the questions raised previously in this journal.[6] The following submissions were made to the MoD Research Ethics Committee (MoDREC);

Protocol 578, Cardiovascular adaptation and recovery in chronic hypoxia. We have previously assessed various methods of recording heart rate variability at HA [7] and this study aimed to collect data on all the trekking teams, investigating changes in a range of physiological variables including heart rate variability (HRV), central aortic blood pressures and pulmonary artery pressures.

Protocol 580, Utility of BNP in diagnosing Acute Mountain Sickness (AMS). We have previous published that brain natriuretic peptide (BNP) may have utility in the diagnosis of altitude illness.[8-11] This study aims to recruit subjects who become unwell on expeditions at HA over the next few years. This will enable us to establish whether BNP can be used to discriminate between those with AMS or other conditions.

Protocol 608, The effects of progressive High Altitude on the development and burden of significant cardiac arrhythmias using an implantable Cardiac Monitor (REVEAL Study). This study used a small implantable (into the subcutaneous fat of the upper chest) cardiac monitoring device, a “Reveal LINQ” made by Medtronic. This has the capability to record and store information about heart rate and rhythm that can then be downloaded to a hard drive for subsequent analysis. The marked hypoxaemia that occurs at altitude could be arrhythmogenic and significant cardiac morbidity is known to occur at HA. This work builds on a smaller study using the predecessor to the current Reveal device that suggested significant arrhythmias do occur at HA.[12]

Protocol 624 Appetite responses during a high altitude expedition. Very little is known about the underlying mechanisms regarding the anorexia and nausea suffered at HA, a topic previously reviewed in this journal.[13] Reductions in appetite contribute to the degradation that ultimately impairs performance at HA. This project investigated nutritional changes at HA using food diaries, an assessment of gut hormones involved in appetite regulation and the novel use at HA of wearable technology assessing continuous subcutaneous interstitial glucose levels.

Protocol 623 Biomechanical changes in walking gait and balance at altitude. Changes in balance may occur at HA and it has been suggested that changes in balance and walking style may be related to the development of AMS and to the incidence of falls and accidents on expeditions. This research examined joint position sense, balance and coordination through a series of assessments including video assessment of gait and balance using a force platform.

Protocol 663 Effects of iron status, manipulated using intravenous iron, on cardiopulmonary physiology during ascent to very high altitude, assessed using echocardiography and self-reported functional performance scores. Exposure to the hypoxia of altitude leads to many physiological changes and a key feature is hypoxic pulmonary vasoconstriction (HPV). HPV increases pulmonary artery systolic pressure (PASP) and contributes to right ventricular strain and exaggerated HPV is a feature of High Altitude Pulmonary Oedema. (HAPE). This study used an intravenous iron infusion to optimise iron stores which at sea-level is known to attenuate the HPV response to hypoxia.[14] There has been one previous trial that has also shown a reduction in AMS following intravenous iron.[15] Participants were randomised to receive iron or placebo and echocardiography used to assess their PASP in the field, while Lake Louise scores collected allow researchers to assess any difference in AMS rates.

Protocol 586 Acclimation and acclimatisation: The effects of Exercise under Normobaric (normal pressure) Hypoxic (reduced Fi02) conditions. We have been investigating the utility of "pre-acclimatisation" in a hypoxic chamber in order to establish if such exposure can improve performance on deployment to HA and reduce HA illness. This protocol compare the effects of 5 days in a normobaric hypoxic chamber at simulated altitudes of between 4300 and 4800m with a control group. Echocardiographic variables, biochemical and endocrine markers of physiological stress and indices of respiratory variables representing acclimatisation were assessed pre- and post-hypoxic exposure as well as during the expedition in order to elucidate any benefit. Additionally, rates of AMS have been assessed in the field to see if prior acclimation can reduce the threat from HA illness.

Protocol 625 Application of Apnoeic training and physiological adaptations to altitude.
Free-divers expose themselves to periods of apnoea and prepare for this by a relatively simple method of "breath-holding". Apnoea training induces changes that could potentially be of benefit at HA, including an increase in haematocrit, haemoglobin, erythropoietin and oxygen saturation.[16] This protocol will employ a 6 week breath hold training programme and compared this with a control group. Variables were assessed in the normobaric hypoxic chamber pre-departure at a simulated 4800 m and while on the trek. These assessments included spleen volume, oxygen saturation, haemoglobin, haematocrit, erythropoietin and rates of AMS. Both protocol 586 and 625 benefit from access not only to the fixed normobaric chamber at Leeds Beckett University but also a portable hypoxic chamber purchased with a grant from Joint Medical Command via the DMS Research Steering Group.

Protocols were submitted to the RAF Scientific Advisory Committee (SAC) and subsequently MoDREC during 2014 to ensure plenty of lead in time and that projects could be in place prior to recruiting participants for the AT activity. The researchers acknowledge the efforts and diligence of both the SAC and MODREC, whose input significantly enhanced the scientific work proposed. Working with sports science specialists at Leeds Beckett University allowed civilian colleagues to make use of an exceptional opportunity for research of this nature and the military researchers to gain from their expertise and equipment. A recce to the area and limited research conducted during February 2015 were hugely useful in finalising research plans and resulted in some limited amendments to protocols.

Participants were all members of HM Forces taking part in an AT exercise and on duty. Selection for this expedition was via Defence Instructions and Notices advertising the event, advertisement through military climbing clubs and via word of mouth. Trekking teams were selected by individual leaders and not by the overall expedition leadership or Principle Investigators. Climbing teams were selected on the basis of previous climbing experience. The climbers were split onto a main team of 12 experienced mountaineers to climb Dhaulagiri and a high altitude development team (HADT), of 12 less experienced high altitude mountaineers to climb Tukuche peak and gain experience. Once involved in the expedition participants were invited to take part in specific research studies. Participants were invited to participate in studies depending on time availability and geographical location before written informed consent was obtained. Where teams were used as controls for an intervention group every effort was made to match military backgrounds of individuals to ensure similar levels of fitness.

All participants received a brief on mountain health including AMS and the military policy of not using prophylactic acetazolamide (Diamox®) in this setting. Baseline data was collected in the UK by a suitably qualified researcher before any pre-acclimatisation training took place.

On the expedition, data was collected by the subjects (daily diaries) and then at three research camps established for the duration of the expedition at 3600m (IBC) , 4600m (Dhaulagiri BC) and 5140m in the Hidden Valley. These camps had resident staff of two trained researchers with at least one medically qualified in each location; additional researchers (military or Leeds Beckett staff) accompanied specific trekking teams to collect specialist data (continuous glucose measurements, cardiac echo, spleen ultrasound and conduct balance testing).

Climbing teams had background data collected at the time of Reveal LINQ device insertion or when enrolled in the iron study. Any potential subject who could not comply with these timings (usually for service reasons) were not included in these studies although data was collected for non-intervention studies. All participants were low altitude dwellers, no trekking team members had exposure to >1500m terrestrial altitude in the four weeks prior to the studies.

Research protocols undertaken by the climbers were developed mindful of minimising the impact of research data collection when in country. All team members flew to Kathmandu via long haul international flights and baseline data was collected the day after arrival or after 4 days in Kathmandu in the case of the advance party. This involved recording symptoms, SpO2 (Nonin Onyx, Nonin Medical Inc, Plymouth, Minnesota), haemaglobin (Haemocue, Haemocue AB, Angelholm, Sweden), cardiac function and pulmonary artery pressures (Vivid I, GE Healthcare, Amersham, UK) and was completed by one experienced cardiologist blinded to the intervention (in the case of the iron study). The team then moved to 2750m by road, where a further data collection period took place (day 4). After day 4 all altitude changes where accomplished on foot carrying moderate loads (5-10Kg). Further altitude changes are given in Table 1. Climbers completed an individual itinerary depending on self-declared fitness to continue with the ascent profile and rest days taken as required. Subjects recorded daily Lake Louise self-reported scores (LLS), AMSc scores, anxiety questionnaires (STAI), SpO2, heart rate and HRV via iThlete app. The iThlete app records HRV over a one minute period of timed ventilation (20 breaths) to give a number indicating HRV. The heart rate is recorded onto a smart phone using the phones' microphone and a finger probe. This number is based on root mean squares of successive differences (RMSSD) of HRV and we have recently published the validity of the iThlete app vs. conventional HRV measurement.[7] HRV recording were not blinded and were taken by the individual first thing in the morning, in a seated position, before food or caffeine wherever possible. Decisions regarding individual fitness to continue with the itinerary or climb higher were made regardless of HRV reading (after consultation with a medical officer who was also unaware of HRV reading where necessary). Borg Rating of Perceived Exertion (RPE) for the "sessional exertion" each day was recorded each evening and subjects asked to record their perception as to how hard the hardest bout of exercise that day had been (on a scale of 6-20). Reveal Linq cardiac rhythm monitors were inserted into members of the climbing team (Reveal LINQ, Medtronic, Dublin, Ireland). These devices were inserted by a consultant cardiologist (CB) at Poole Hospital during January 2016. The device automatically records any tachycardia, bradycardia or arrhythmia. Baseline data was collected automatically via the Carelink system in the UK and downloaded every few days using a larger programmer device in Nepal.

Table 1. Climbing team Itinerary and altitude changes

Day	Sleeping altitude	Activity (evening Location
0	1400m	Arrive Kathmandu
1	1400m	Kathmandu – baseline data collected
2	848m	Beni
3	2679m	Move to Marpha by vehicle
4	2679m	Marpha, subjects free to do own trekking acclimatisation
5	3720m	Trek Alu Bari Lower Camp, 3650m, o/n camp
6	3720m	Alu Bari Lower Camp, 3650m, Acclimatisation day.
7	4150m	Trek Yak Kharta
8	4150m	Yak Kharta, 4600m, acclimatisation day, o/n camp
9	4150m	Yak Kharta, 4600m, acclimatisation day, o/n camp
10	5140m	Trek Hidden Valley 4975m (via Dhampus Pass 5250m)
10		Hidden Valley, 4975m, acclimatisation day,
11-24		Hidden Valley basecamp for attempts on Dhampus peak **6035m** and Tukuche peak **6800m** – individual itineraries
25	4800m	Team reduces to 12 and move to Dhaulagiri BC
26-50		Dhaulagiri BC – individual itineraries. Altitude of **7500m n**achieved by 5 team members.
51		Trek to Hidden Valley
52		Trek to Marpha
		Rest Marpha
		Rest Marpha
		Drive to Pokhara
		Drive to Kathmandu
		Fly to UK

Trekking teams were invited to take part in studies 580, 578, 586, 623, 624 and 625.

Recruitment and interest in the studies was high.

Trekkers all arrived in Kathmandu by long haul air travel and travelled by road to 1123m before attempting a trek of the Dhaulagiri circuit. Each team was accompanied by a medical officer who advised on any changes in itinerary based on team or individual acclimatisation. Further medical support was available at 3600m, 4650m and 5140m. The itinerary (Table 2) and altitude profile (Figure 1) are below. Changes of itinerary where made as necessary when trekkers showed signs of acute mountain sickness. Trekkers completed a daily recording of LLS, AMSc scores, STAI, SpO_2, heart rate. At 3600m, 4650m and 5140m heart rate variability was recorded via a Checkmyheart™ HRM device (Daily Care Medical, Naihu, Taiwan). This was a conventional single lead ECG and data were downloaded to a laptop to be analysed offline by a cardiologist who was blinded to the individuals' performance and LLS.

Table 2. Trekking team itinerary

	Activity	Sleeping altitude
Day 1	Fly from UK	
Day 2	Arrive Kathmandu	
Day 3	In Kathmandu. Sightseeing tour	
Day 4	Drive Beni via Pokhara	
Day 5	Drive Darbang and trek Riverside	
Day 6	Trek Jugepani 1456m	
Day 7	Trek Bagar	2017m
Day 8	Trek Doban	2430m
Day 9	Trek Sallagari	3107m
Day 10	Trek Italian BC	3619m
Day 11	Rest day at Italian BC	
Day 12	Trek to Japanese Camp	4072m
Day 13	Trek Dhaulagiri Lower BC	4600m
Day 14	Rest Day, Dhaulagiri Lower BC	4600m
Day 15	Trek Hidden Valley	5140m
Day 16	Rest day in Hidden Valley	5140m

Results

129 military participants took part in the expedition including 7 research/medical staff. Two trekkers were removed from the trail with minor illness before exposure to any significant altitude. Three trekkers descended earlier than planned via IBC from higher on the trail; four trekkers required extraction from the Hidden Valley by helicopter. One member of the HADT withdrew on day 4 of the trek due to non-altitude related illness. Overall, 22 of the remaining members of the HADT and main team reached 6035m and five reached 7500m on Dhaulagiri.

AMS was diagnosed by the Lake Louise or AMSc Scores from the daily symptoms scores recorded. Subjects were included in analysis with a positive diagnosis of AMS if they took drugs to aid acclimatisation or if they were evacuated by helicopter with no symptom scores recorded. Data collection was completed well with relatively few missed data collection points. The Dhaulagiri circuit is extremely remote and the satellite communication between camps was patchy which reduced the ability to trouble shoot and provide rigorous oversight. Specific research projects will be analysed individually and results submitted for publication in due course.

Conclusion

The BSDMRE 2016 provided a unique opportunity to perform high quality research projects in the most challenging and austere of situations. Strong collaboration between civilian universities and military personnel drew on specialist expertise, maximised funding opportunities and enabled a range of projects to be completed. The combination of AT and research on an exercise of this scale was a novel undertaking and organisationally challenging but will result in significant and militarily relevant outputs. After the enduring operations of TELIC and HERRICK research strategies must now focus on support of the wider military as we return to contingency. Remote, mountainous environments remain a safe haven for potential enemies and presents significant challenges for non-acclimatised troops operating in those areas. BSDMRE ranks as one of the largest participation HA research expeditions ever conducted and continues a tradition of military leadership in this field.

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Fig 1. Altitude profile for trekking teams
210x297mm (300 x 300 DPI)