Intraocular Pressure during a Very High Altitude Climb

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Purpose. Reports on intraocular pressure (IOP) changes at high altitudes have provided inconsistent and even conflicting results. The purpose of this study was to investigate the effect of very high altitude and different ascent profiles on IOP in relation to simultaneously occurring ophthalmic and systemic changes in a prospective study.

Methods. This prospective study involved 25 healthy mountaineers who were randomly assigned to two different ascent profiles during a medical research expedition to Mt. Muztagh Ata (7,546 m/24,751 ft). Group 1 was allotted a shorter acclimatization time before ascent than was group 2. Besides IOP, oxygen saturation (SaO_2), acute mountain sickness symptoms (AMS-c score), and optic disc appearance were assessed. Examinations were performed at 490 m/1,607 ft, 4,497 m/14,750 ft, 5,533 m/18,148 ft, and 6,265 m/20,549 ft above sea level.

Results. Intraocular pressure in both groups showed small but statistically significant changes: an increase during ascent from 490 m/1,607 ft to 5,533 m/18,148 ft and then a continuous decrease during further ascent to 6,265 m/20,549 ft and on descent to 4,497 m/14,750 ft and to 490 m. Differences between groups were not significant. Multiple regression analysis (IOP-dependent variable) revealed a significant partial correlation coefficient of $\beta = -0.25$ ($P = 0.01$) for SaO_2 and $\beta = -0.23$ ($P = 0.02$) for acclimatization time.

Discussion. Hypobaric hypoxia at very high altitude leads to small but statistically significant changes in IOP that are modulated by systemic oxygen saturation. Climbs to very high altitudes seem to be safe with regard to intraocular pressure changes. (*Invest Ophthalmol Vis Sci.* 2010;51:1609–1613) DOI: 10.1167/iovs.09-4306

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Traveling to high altitudes for recreational reasons is becoming increasingly popular and has been a subject of scientific interest. Technical progress enables researchers to gain new insights into changes that occur within the human body on exposure to naturally hypobaric atmospheric conditions.

Intraocular pressure (IOP) changes at high altitudes have been the subject of several publications.[1–9] Yet results have been inconsistent. Findings range from a decrease[1,4,6,8,9] through no change,[5] to an increase[1] in IOP at moderate to high altitudes. Changes in IOP during an expedition to very high altitudes (i.e., >5,500 m/18,045 ft) have not been documented yet.

Depending on the degree of hypoxia,[10] ascent rate,[11] and individual susceptibility,[12] acute mountain sickness, or even the less common high-altitude cerebral edema (HACE) may occur. HACE results in increased intracerebral pressure (ICP) and hence in cerebral hypoperfusion with possible severe and fatal dysfunction.[13] Several studies suggest that an increase in ICP leads to an increase in IOP, and thus that IOP measurement could be a minimally invasive method of detecting an increase in ICP.[14–16] Therefore, a correlation of IOP with parameters indicating cerebral affection due to hypoxia would be of great interest.

The Muztagh Ata medical research expedition study included researchers from various medical specialties, such as pneumology, neurology, hematology, and ophthalmology, who used a holistic approach to prospectively assess hypoxia-induced changes in the body. A list of the discipline-specific studies along with references can be found in Table 1. We set out to investigate changes in IOP at very high altitudes (>6,000 m/19,685 ft) with two different ascent profiles and place these results into perspective with simultaneously occurring ophthalmic and systemic changes (e.g., optic disc status; cerebral acute mountain sickness [AMS-c]scores, including possible HACE; and pulse oximetry).

Methods

Our working hypothesis was that IOP would decrease with altitude, because of lower systemic oxygen saturation (SaO_2) and decreased aqueous production.

Volunteers

This randomized, prospective, multidisciplinary, observational cohort study[17–20] was performed within the scope of a high-altitude medical research expedition on Mt. Muztagh Ata in China (7,546 m/24,751 ft; Fig. 1). Mountaineers in good physical condition were included. Exclusion criteria were any type of ocular, cardiac, or respiratory disease; a history of high-altitude pulmonary edema or high-altitude cerebral edema; a history of ophthalmic disease or ophthalmic surgery (including cataract); a history of contact lens wear; and intake of drugs other than nonsteroidal antirheumatic agents during the expedition. The study was approved by the Ethics Committee of the University Hospital, Zurich, and adhered to the tenets of the Declaration of Helsinki

Table 1. High Altitude Medical Research Expedition to Mt. Muztagh Ata, 2005

Discipline	Discipline-specific Studies	References
Ophthalmology	Incidence of optic disc swelling at very high altitudes	Bosch et al.[17]
	Effect of high altitude on ocular blood flow	Bosch et al.[18]
	Effect of high altitude on corneal thickness in healthy mountaineers	Bosch et al.[19]
	Incidence of retinal hemorrhages and their implications during a high altitude climb	Barthelmes D, et al., manuscript submitted
	Effect of high altitude on corneal topography	Bosch MM, et al., manuscript in preparation
Internat medicine and pneumology	Effect of ascent protocol on acute mountain sickness; randomized, controlled study	Bloch et al.[20]
Neurology	Effect of high altitude on cognitive function	Merz TM, et al., manuscript submitted
Hematology	Effect of high altitude on glomerular filtration rate	Pichler et al.[21]
	Changes in coagulation parameters during a high altitude climb	Pichler-Hefti J, et al., manuscript submitted

(1983 revision). Informed, written consent was obtained from all subjects before the examinations.

Ascent Profile

For security reasons and to study the effect of acclimatization, the participants were randomly distributed into two groups with different ascent profiles (Fig. 2). The average ascent rate was 190 and 200 m/d (623 and 656 ft/d), for groups 1 and 2, respectively. The climb began at 3,750 m/12,300 ft in the village of Subash and progressed to base camp (BC = 4,497 m/14,750 ft), camp 1 (C1 = 5,533 m/18,148 ft), camp 2 (C2 = 6,265 m/ 20,549 ft), camp 3 (C3 = 6,865 m/22,517 ft), and the summit (7,546 m/24,751 ft) within 20 (group 1) and 19 (group 2) days.

Measurements

All participants underwent general and ophthalmic baseline examinations 1 month before the expedition (ZH) at the University Hospital of Zurich (490 m/1607 ft). At the time of the expedition, examinations were performed during the ascent on the subsequent day on arrival at each new high camp (i.e., from BC to C2), and at the return to base camp (BC2). Each mountaineer had to have reached at least C2 to be included in the evaluation.

IOP was measured with a handheld tonometer (Tono-Pen XL; Reichert, Inc., Depew, NY) by placing the tip of the device onto the central cornea after local anesthesia with oxybuprocaine 0.4% (SDU Faure; Novartis Pharma AG, Basel, Switzerland). Three complete measurements were taken, and the average was calculated and recorded. All three readings used for calculating the average were required to have an SD of ≤5%, as shown on the instrument's digital display. The tonometer was calibrated according to the manufacturer's guidelines before each examination session.

Central corneal thickness (CCT) measurements during the expedition[19] were performed with a precision pachymeter (Pocket II; Quantel Medical, Clermont-Ferrand, France) after IOP measurements. CCT was determined in micrometers by averaging five successive readings in each eye. A maximum SD of 15 μm was defined a priori, and if it was exceeded, the complete measurement was repeated.

Fundus photographs were acquired with a handheld digital fundus camera (Genesis-D; Kowa Inc., Tokyo, Japan). Photographs were analyzed by three independent ophthalmologists. Optic discs were assessed as not swollen, equivocal, or swollen.[17]

Measurements were performed after one night of acclimatization[20] at similar times of the day, to minimize the effect of strenuous exercise[22] and diurnal variation.[23]

AMS-c scores on the Environmental Symptoms Questionnaire III[24] were assessed daily during the expedition. The AMS-c score represents symptoms that seem to reflect altered cerebral function. A score of 0.7 or greater reliably identifies a person with AMS, with symptoms that may include light-headedness, headache, dizziness, dim vision, lack of coordination, gastrointestinal tract upset, and weakness. The score is

Figure 1. Photograph of Mt. Muztagh Ata (7,546 m/24,751 ft) in Western Xinjiang Province, China. *Inset*: a climber having his fundus photographed in a high camp examination tent.

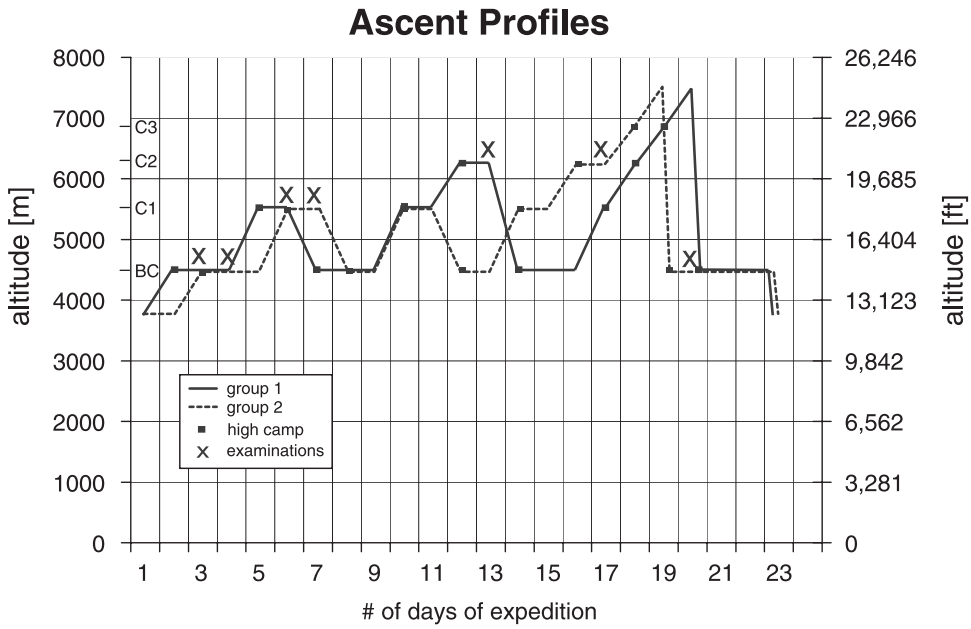

FIGURE 2. Ascent profiles of both climbing groups on Mt. Muztagh Ata. X, examination time points.

calculated by the sum of all item scores (range, 0–5) multiplied by their respective factorial weight and then multiplied by 0.1927.

Daily pulse oximetry was performed in the evening during a quiet rest in a standing position with a finger pulse oximeter (Onyx 9500 SportStat; Nonin Medical Inc., Plymouth, MN). Stable values after at least 3 minutes were recorded. Temperature was measured with a digital thermometer in the examination tent.

Statistical Analysis

Statistical analysis was performed with commercially available statistical software packages (SPSS 13; SPSS Inc., Chicago, IL, and Statistica 6; Statsoft Inc, Tulsa, OK). A test for normal distribution was performed with the Kolmogorov-Smirnov test. Measurements at each altitude between the two groups were compared by using the unpaired Student's *t*-test (including the Welch correction). Repeated-measures analysis of variance (ANOVA) was performed with combined data of groups 1 and 2, to assess changes in IOP over the different altitudes. Assumption of sphericity was assessed with Mauchly's test. In case of a statistically significant result, post hoc testing with Bonferroni's correction was applied.

Multiple regression analysis was used to analyze correlations between IOP as the dependent variable and independent variables (ascent group and different times of acclimatization, SaO_2, AMS-c score, central corneal thickness (CCT), altitude, optic disc appearance), and age. The time of acclimatization was defined as the number of days during the expedition starting from Subash. Correlation between environmental temperature and IOP, as well as pachymetry and IOP, was analyzed using bivariate regression analysis. Normally distributed data are expressed as the mean ± SD, and non-normally distributed data are expressed as the median and range (minimum–maximum). A two-sided α error (P) < 0.05 was considered statistically significant.

RESULTS

Seven of the total group of 32 climbers included in the ophthalmic branch of the study were excluded because of incomplete data collection during the expedition ($n = 4$), a history of refractive surgery on both eyes (LASIK, $n = 1$), or drug intake during the examination period ($n = 2$). Of the 25 climbers included, 5 were women and 20 were men. Mean ages in groups 1 and 2 were 42 ± 12 years and 45 ± 9 years, respectively, with no a significant difference between the groups ($P = 0.54$). Seventeen mountaineers (nine in group 1 and eight in group 2) reached the summit.

IOPs in both ascent groups increased from ZH to C1 and then continuously decreased with further ascent to C2 and descent to BC2 as shown in Table 2. Maximum IOP measurements never exceeded 21 mm Hg in both groups. For logistic reasons, group 1 could not be examined at BC2. No significant differences between ascent groups were found at any altitude (ZH, $P = 0.78$; BC1, $P = 0.77$; C1, $P = 0.65$; and C2, $P = 0.82$). Thus, for further analyses, measurements of both groups were combined. Mean IOP changes for both groups are shown in Figure 3. ANOVA revealed a significant IOP/altitude interaction ($P = 0.01$). The significant differences between IOPs at each altitude found in post hoc testing are illustrated in Figure 3.

CCT increased from 537 to 572 μm in group 1 and from 534 to 563 μm in group 2 with increasing altitude and decreased after decent.[19] SaO_2 measurements, and AMS-c scores are shown in Table 3. IOP measurements were undertaken in the same windless tent, with temperatures varying from 9°C (minimum temperature at C2) to 37°C (maximum temperature at BC) during the day with a mean of 21 ± 7°C.

Multiple regression analysis with IOP as the dependent variable revealed a partial correlation coefficient of $\beta = -0.25$ ($P = 0.01$) for SaO_2, -0.23 ($P = 0.02$) for acclimatization time, -0.11 ($P = 0.18$) for ascent group, 0.02 ($P = 0.85$) for AMS-c

TABLE 2. Summary of IOP Measurements in Groups 1 and 2 at Each Examination Height

	Mean	SD	Minimum	Maximum
Group 1				
ZH	13.4	2.5	8.0	17.3
BC1	13.9	2.6	9.0	20.6
C1	14.7	2.4	10.6	19.6
C2	13.5	2.2	9.6	17.6
Group 2				
ZH	12.8	3.4	6.3	21.0
BC1	13.9	3.2	8.3	20.3
C1	13.9	3.4	8.3	19.3
C2	13.2	2.4	8.6	18.3
BC2	12.3	3.0	7.6	19.3

All data are expressed in mm Hg. Group 1, $n = 13$, each altitude; group 2, $n = 12$, each altitude.

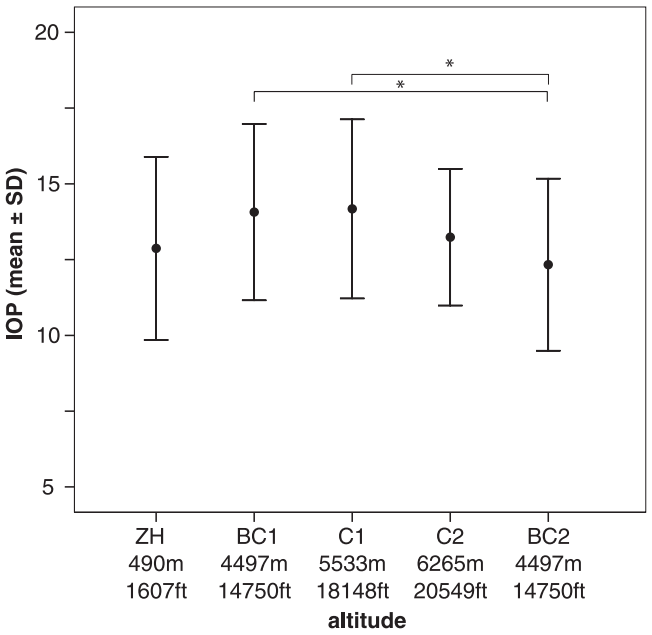

FIGURE 3. Development of IOP in both groups. The combined values of both groups are normally distributed. *Circles*: mean; *whiskers*: the SD of IOP at different altitudes. *Statistically significant differences between altitudes connected by brackets.

score, −0.09 ($P = 0.32$) for optic disc swelling, and 0.13 ($P = 0.13$) for age. No multicollinearity was detected. No statistically significant correlation between environmental temperature and IOP were found (ZH, $r = 0.16$, $P = 0.26$; BC1, $r = -0.18$, $P = 0.20$; C1, $r = 0.17$, $P = 0.24$; C2, $r = -0.10$, $P = 0.49$; and BC2, $r = -0.21$, $P = 0.32$). Analysis testing for a correlation between pachymetry and IOP at each altitude did not reveal significant results (ZH, $r = 0.05$, $P = 0.95$; BC1, $r = 0.19$, $P = 0.19$; C1, $r = 0.23$, $P = 0.11$; C2, $r = -0.93$, $P = 0.52$; and BC2, $r = 0.25$, $P = 0.24$).

DISCUSSION

This study reveals two main findings: First, only small but statistically significant changes in IOP over time were found during an expedition to very high altitudes. Second, IOP correlated with SaO_2 at various altitudes.

Our findings for the initial but statistically insignificant increase in IOP at 4,497 m/14,750 ft parallel the results of Somner et al.[1] Thereafter, the decline in IOP at further ascent to higher altitudes (at 6,265 m/20,549 ft), at which severe systemic hypoxia occurs, may be due to depleted oxygen supply to the nonpigmented ciliary epithelium and hence to decreased aqueous humor production. Aqueous production seems to become impaired after a certain systemic hypoxia threshold has been reached, which is supported by the statistically significant negative correlation between SaO2 in the participants at various heights and IOP. The pathophysiology behind this phenomenon may be comparable to that reported in other conditions with impaired oxygen supply to the ciliary body, such as in ocular ischemic syndrome.[25] or in severe cases of giant cell arteritis.[26]

The rationale behind randomizing the climbers into two groups with different ascent profiles was to assess the differences in the measured parameters that may have been due to distinct acclimatization times. Safety considerations also played a role in keeping the ascent groups limited. The duration between examinations at BC1 and C2 was 7 days in group 1 and 11 days in group 2 (Fig. 2). As no significant differences in IOP in the ascent groups were found, the differences in acclimatization time may have been too little to detect IOP changes between the two groups. IOP reduction over time did occur, however, and a significant negative correlation between acclimatization time and IOP measurements was found in our analysis. Pressures at BC2 (4,497 m), 13 days after the volunteers climbed to substantially higher altitudes after the initial measurements, were significantly lower than the ones at the same altitude (BC1). Thus, hypoxia during a prolonged stay at high altitudes may also lead to reduced aqueous production and therefore to the decline in IOP measured at 6,250 m (C2).[1,27] But overall, the duration of systemic hypoxia seems to play a greater role in IOP reduction compared with the extent of hypoxia. Yet, from the current data, no estimation can be made of the amount of contribution of acclimatization toward IOP reduction.

No statistically significant correlation was found between IOP and optic disc swelling or AMS-c scores. As reported earlier,[28] a high incidence of optic disc swelling has been observed in more than half of our volunteers with increasing altitude, representing increasingly severe hypoxia. All evidence pointed toward a hypoxia-induced increase in brain volume as the most probable etiology of the optic disc swelling, with a potential consecutive increase in ICP. Several studies support the hypothesis that an increase in ICP leads to an increase in IOP. Thus, IOP measurement could be used as a minimally invasive method to detect increased ICP.[14–16] Other investigators[29,30] found no correlation between IOP and optic disc swelling (i.e., an increase in ICP). Nevertheless, because of the small changes in IOP noted at different altitudes, which were clinically insignificant, we suggest that measuring the IOP in climbers at high altitudes is not an appropriate method to detect an increase in ICP.

In addition, acute strenuous exercise is known to lower IOP.[22] However, 10 minutes after stopping exercise, Price et al.[22] detected no significant IOP difference to baseline data. Our participants were examined on the day after ascent to a new high camp, thus allowing for at least 15 hours of rest. Based on the study design with moderate ascent rate, the influence of physical exercise on all our measured parameters should have been minimal.

IOP readings are largely influenced by mechanical properties of the eye. These properties may be altered by the development of corneal edema and are neither linear nor measur-

TABLE 3. Oxygen Saturation Measurements in Both Groups at the Different Altitudes

	ZH	BC1	C1	C2	BC2
Group 1					
SaO_2	98 ± 0.89	91 ± 8.31	79 ± 6.13	74 ± 7.79	87 ± 5.34
AMS-c	0 (0–0)	0.08 (0–0.88)	0.13 (0–1.15)	0.17 (0–2.42)	0 (0–0.18)
Group 2					
SaO_2	98 ± 0.79	83 ± 2.69	74 ± 3.92	73 ± 4.52	N/A
AMS-c	0 (0–0)	0.04 (0–0.74)	0.09 (0–0.57)	0.08 (0–0.76)	N/A

SaO_2 is expressed as mean percent ± SD; AMS-c scores are expressed as the median (range).

able to date.[31,32] Previous reports indicate a greater accuracy in IOP measurements by the TonopenXL tonometer (Reichert, Inc.) on edematous corneas.[33–35] On normal corneas, the TonopenXL has been shown to be the least affected by CCT when compared with other transportable handheld tonometers.[36] Because of its portability and ease of use, we chose this lightweight tonometer for our expedition. Concerning temperature variations during the expedition, especially low temperatures that may decrease battery voltage output, the manual of the tonometer explicitly states that, in the event of low battery output, the display shows the letters LoB. In the event of low temperature that may affect the transducer, the device may be inactivated or the calibration process may be slowed down. During our expedition, no such events occurred.

Measuring IOP in such conditions as a low-temperature environment can alter the measurement results by causing a decrease in episcleral venous pressure.[37] There was no correlation between temperature and IOP measurements at any altitude in this study.

As shown in our study, changes in IOP during very high-altitude mountaineering are small and insignificant from a clinical point of view, which is in conjunction with results in previous studies. In essence, exposure to very high altitudes results in a slight decrease in IOP. Considering our data from the highest IOP examinations to date, in addition to already existing data, we conclude that measuring the IOP is not a useful screening method for incipient and potentially harmful altitude-dependent diseases. In summary, in healthy persons, climbs to very high altitudes seem to be safe with regard to change in IOP.

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