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Degree of Hypoxia and Physiological Differences Between Fast and Slow Ascents to Very High Altitude

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Abstract

Introduction: Rapid ascent to altitudes of over 5000 m above sea level are associated with dramatic changes in adaptive physiology. The effects of a gradual ascent on symptoms, oximetry, and heart rate are described and compared with the effects of a rapid ascent to the same altitude by a comparable cohort. **Methods**: A group of 13 individuals (six females) representing 10 countries from five continents ascended gradually from Lukla (2300 m) to Everest Base Camp (5300 m) in Nepal over an 8-day period, then descended over a further 4 days. All symptoms and medication were recorded, along with pulse oximetry (SpO_2) and heart rate (HR) every 500 m of ascent. The results were then compared with those obtained at equivalent altitudes using similar methodology from a fast ascent of Mount Kilimanjaro to an equivalent altitude by a comparable cohort over 4 days. **Results**: The gradual ascent group had a median age of 33 years (range 25–66), and all successfully completed the trek. No severe headache, vomiting, orthopnoea, or productive cough occurred, although minor nausea and mild headache were common. Baseline oximetry fell from a median of 96% (93–97%) to a median of 78% (53–86%) at 8 days but recovered to 94% (89–99%) inside 4 days. Corresponding HR rose from a baseline median of 72 bpm (57–85) to a median of 103 bpm (78–115) at 8 days, then recovered to 80 bpm (54–94) after 4 days. Neither age nor gender correlated with outcomes. Individually, HR correlated inversely with oximetry, but there was no group correlation between these two variables. By contrast, a more rapid 4-day ascent from the same starting height, with similar baseline values for HR and oximetry, to the same final altitude was associated with more severe headache, breathlessness, and vomiting. Fast ascent was associated with a significantly more marked reduction in oximetry to a median of 71% (52–76) and an increase in HR to a median of 110 bpm (88–140). The fast ascent group also required significantly more medication, rated their experience as less enjoyable, and had a 100% incidence of acute mountain sickness compared to 0% in the slow ascent group. **Discussion**: Oxygen desaturation and tachycardia are inevitable consequences of ascending above 5000 m, but the degree to which this occurs can be reduced by slowing ascent times and taking rest days every 1000 m of ascent. This practice is associated with fewer symptoms and greater safety, with less need for either prophylactic or therapeutic medication. Careful consideration should be given to rates of ascent when climbing to altitudes at or above 5000 m.

Keywords: altitude; Everest; Kilimanjaro; acute mountain sickness; physiology; oximetry; hypoxia; hypothermia

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1. Introduction

Climbing to very high altitudes has become much commoner in recent years as access to remote areas has rapidly improved and the associated expense has fallen in relative terms. However, limitations imposed on time and resources have led to many ascents being made more rapidly. Rapid ascent to very high altitude is known to carry greater risks than a more gradual ascent, but we have only found one comparative study of fast versus slow ascent to very high altitudes under similar conditions [1].

The human body is exposed to many risks when ascending to high elevations. Adverse and changeable weather conditions, cold, high winds, and the risk of ice, rock fall, or avalanche may be encountered even at relatively low altitudes. Likewise, the dangers posed by poor visibility, difficult terrain, and dehydration are often under-appreciated by climbers [2]. More predictable is the change in the partial pressure of oxygen (pO2) in inspired air, which can have profound effects on human physiology [3].

Failure of the human body to adjust adequately to the physiological challenges imposed by hypoxia can cause altitude illness. Physical fitness does not predict the probability of developing this, while genetic factors play a part in susceptibility. Blood oxygen levels drop more at night, so ascending slowly and taking occasional 'rest days' to climb high and then return to lower elevations to sleep greatly reduce stress and facilitate acclimatisation. This approach protects against the development of acute altitude sickness, but the effectiveness of this approach diminishes above 8000 m, close to the height of Mt Everest [3,4]. Acclimatisation increases the climber's sense of well-being and enjoyment, while improving their sleep and capacity for physical endurance.

Mountain medicine defines three altitude zones which correspond with reducing pO2 and are associated with increasing risks of developing acute mountain sickness (AMS) [5]. These zones are high altitude (1500–3500 m), very high altitude (3500–5500 m), and extreme altitude (>5500 m). Medical problems at these altitudes also include the risks of high-altitude pulmonary oedema (HAPE) and high-altitude cerebral oedema (HACE). Treatment with nifedipine and/or dexamethasone [6] may be required, while the risk of neurological damage is increased at extreme altitude [7]. People who develop AMS demonstrate alterations in anti-diuretic hormone (ADH), and those at risk of developing HAPE may notice reduced urine production prior to developing respiratory symptoms [8]. A reduction in the efficiency of digestion occurs at high altitude [9], and other adverse effects include dehydration, hypothermia, and sunburn.

As altitude increases, atmospheric pressure falls, and there is an associated reduction in pO2. Atmospheric pressure is reduced by half at 5500 m above sea level to 380 mm Hg, with a corresponding fall in pO2 to 69 mmHg. At an altitude of 8900 m, near the height of mount Everest, these values fall to around 30% of their sea level baseline. At half this height, arterial oxygen saturation is around 70% in unacclimatised trekkers but rises significantly within a few days [4]. The stress on the body brought upon by hypoxia is also influenced by ascent rate and the severity and duration of exposure [10]. Other factors shown to be relevant to the development of AMS at an altitude of 3350 m included body mass index > 24 and lower initial SpO_2 [11]. In this study, the incidence of AMS was not associated with the rate of ascent. However, a larger study up to a higher altitude of 4400 m showed a more complex association between rate of ascent and development of AMS. Here, a faster ascent protocol was initially a risk factor for AMS but then evolved to become protective against AMS after ascent to higher altitudes [12].

Hypoxic pulmonary vasoconstriction leads to improved matching of ventilation and perfusion within the lung. The subsequent elevation in pulmonary artery pressure may ultimately lead to right ventricular hypertrophy [13]. There are corresponding cardiovascular changes, with tachycardia, increased cardiac output, and rising blood pressure

mediated by increased sympathetic drive. Increased diuresis leads to a higher haematocrit as plasma volume reduces and blood becomes more concentrated [14]. Despite these early adaptations, there is a reduction in cognitive function with hypoxia, which contribute towards accidents and poor decision-making at extremes of altitude.

Further acclimatisation occurs over several days. The body slowly adapts to the resulting respiratory alkalosis by increasing renal excretion of bicarbonate. This compensatory mechanism takes about 100 h and is accelerated by acetazolamide [15]. Lactate production falls as capillaries proliferate in skeletal muscle to maintain muscle function [16]. Increased production of erythropoietin by the kidney in response to hypoxia stimulates haematopoiesis. Haematological adaptation to altitude is complete when polycythaemia occurs [17]. Haemoglobin concentrations can rise to 200 g/L, and greater blood viscosity increases the risk of venous thromboembolism, retinal damage, and stroke [18].

Hypoxia is the main factor in the development of acute altitude illness, which can be separated into three related categories: AMS, HAPE, and HACE [19]. AMS is the most common, and diagnosis is based on recent ascent to high elevation with the development of headache in all sufferers, typically accompanied by anorexia, fatigue, syncope, insomnia, nausea, or vomiting. These symptoms usually develop within 12 h of ascent to an elevation above 3000 m and often develop overnight. The present study was designed to compare the effects of a gradual ascent to very high altitude with those of a rapid ascent on human physiological responses and symptoms of AMS. Comparative data on this subject are presently very limited and is well overdue.

2. Methods

2.1. Aim

In this report we compare and contrast the effects on human physiology of rapid versus slow ascent to 5300 m by comparable groups under similar conditions using pulse oximetry. Our data extend previous observations at lower altitude. We also compare cardiac adaptation, symptoms, pharmacological consumption, and AMS scores between the two groups to provide a comprehensive and clinically relevant comparison of the two approaches. Inclusion criteria were that individuals had no pre-existing cardiopulmonary disease. Exclusion criteria were refusal to train adequately, refusal of consent to regular physiological assessment, exceeding 1000 m altitude during the previous 3 months, and failure to achieve an altitude of at least 5300 m.

2.2. Details Group 1

Over 21 days in early March 2024, 13 people (six females) from 10 countries across five continents met in Kathmandu in Nepal to climb to Everest Base Camp (Group 1). The group had a median age of 33 years (range 25–66). Led by two male Nepali guides, the group ascended gradually from 2300 m, via Lukla (2860 m), to Everest Base Camp at 5300 m, and then further up to Kala Patthar (5700 m) over an 8-day period. The average cumulative ascent gained each day was 500 m, as the group had 2 rest days when they climbed then descended, spending 2 consecutive nights at the same altitude.

Given that the route was undulating, their total ascent amounted to 6300 m, with an average daily height gain of 788 m. The group then descended back to Lukla over a further 4 days before flying back to Kathmandu. The group all used four-season sleeping bags to help cope with nocturnal temperatures, which dropped to −15 °C.

All symptoms, signs, and medication used were recorded by a physician (CK). Polyuria was defined as the passing of >2.5 L urine over 24 h, but practicalities prevented objective assessment of this while trekking. Hence, daily urine volumes were estimated by each individual with reference to frequency and duration of micturition. The AMS score for

each individual was calculated from symptoms recorded, using the 2018 modification of the Lake Louise score, classifying mild AMS as a score of 3–5 and moderate AMS as a score of 6–9 [20].

Each person's SpO_2 and heart rate (HR) was measured every 500 m. The highest altitude at which recordings were taken was 5300 m. On each occasion, the highest of three readings for SpO_2 and the lowest of three readings for HR were recorded using a finger probe (Oxypulse, Ecomerzpro, Madrid, Spain). Participant enjoyment of each trek was assessed on a simple Likert scale from 0 (worst experience) to 10 (best experience) after descent.

2.3. Details Group 2

The results from this trek were compared with those obtained in late February 2018 from Group 2 comprising seven people (four female) who ascended Mount Kilimanjaro in Tanzania. This group had a median age of 29 years (range 25–60 years). They ascended rapidly, using the Machame route from a starting height of 1800 m to the summit at 5900 m, over a 4-day period.

Their total ascent was therefore 4160 m, and the average cumulative height gained each day was 1040 m, with no rest days and no descent on the way to the summit. They then descended back to 1740 m over a further day. They camped and required four-season sleeping bags to cope with night-time low temperatures of −7 °C. The ascent profiles for both routes are available in the Supplementary Materials.

All symptoms, signs, and medication were recorded by a physician (CK). Polyuria was defined as the passing of >2.5 L urine over 24 h, but practicalities prevented objective assessment of this while trekking. Hence, daily urine volumes were estimated by everyone with reference to frequency and duration of micturition. The AMS score for each individual was calculated from the recorded symptoms using the 2018 modification of the Lake Louise score, classifying mild AMS as a score of 3–5 and moderate AMS as a score of 6–9 [20].

Each person's SpO_2 and heart rate (HR) was measured every 500 m of ascent, with the highest of three readings for SpO_2 and the lowest of three readings for HR all recorded using a finger probe (Oxypulse, Ecomerzpro, Madrid, Spain). Again, the highest altitude at which recordings were taken was 5300 m. On this trek, systolic blood pressure (SBP) was also measured each evening at 6 pm using an automatic sphygmomanometer (Vital Track, Blue Ocean Company Ltd., Lancashire, UK), and the lowest of three readings was recorded. Participant enjoyment of each trek was assessed on a simple Likert scale from 0 (worst experience) to 10 (best experience) after descent, and the mean results were compared.

2.4. Group Comparisons

The weather was dry, stable, and free of significant windchill for each of the expeditions, with equivalent daytime temperatures peaking at 16 °C on both trips. Participants were comparable between the two groups in terms of racial origin, male-to-female ratio, age, body mass index, training, and preparation. All but one participant in each group were Caucasian or Asian. All participants had trained for over 3 months at altitudes between sea level and 1000 m, exercising at least thrice weekly for a minimum of 30 min. All females were premenopausal, and none of the subjects in either group had lived at an altitude of above 1000 m in the decade prior to the expeditions described. The SPSS software (version 3) package program (IBM) was used for statistical analysis. The Shapiro–Wilk test showed that the data were not normally distributed, and hence comparisons were made by modified ANOVA testing between data sets within each group using the Wilcoxon signed rank test, while those between groups were made using the Kruskal–Wallis test. Significance was expressed at the $p = 0.05$ level. All trekkers in both groups provided

informed consent to the collection and use of their physiological and pharmacological data, both as a means of monitoring their well-being during the treks, as well as for the purposes of writing this paper. The study was approved by the Ethical Committee at Kilimanjaro Christian Medical Centre in Moshi.

3. Results

All of those in Groups 1 or 2 met the inclusion criteria, and none met the exclusion criteria. Neither the trek to Everest Base Camp, nor to Kilimanjaro summit, required any significant technical expertise, and the mean daily distance covered in each was very comparable, at 11 km. There were no significant differences between the groups in terms of age or gender mix. Barometric pressures at the latitude of Kilimanjaro and Everest are similar up to 5000 m [21]. All members of both groups completed the treks, and none of the trekkers had established prior cardiorespiratory disease. Table 1 compares the symptoms experienced by both groups. None of Group 1 in Nepal met the criteria for AMS. The main symptoms reported by members of this group were mild headache, fast heart rate, sunburn, sinusitis, and a dry cough. The latter two symptoms were not reported by five people who wore masks to minimise dust inhalation. Four also exhibited mild peripheral oedema, affecting the hands, feet, and face, above altitudes of 4000 m. Polyuria was also reported by four and was a significant inconvenience, especially at night. Symptoms reported by Group 2 in Tanzania were much more significant. Two people had severe headache, and one had recurrent vomiting with abdominal pain and became dehydrated. Five had polyuria, and all reported anorexia and nausea, with moderate headache and some breathlessness. Five (71%) met the criteria for mild AMS, while two (29%) met the criteria for moderate AMS. The median peak (range) AMS score in Group 1 was 1 (0–2), which was significantly lower than that in Group 2, at 4 (3–6) [H-stat = 20, $p = 0.0031$]. Table 2 shows the AMS scores in both groups correlated with increasing altitude. None of Group 1 developed AMS, while the percentage of trekkers with AMS in Group 2 rose from 43% at 4300 m to 57% at 4800 m and to 100% by 5300 m. All members of Group 2 developed peripheral oedema. Neither age nor gender were correlated with any outcome measures.

Table 1. Comparison of the symptoms experienced by Group 1 ascending to 5300 m over 8 days (slow) versus Group 2 ascending over 4 days (fast), along with the altitude at which symptoms were first reported and percentage of subjects affected.

Altitude (m)	Symptoms (Group 1)	Symptoms (Group 2)
1800		
2300		
2800		Sunburn *n* = 2 (28%)
3300	Chest infection *n* = 1 (8%)	Tachycardia *n* = 3 (42%)
		Mild dyspnoea *n* = 2 (28%)
3800	Polyuria *n* = 4 (30%)	Mild headache *n* = 7 (100%)
	Sunburn *n* = 3 (22%)	Peripheral oedema *n* = 7 (100%)
		Polyuria *n* = 5 (70%)
4300	Peripheral oedema *n* = 4 (30%)	Anorexia *n* = 7 (100%)
	Nausea *n* = 2 (15%)	Moderate headache *n* = 7 (100%)
		Diarrhoea *n* = 1 (14%)

Table 1. *Cont.*

Altitude (m)	Symptoms (Group 1)	Symptoms (Group 2)
4800	Sinusitis *n* = 8 (60%)	Nausea *n* = 7 (100%)
	Tachycardia *n* = 2 (15%)	Moderate breathlessness *n* = 3 (42%)
	Anorexia *n* = 2 (15%)	Severe headache *n* = 2 (28%)
5300	Mild headache *n* = 3 (22%)	Vomiting *n* = 2 (28%)
	Dry cough *n* = 3 (22%)	Severe breathlessness *n* = 2 (28%)

Table 2. Comparison of the median (range) of AMS scores in Group 1 with those in Group 2, along with the altitude at which they were recorded.

Altitude (m)	AMS Scores (Group 1)	*p* Value	AMS Scores (Group 2)
3800	0 (0–0)		0 (0–2)
4300	0 (0–1)	0.03	2 (2–3)
4800	0 (0–2)	0.01	3 (2–4)
5300	1 (0–2)	0.003	4 (3–6)

Table 3 records the medication required by each group. Five members of Group 1 chose to use low-dose acetazolamide prophylaxis, and a further three were advised to use ibuprofen for symptomatic relief. One person was given a course of antibiotics for a chest infection, and five required decongestants for sinusitis. By comparison, all of Group 2 took prophylactic acetazolamide, and five needed additional ibuprofen for persistent symptoms. Two were administered low-dose (2 mg) dexamethasone, and one needed nifedipine (20 mg). No one required oxygen, but rapid descent was mandated because of the severity of symptoms at the summit. Polyuria was associated with taking acetazolamide, occurring in 9 out of 12 (75%) of climbers on this agent across both groups. Group 1 participants generally rated their experience as more enjoyable than did those in Group 2 (7.9 versus 6.7).

Table 3. Comparison of the percentage of subjects requiring specific medication in Group 1 ascending to 5300 m over 8 days vs. Group 2 ascending over 4 days.

Altitude (m)	Medication (Group 1)	Medication (Group 2)
1800	Acetazolamide *n* = 5 (38%)	Acetazolamide *n* = 7 (100%)
2300		
2800		Paracetamol *n* = 5 (70%)
3300	Co-amoxiclav *n* = 1 (8%)	
3800		Ibuprofen *n* = 5 (70%)
4300	Paracetamol *n* = 3 (22%)	Loperamide *n* = 1 (14%)
4800	Decongestants *n* = 5 (38%)	Dexamethasone *n* = 2 (28%)
5300	Ibuprofen *n* = 3 (22%)	Nifedipine *n* = 1 (14%)
	Salbutamol *n* = 1 (8%)	Cyclizine *n* = 2 (28%)

Table 4 shows the results of the physiological measurements undertaken. In Group 1, baseline SpO_2 fell from a median of 96% (93–97%) at 2300 m to a median of 78% (53–86%) at 5300 m 8 days later [R1 = 91; $p = 0.0001$] but recovered to 94% (89–99%) within 4 days on returning to 2860 m. Corresponding HR rose from a baseline of 72 bpm (57–85 bpm) to a median of 103 bpm (78–115 bpm) at 5300 m [R1 = 98.5; $p = 0.0001$], then recovered to 80 bpm (54–94 bpm) after 4 days on returning to 2860 m. Neither age nor sex correlated

with outcomes. Individually, HR correlated inversely with SpO_2, but there was no group correlation between these two variables. By contrast, in Group 2, baseline SpO_2 fell from a median of 96% (94–98%) at 1760 m to a median of 71% (52–76%) at 5300 m at 4 days [R1 = 77; $p = 0.001$] but recovered to 95% (92–98%) within 1 day on descending to 1800 m. Corresponding HR rose from a median baseline of 70 bpm (58–80 bpm) to a median of 110 bpm (88–140 bpm) at 5300 m after 4 days [R1 = 77, $p = 0001$], then recovered to 80 bpm (54–94 bpm) after a day on returning to 1760 m. Again, neither age nor sex correlated with outcomes. In Group 2, SBP rose from a median of 122 mm Hg (98–138 mm) at baseline to a median of 164 mm Hg (139–198 mm) at 5300 m [R1 = 28; $p = 0.001$] but returned to normal slowly over 5 days. No residual neurological features were noted after descending, and careful screening showed no evidence of retinal haemorrhages in any of the group the day after descent. Everyone in both groups experienced complete resolution of symptoms within 48 h of returning to starting height. There were no long-term sequelae in any participants, and interestingly there were no differences in symptoms or oxygen saturation between those who took acetazolamide and those who did not.

Table 4. Comparison of heart rate (HR) and pulse oximetry (SpO_2) in Group 1 ascending to 5300 m over 8 days (slow) versus Group 2 ascending over 4 days (fast).

Altitude (m)	**HR (bpm)**		**SpO_2 (%)**	
	Group 1	Group 2	Group 1	Group 2
1800		66 (48–72)		98 (95–99)
2300	72 (57–85)	70 (58–80)	96 (93–97)	96 (94–98)
	NS		NS	
2800	78 (58–95)	76 (60–88)	94 (90–98)	94 (91–97)
	NS		NS	
3300	83 (67–103)	84 (78–105)	91 (83–94)	91 (88–95)
	NS		NS	
3800	83 (63–102)	88 (70–104)	87 (81–94)	85 (74–92)
	NS		NS	
4300	94 (70–112)	96 (76–120)	86 (74–94)	82 (71–89)
	NS		NS	
4800	94 (69–116)	98 (81–118)	82 (55–93)	77 (58–86)
	NS		$p = 0.047$	
5300	103 (78–115)	110 (88–140)	78 (53–86)	71 (52–76)
	$p = 0.061$		$p = 0.036$	

Statistical differences relate to intergroup comparisons.

Although the rises in HR from baseline to 5300 m altitude were highly significant in both groups, the difference between the two groups in the degree of change in HR did not quite meet statistical significance [H stat = 4.31, $p = 0.061$]. The falls in SpO_2 were also highly significant in each group, but the degree of reduction in SpO2 was significantly less in Group 1 than in Group 2, both at 4800 m [H stat = 16.9, $p = 0.035$] and at 5300 m [H stat = 13.5, $p = 0.013$].

There was significant inter-individual variation in both groups. In Group 1 at 5300 m, HR, SpO_2, and AMS scores ranged from 78 bpm, 86%, and 0, respectively in the best-adapted individuals to 115 bpm, 53%, and 2, respectively, in the worst-adapted individuals. In Group 2 at 5300 m, HR, SpO_2, and AMS scores ranged from 88 bpm, 76%, and 3,

respectively, in the best adapted individuals to 140 bpm, 52%, and 6, respectively, in the worst adapted individuals.

4. Discussion

To our knowledge, this is the first paper to compare SpO_2 during fast and slow ascents to very high altitudes by equivalent groups using the same protocol. A previous study [11] compared larger groups ascending to 3350 m using a fast vs. slow ascent profile and demonstrated earlier onset of AMS symptoms in the fast ascent group and an association of AMS with initial reductions in SpO_2. However, the overall incidence of AMS was not associated with the rate of ascent. The differences between fast (3 days) and slow (4 days) ascent, and the maximum altitude reached, were both much less in that study [11] than in our present study, which demonstrated that the differences in SpO_2 only became statistically significant at and above 4800 m.

Although our group sizes were small, the time of year, group composition, and conditions experienced were all very similar. Despite the small numbers, a significant difference in oxygen saturation was found between fast and slow ascents, confirming what had previously been predicted by other authors. In the only other study to directly compare fast and slow ascents to very high altitude, reported 15 years ago, the differences in rate of ascent were less marked than in ours, SpO_2 was not measured, and between-group differences were primarily assessed using an estimate of severity of AMS [1], prior to the 2018 criteria reclassification [20]. We also found a very significant difference in AMS scores between fast and slow ascenders. The number of climbers within the slow ascent group in the 2009 study was comparable to ours, emphasising how difficult it can be to undertake large, controlled studies at very high altitude while ensuring both participant safety and scientific validity.

The highest altitude at which people have been recorded as living long term is 5100 m [22]. Different populations have evolved different adaptations to living at high altitude, with genetic changes resulting over time [23]. Indigenous inhabitants can thrive at high altitude because of evolutionary changes in their respiratory and cardiovascular systems [24,25]. Adaptation to altitude leads to genetic advantages, such as larger lungs [26]. Residents of the Andes exhibit polycythaemia [27], while Himalayan inhabitants compensate via increased ventilatory rates and cerebral blood flow [28].

Hypothermia (a body core temperature of below 35.0 °C) is a constant threat at any altitude, but the risk rises with increasing distance from the equator. During the climbing season, the mean temperature at the summit of Everest is −26.0 °C [29]. The risk of dehydration is accentuated by breathing cold air, as moisture from the upper airways is required to warm inhaled air to body temperature [8]. Conversely, severe sunburn can accentuate nausea and fatigue and may accelerate fluid loss in the case of severe skin damage [30]. The lower mean temperatures experienced by the slow ascent group may have protected them from excessive fluid loss by comparison with the fast ascenders in our study.

The presence and severity of AMS, as quantified by the Lake Louise score [20] offer a useful comparison between both individuals and groups, as well as the effect of the speed of ascent. In this study, the individuals in each group were well matched, which allowed for comparison of the effects of fast versus slow ascent on the prevalence and severity of AMS. The prevalence of AMS increases with altitude and typically affects just 7% at 2200 m, but as many as 52% at 4560 m [31]. Younger people appear more susceptible to AMS [32], as do females [33]. The present study showed that AMS was confined to the fast ascenders (Group 2), where all were affected to some degree.

Mild AMS usually resolves within a day if trekkers do not climb any higher [34]. It is usually self-limiting, but can be treated with paracetamol or ibuprofen. Acetazolamide facilitates acclimatisation and can be used to treat AMS, but it is more typically used as a prophylactic agent. It causes bicarbonate diuresis with metabolic acidosis, increasing ventilatory drive and oxygenation [35]. It accelerates acclimatisation and reduces periodic breathing, which is common at night over 4000 m. It may induce polyuria and paraesthesia of extremities. A dose of 125 mg twice daily, starting 1 day prior to ascent and continuing until descent commences, reduces the probability of developing AMS. This can be administered at the treatment dose of 250 mg twice daily if AMS occurs in climbers not already taking it [5,36]. Acetazolamide reduces the incidence of AMS and is likely to affect the values of the Lake Louise clinical score and might also alter SpO_2 by improving arterial oxygen saturation. In more severe cases of AMS, dexamethasone is effective in providing rapid symptomatic relief [37]. In the most severe cases, oxygen supplementation provides immediate benefit but must be combined with a prompt reduction in height of at least 300 m [38].

The incidence of severe AMS among all trekkers on Kilimanjaro has been shown to be 8.6%, with over 1% of all climbers hospitalised [39]. An earlier study of 130 Finnish trekkers reported a prevalence of at least mild AMS of 75% and a summit success rate of under 50% [40]. These results are broadly in keeping with our findings, with 29% experiencing moderate AMS, while 71% had mild AMS, although all managed to summit. By comparison, the prevalence of any AMS among trekkers to Everest Base Camp in a South African study was 42% [41], though the prevalence in our study was 0%.

More serious manifestations of altitude illness may occur above 4300 m, with a rough incidence of HAPE occurring in 1% of climbers [42]. It typically manifests as a productive cough with frothy phlegm and associated dyspnoea at rest. In severe cases, sputum is often blood-stained. Oxygen saturation falls dramatically, and SpO_2 shows levels at least 10% below those recorded by healthy people at the same altitude, with values invariably below 70% and often much lower [43]. The commonest cause of death among trekkers on Kilimanjaro is HAPE [44]. Urgent descent is mandatory, with the use of supplemental oxygen if available. Nifedipine has long been known to be effective in preventing or reducing pulmonary oedema in the short term, but does not replace the need for oxygen and descent from altitude [45]. Less common is HACE, which may be triggered by the worsening hypoxia associated with HAPE [46]. HACE is a medical emergency and may lead to confusion, drowsiness, and coma [47]. Urgent descent is mandated, along with the use of dexamethasone and oxygen, where available. Low-dose dexamethasone also helps prevent HACE in susceptible individuals [48] and can save lives [49].

In keeping with previous work [50], our study showed that a gradual ascent to 5300 m over 8 days, incorporating 2 rest days where the participants slept at the same altitude, was associated with significant benefits when compared to a rapid ascent over 4 days without taking time to acclimatise. Guidelines on safe ascent rates have been published [51] and evaluated [52]. None of the slow ascenders in our study developed features of AMS, while all of those in the fast ascent group developed symptoms of at least mild AMS, with one person (14%) also exhibiting features of early HAPE. Drinking adequate volumes of fluid to prevent dehydration was offset by the unwanted developments of either peripheral oedema from fluid retention or polyuria from acetazolamide use in many trekkers. Acetazolamide is a diuretic and therefore accentuates polyuria. Acetazolamide was used less by slow ascenders (38%) than by fast ascenders (100%), as were both ibuprofen and paracetamol, which would suggest that, without these agents, differences between fast and slow ascenders with regards to AMS scores, and possibly physiological adaptation, might have been even greater. The use of nifedipine and dexamethasone was confined to the fast ascent

group, and it is possible that a degree of dehydration might offer some protection against both HAPE and HACE. At and above 4800 m, oxygen saturations were significantly higher among those who ascended slowly, and this group also exhibited slightly lower pulse rates. Overall, those who ascended slowly adapted more effectively to increasing altitude and reported a more comfortable and enjoyable experience. Our findings support those previously published, showing a greater propensity for problems among high altitude trekkers in Africa than Asia [53], associated with higher levels of AMS [40,41]. This is likely to be at least in part due to the nature of the terrain and the speed of ascent.

Limitations of our study include the small, uneven numbers in each group. However, these were matched as closely as possible for age, gender, and baseline fitness. Furthermore, weather conditions, temperatures, and the terrain were very similar for both expeditions. Despite the small numbers, our findings did demonstrate significant differences in outcome between the groups. A further methodological flaw was the lack of objective assessment of urinary volumes. A major strength is the direct comparison of fast and slow ascents by age- and gender-matched groups using objective measures under similar conditions at the same altitudes.

5. Conclusions

We found that gradual ascent to very high altitudes was protective against the onset of AMS when compared to a more rapid ascent to the same altitude. We showed that the fall in SpO2 at 5300 m was less severe among slow ascenders when compared to fast ascenders. The corresponding rise in pulse rate at this altitude was also less dramatic than among fast ascenders. The differences in SpO_2 were significant from 4800 m.

Those who ascended more slowly required significantly less medication and rated their experience as more enjoyable than those who ascended quickly. We found no correlation between either age or sex and any of the clinical or physiological variables we measured. Graduated ascent with rest days to allow acclimatisation reduced the body's physiological stress and was linked with fewer symptoms and less medication.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/oxygen5030013/s1.

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