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富士山における急性高山病に影響を及ぼす要因

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Influencing factors of acute mountain sickness on Mount Fuji - A pilot study

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Abstract

The present study investigated influencing factors of acute mountain sickness (AMS) on Mount Fuji using questionnaires, and also complementary experimental study. In survey study, 395 people participated and the data of 376 participants were used for further analysis. Univariate analysis revealed that risk factors for developing AMS include; women (P=0.007, compared to men); less experience with climbing Mt. Fuji (P<0.001, compared to many experiences); overnight mountain climbers (P=0.035 compared to single-day climbers); and incidence participant with greater numbers of toilet break (P=0.013). Moreover, multiple analyses demonstrated that less experience was extracted to explain both the incidence (P=0.002) and the severity of AMS (P<0.001). In experimental study, arterial oxygen content was evaluated using a finger pulse oximeter (SpO_2). SpO_2 decreased gradually in accordance with increasing altitude, however, changes in SpO_2 were not associated with the severity of AMS. Fluid inbalance, that is, the ratio between fluid intake and urine output, was associated with the severity of AMS obtained by quadratic curve regression ($y=0.008x^2+0.524x+9.733$, r=0.841, n=9, P=0.025). Collectively, these preliminary data suggest that, in addition to less experience, fluid balance may also accentuate the severity of AMS.

Key words:less experience, women, fluid balance, rapid ascent

要　旨

本研究は、富士山における急性高山病の要因を明らかにするために、富士登山者395名に対して、吉田口五合目でアンケート調査を行った。さらに、その結果を補足するために、別に9名の被験者に対してフィールド実験を行った。調査対象者395名のうち、アンケート記入に不備があった者を除き、376名を分析対象とした（有効回答率 95.2%）。急性高山病の診断にはレイク・ルイーズの質問表を用い、1）頭痛、2）消化器症状、3）倦怠感/脱力感、4）めまい/ふらつき、5）睡眠障害の５項目について、4件法で回答を得た（0-15点満点）。この質問表で4点以上の者を急性高山病発症者と診断した。単変量解析の結果、1）女性であること、2）富士登山の経験が少ないこと、3）１泊以上の宿泊登山であること、4） 登山中のトイレ休憩回数が多いことが、急性高山病の発症（４点以上の者）や重症度（素点）に影響を及ぼす要因として抽出された。多変量解析の結果、富士登山の経験回数が少ないことが最も強く急性高山病の発症と重症度に影響していた。

フィールド実験では各被験者に対して、登山前、各休憩地点においてパルスオキシメータにより経皮動脈血酸素飽和度（SpO_2）が測定された。さらに、登山中の飲用量と尿量が正確に測定された。SpO_2は高度の上昇とともに、有意に低下し、スタート時点と山頂では約10%ほどの低下が認められた。しかしながら、高山病の重症度とSpO_2との間に関連は認められなかった。登山中休憩時の心拍数は、高度の上昇とともに増加する傾向にあったが、統計的に有意な差は認められなかった。また、飲用量と尿量の差が大きい者ほど、すなわち、飲用量に対して尿量が少なすぎても多すぎても、急性高山病の重症度と関係していた。

以上のことから、富士山における急性高山病発症の危険因子として、富士登山経験の少なさは、急性高山病の発症と重症度の双方に強く関係していた。さらに、体水分量調節機能も、急性高山病の重症度と関係している可能性が示唆された。

キーワード：未経験、女性、体液バランス、急上昇

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Introduction

Mount Fuji is the highest mountain (3,776m) in Japan, and now, this mountain is awaiting UNESCO world cultural heritage. Recently, more people are climbing Fuji, for example, in 2005, more than 200,000 people climbed, increasing to more than 320,000 people in 2010 (http://www.env.go.jp/park/fujihakone/index.html). Furthermore, it is supposed that ratio of aged people and younger women to climb Fuji, is increasing. Under these conditions, it is important to prevent acute mountain sickness (AMS) because the designation as a World Heritage Site is expected to lead to an increase in the number of climbers.

Risk factors for AMS seem to be complicated and are not yet completely clear. It is well known that rapid ascent is a major risk factor for developing AMS (Hacket et al. 1976, Hacket and Roach, 2001, Basnyat and Murdoch, 2003, Bartsch et al. 2004 Basnyat et al. 2001, Schneider et al. 2002). However, effects of other relevant factors on AMS, for example, age (Chen et al. 2012, Gaillard et al. 2004, Hacket et al., 1976, Honigman et al. 1993, Maggiorini et al. 1990, Roach et al. 1995, Schneider et al. 2002, Vardy et al. 2006, Wang et al. 2010, Wu et al. 2010), gender (Hacket et al. 1976, Harris et al. 1966, Honigman et al. 1993, Johnson et al. 1988, Maggiorini et al. 1990, Snhneider et al. 2002, Vardy et al. 2006, Wang et al. 2010, Wu et al. 2010), body mass index (Hirata et al. 1989, Honigman et al. 1993, Schneider et al. 2002, Wang et al. 2010), arterial oxygen saturation (Chen et al. 2012, Karinen et al. 2010, Oliver et al. 2012, Roach et al. 1998, Wagner et al. 2012), and population difference (Honigman et al. 1993), are still controversial.

At high-altitude, highly critical illnesses include lung or cerebral edma. Generally, acute hypoxia may produce hypoxemia and hypercapnemia, resulting in transcellular water shift from intracellular fluid to extracellular fluid, induced by de-conditioning of the aqueous electrolyte metabolic hormone regulation. Hence, it is considered that AMS is a result of edma in the interstitium caused by abnormality in aqueous electrolyte metabolism. Additionally, it was suggested that several hormones such as vasopressin, Rennin-Angiotensin-Aldosteron, atrial natriuretic peptide may play an important role to regulate fluid balance (Bartsch et al. 1991). Indeed, a recent study has demonstrated that aggressive fluid intake is protective for developing AMS (Nerin et al. 2006). It is likely that greater fluid intake might cause greater urine output, but they also reported that developing AMS was associated with reduced urine output (Nerin et al. 2006). Given their study, fluid balance, for example, total amount of fluidintake and urine output should be considered to elucidate related factors for AMS. Moreover, dehydration was associated with worsening altitude illness (Cumbo et al. 2002).

Although numerous studies into the incidence of AMS have investigated mountaineers and trekkers in the Himalayas, Alps, and Rocky Mountains (Bärtsch et al. 2004, Basnyat and Murdoch, 2003, Hackett et al. 1976, Hackett and Roach 2001, Honigman et al. 1993), to date, no study was conducted at Fuji. As mentioned above, an AMS study at Fuji would become increasingly important from the view point of the pending condition of the for world heritage. Moreover Fuji stands 3,776m above sea level, however, the "standard" climbing routes start around 2,000m, that is, climbers can drive around 2,000m by their own vehicle. Thus the vertical elevation gain is about 1,800m, indicating that relatively aged people and/or less physical fit people, can climb Fuji. Under these conditions, appropriate advice and management can prevent risk of AMS, may result in needless suffering of climbing Fuji.

Therefore, in this study, we surveyed the current status of AMS for Fuji mountain climbers and investigated influencing factors for AMS. We also performed complementary study for several participants to extend and confirm fluid balance during actual climbing of Fuji beyond the questionnaire survey.

Methods

Survey study

Participants

On July 28th, 29th and August 11th, 12th in 2012, an epidemiological study was performed on descending climbers at the 5th step. Survey time was between 9:00 am and 1:00 p.m., suggesting that people who were surveyed began to descend during the first hours of the morning. In total, 395 Japanese participants age >20 were surveyed. Of them, 19 were excluded for further analysis due to lack of information in the survey form. Thus, the quantity of valid responses was 376 and the valid response rate was 95.2 %. Notably, 33 participants could not reach the summit of Fuji, however, these data was also included for further analyses as the purpose of the presents study was to investigate influencing factors of AMS irrespective of whether or not they summited.

Weather conditions

Barometric pressure and climate conditions at the summit of Fuji on each survey day are shown in Table 1. According to this table, people were exposed to a hypobaric hypoxia, and cold environment.

Questionnaires

All participants completed the following questions, 1) basic attribute; age, gender, and climbing experience at Fuji, 2) climbing schedule; with or without staying during climbing, 3) fluid balance; total amount of fluid intake, and number of toilet breaks, and 4) AMS scores.

Table 1 Barometric pressure (BP) and climatic conditions of the four surveying days at the summit of Mt. Fuji.

	July 28th	July 29th	Aug 11th	Aug 12th
BP (hPa)	651	650.2	648.3	647.5
Temperature(℃)	8.4	8.2	5.5	6.5
RH (%)	73	70	94	89
Sunshine hours (h)	11.9	11.9	9.1	6.5

All values are averaged through one day. RH: relative humidity

AMS assessment

The Lake Louise Symptoms Score (LLSS) consists of a self-reported assessment of five AMS symptoms. This includes symptoms of 1) headache, 2) digestive, 3) fatigue and weakness, 4) dizziness and lightheadedness, and 5) difficulty sleeping. Each questionnaire uses a scale of 0-3, indicating nil, mild, moderate, and severe, therefore, total minimum score is zero and maximum score is 15. Criteria of AMS was defined as : 0-3 points mean "no AMS", and above 4 points mean "AMS" (Roach et al. 1993).

Experimental study

Subjects

Twelve healthy adults (9 men and 3 women) with a mean age of 42 yrs participated in this study. The purpose, procedure, possible risks, and benefit were explained and each subject took part in this study voluntarily.

Procedures

Nine subjects (6 men and 3 women) climbed Fuji on August 27th and three subjects (3 men) on August 30th. They ascended to the 5th step with vehicles and started to climb around noon. On the first day, subjects reached the altitude of 3,200 m in the evening and stayed one night at a mountain lodge. Around 2:00 a.m., subjects started climbing again to reach the summit. Only one subject did not stay at a lodge due to personal reasons, and he continued to climb through the night. After reaching the summit, he descended by himself.

Weather conditions

Barometric pressure and climate conditions at the summit of Fuji on each experimental day are shown in Table 2. According to this table, people were exposed to a hypobaric hypoxia, and cold environment. Moreover, weather conditions in two days were almost the same conditions, suggesting that none of the problem exists to compare physiological responses.

Measurement

Heart rate (HR) and arterial oxygen saturation (SpO_2) were monitored using finger pulse oximeter (Oxiboy S-107, Oxim, Shiga, Japan) at the altitude of 2,300m, (i.e., 5th step and start point), 2,520m, 2,850m, 3,200m at a mountain lodge and the summit of Mt. Fuji (3,720m altitude). Measurement was performed during resting time at each altitude except at 3,250m. At 3,200m altitude of a mountain lodge, each participant was measured in the morning before restart. Each subject took their preferred drink bottle and total fluid intake after starting was recorded throughout the climbing. Subset of subjects were given handmade measuring cups with 450 ml, and they self-reported the total amount of urine output at mountain lodges and on the summit.

Moreover, one subject wore a HR monitor (RS-800, Polar, Finland) and HR was recorded throughout the climb until reaching a mountain lodge at the altitude of 3,200m.

Table 2 Barometric pressure (BP) and climatic conditions of the two experimental days at the summit of Mt. Fuji.

	Aug 27th	Aug 30th
BP (hPa)	652.9	650.7
Temperature(℃)	6.5	8.3
RH (%)	53	59
Sunshine hours (h)	10.5	8.7

Data analysis

Fluid balance was calculated using the following equation; Total urine elimination / total fluid intake *100 (%).

Statistics

Statistical analysis was performed using Sigma Stat 3.5 software (Systat software Inc., Chicago, IL, USA). For the categorical variables, chi-square test and, for the continuous variables, unpaired t-test, and one-way analysis of variance (ANOVA) were applied. A multiple logistic regression analysis was applied to elucidate the incidence of AMS and a multiple linear regression analysis was also applied to elucidate the effects of potential risk factors on the severity of AMS. Prevalence (total AMS score is above 4) or absence (below 3) was used as a dependent variable. Following six valuables, age, gender, experiences of climbing, with and without a stay at the mountain lodge, total amount of fluid intake, numbers of toilet break, were used as independent variables for all participants (n=376). One-way repeated ANOVA was conducted for comparison in SpO_2 and HR. Data are expressed as are mean ± standard deviation (S.D) with significance for all tests set at $P<0.05$.

Results

Survey study

The overall incidence of AMS, i.e., AMS score ≧4, in the study population, was 38.7%. Although LLSS diagnostic criteria of AMS defines that symptoms of "headache" is an essential qualification, 18.5% of AMS participants did not complain of a headache. In contrast, 53.7% of participants without AMS symptoms complained of a headache. Among the 33 participants who could not reach the summit, more than 80 % stated they had retired due to AMS. Other reasons given were bad weather, lack of time and personal training.

Univariate analysis

Gender

There was a tendency that incidence of AMS in women was greater than men (df=1, χ^2=2.923, P=0.087), but no statistical significance was observed either between AMS incidence and gender (35.6% of men, and 44.1% of women). Moreover, the severity of AMS, i.e., mean values of AMS score in women was significantly higher compared to men (2.93±0.15 in men and 3.63±0.21 in women, P=0.007, Figure 1A).

Age

To assess the relation between age and AMS, the participants were divided into four age groups, i.e., 20-29, 30-39, 40-49, and >50 yrs, respectively. Although younger participants showed a trend towards higher AMS scores (Figure 1B), no significant differences were observed either between AMS incidence and age (42.3 % of 20-29 yrs, 40.4% of 30-39 yrs, 28.5 % of 40-49 yrs,40% of >50 yrs, df=3, χ^2=3.828, P=0.281). This resulted in no significant observation about severity of AMS score age (3.31 ±0.20 of 20-29 yrs, 3.35±0.25 of 30-39 yrs, 3.04±0.28 of 40-49 yrs, and 2.78±0.25 of >50 yrs, P=0.317) (Figure 1B).

Effect of stay

Surprisingly, there were also statistical significant differences either between AMS incidence and staying at mountain lodge (31.6 % of a single day and 42.7% of one or more stay, df=1, χ^2=4.105, P=0.043). In addition, severity of AMS in participants, who did not stay a mountain lodge was significantly lower compared to participant who stayed one or more night at a mountain lodge. 2.77±0.21 of single day and 3.40±0.15 of one stay or more (P=0.013, Figure 1C).

Previous experience climbing Fuji

Interestingly, there were statistically significant differences between AMS incidence and previous experience climbing Fuji (45.0 % of zero, 36.1 % of one to three times, 15.3% of more than four times, df=2, χ^2=15.085, P<0.001). Moreover, the severity of AMS of the participants with no experience, i.e. “zero”, was significantly higher compared to other groups (zero vs. one to three times, P<0.001 and zero vs. more than four times, P=0.023, respectively), whereas no difference was observed in the severity of AMS between participants who had climbed Fuji one to three times and more than four times (P=0.099). Observed score were 3.59±0.18 of zero, 2.88±0.19 of one to three times, and 2.07±0.29 of more than four times, respectively (Figure 1D).

Fluid intake

The mountaineers consumed a variety of fluids, including water, isotonic drink, orange juice, tea, coffee, soup (including miso soup) and coke. Table 3 shows the different amount of fluid intake in participants with and without AMS. There was no significant difference in the amount of fluid intake in two groups.

Number of toilet breaks

In contrast, the number of toilet breaks in participants with AMS was significantly greater compared to participants without AMS (P=0.013), suggesting a greater amount of urine output among participants suffering AMS (Table 3).

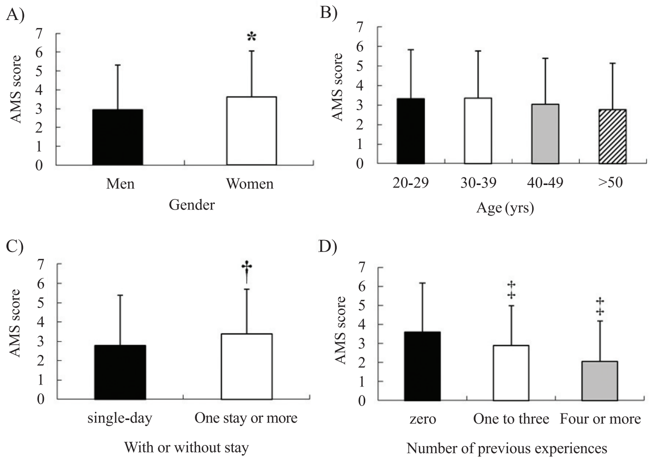

Figure 1 Severity of acute mountain sickness (AMS) in gender (A), age (B), effect of stay (C), and effect of experience (D) differences. Values are mean ± standard deviation (S.D.). *, P<0.05 vs. men, +, P<0.05 vs. single day, ‡, P<0.05 vs zero.

Table 3. Fluid balance in participants with and without AMS.

	Without AMS	With AMS	P value
Fluid intake（mL）	1574 ± 938	1653 ± 695	0.370
Number of toilet breaks	2.61 ± 198	3.03 ± 1.78	0.035

Values are mean ± S.D. (standard deviation). AMS: acute mountain sickness.

Multiple analysis

Table 4 and 5 represents the results of multiple analysis for independent risk factors of the incidence or the severity of AMS. Only less experience was extracted as a potential risk factor for the incidence of AMS by multiple logistic regression analysis (P=0.002, Table 4). A multiple linear regression analysis also revealed that less experience was strongly associated with the severity of AMS (P<0.001), moreover, there were tendencies that “women” and “staying at a mountain lodge” were associated with the severity of AMS, but no statistical significance was observed (P=0.060 and P=0.069, respectively, Table 5).

Experimental study

AMS

Two subjects indicated symptoms of AMS, and the average score of AMS in all participants (n=12). was 2.5±1.4 (a range was 1-6). Participants who complained of AMS symptoms included one man and one woman.

Table 4. Results of multiple logistic regression analysis for independent risk factors of the incidence of AMS.

	P value	OR
Age	0.509	1.006
Gender	0.501	0.853
Experience climbing Fuji	0.002	1.675
Effect of stay	0.265	0.776
Numbers of Toilet break	0.167	0.919
Fluid intake	0.825	1.000

OR, Odds ratio.

Table 5. Results of multiple linear regression analysis for independent risk factors of the severity of AMS.

	P value	t value	Std.partial. reg. coeff.
Age	0.137	-1.489	-0.079
Gender	0.006	1.886	0.099
Experience climbing Fuji	<0.001	3.477	-0.183
Effect of stay	0.069	1.823	0.096
Numbers of Toilet break	0.581	0.552	0.030
Fluid intake	0.177	1.354	0.072

R^2=0.083, P<0.001,St. partial reg. coeff, standardized partial regression coefficient.

SpO_2 and HR

Figure 2 shows HR changes for one subject and average values of SpO_2 and HR measured by pulse oximeter during climbing. Despite longer rest stops, resting HR seemed to show a slight increase at higher altitudes.. Mean values of HR and SpO_2 were also shown in Figure 3 (n=9). At the 5th step, SpO_2 showed about 96 %, then, gradually decreased in accordance with increasing altitude, finally it reached around 85% at the summit. One-way repeated ANOVA revealed that significant differences were observed between 5th place and other altitudes (Figure 3).

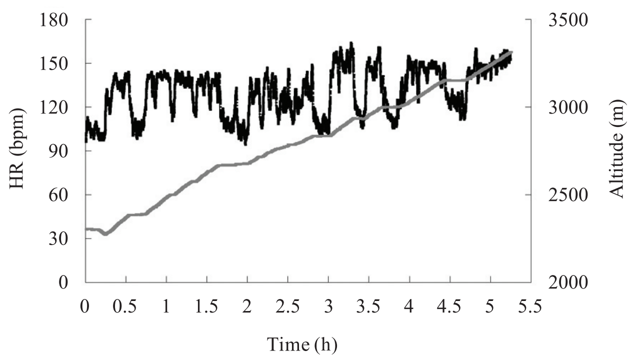

Figure 2 An original data of heart rate (HR) changes in accordance with an increasing of altitude for a single subject. Black lines shows HR changes and gray line shows altitude changes.

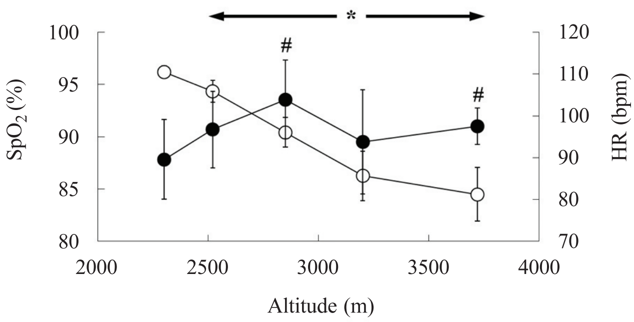

Figure 3 HR and arterial oxygen saturation (SpO_2) estimated by a finger pulse oximeter at each altitude. Values are mean ±S.D. * and #, significant differences between the altitude of 2,300m.

In contrast, HR gradually increased in accordance with increasing altitude though it slightly decreased at a mountain lodge, probably due to different measurement conditions. On the second day, HR increased again and the HR value at the altitude of 2,850m and 3,720m, i.e., the summit, was significantly higher than that of 5th step (Figure 3).

The mountaineers consumed a variety of fluids, including water, isotonic drink, orange juice, tea, coffee, soup (including miso soup) and coke. Total amount of fluid intake ranged from 400 to 2,400ml, and total amount of urine output ranged from 140 to 1,180 ml, respectively (n=9). The relationship between fluid balance and AMS scores is shown in Figure 4.

Discussion

The primary findings in the present study were threefold. 1) Univariate analysis revealed that the incidence and severity of AMS was associated with gender, previous experience climbing Fuji, stay at a mountain lodge, greater numbers of toilet breaks, and shorter sleeping time at a lodge. 2) A multiple forward logistic regression analysis accentuated that less experience climbing Fuji and shorter sleeping time were risk factors for AMS. 3) Both greater and less urine discharge may affect developing AMS. Collectively, these preliminary data suggested that enough experience and

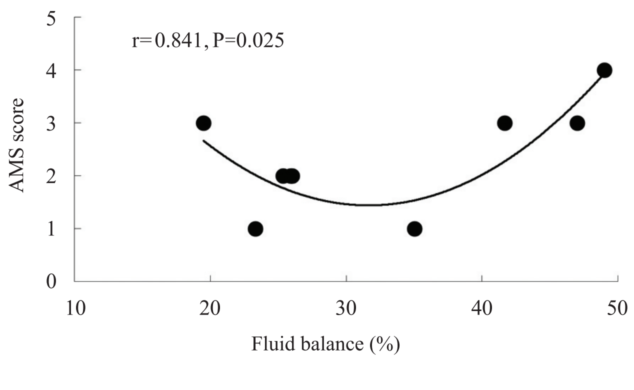

Figure 4 The relationship between fluid balance and severity of AMS.

sleeping time and appropriate fluid balance may play an important role in reducing and/or preventing AMS.

Effect of gender

Previous studies demonstrated that effects of gender differences on AMS are still controversial. For example, it was reported that incidence and severity of AMS in women was higher compared to men (Honigman et al. 1993, Wu et al. 2010), while other studies showed that women could be protected from AMS (Harris et al. 1966, Johnson et al. 1988). In addition to these conflicting results, several studies indicated that there is no gender difference in the incidence and severity of AMS (Hacket et al. 1976, Maggiorini et al. 1990, , Schneider et al. 2002, Vardy et al. 2006, Wang et al. 2010). In the present study, women showed a slightly higher incidence of AMS and significantly greater severity of AMS. These results were consistent with some previous studies, but not others. Although this discrepancy is unclear, one possible explanation is due to the smaller sample size in women compared to men.

Effect of age

We found a tendency that younger participants showed a higher severity of AMS but no statistical differences were observed. Previous studies suggested a higher risk of AMS among young people (Chen et al., 2012, Gaillard et al. 2004, Hacket et al., 1976, Honigman et al. 1993, Roach et al. 1995), indicating similar tendencies between our study and previous studies. Conversely, it was reported that older people have a higher risk factors of AMS due to coexisting symptoms of cardiovascular diseases with advancing age, suggesting that administration of medications (Maggiorini et al. 1990, Wu et al. 2010.) Moreover, several studies revealed that age differences had no effect on the prevalence of AMS (Schnider et al. 2002, Vardy et al. 2006, Wang et al. 2010). In this study, symptoms of cardiovascular disease were not investigated, however, only 10% (n=9) of subjects above 50 yrs were taking medication such as hypotensor. Moreover, of them, four participants were without AMS, and five were with AMS. Thus, it is likely that age differences were of minor importance regarding the incidence and severity of AMS.

Effect of stay

One surprising finding was that the incidence and severity of AMS among participants who stayed at a mountain lodge was significantly greater than those in single-day participants. It is well known that rapid ascent was a most serious risk factor for AMS (Hacket et al., 1976, Hacket and Roach, 2001, Basnyat and Murdoch, 2003, Bartsch et al., 2004 Basnyat et al. 2001, Schneider et al. 2002). Our results showed an obvious discrepancy with previous studies. Although it can not be elucidated these inconsistent results, there are several possibilities to explain this dissociation. First, it was reported that severity of AMS symptoms peaked during the first 1-2 days (Anderson et al. 2011), indicating that participants who stayed at a mountain lodge might develop AMS after a one night stay. Moreover, interesting findings demonstrated that there were no differences between the incidence of AMS in climbers who did or did not take a rest day at 3,700m while climbing Mount Kilimanjaro (altitude 5,895m) (Jackson et al. 2010). Second, in this study, we did not ask the actual climbing hours, thus, there is a possibility that rapid ascent does not necessarily correspond to the participants who did not stay at a mountain lodge. Further studies are needed and should be focused on detailed climbing schedules.

Effect of experience climbing Fuji

In the present study, mountaineers with more experience climbing Fuji demonstrated lower risk of AMS, and this factor was most strongly associated with the incidence and severity of AMS. Since the Fuji climbing season is only summer, it is quite unlikely that participants climb several times in the same season. Even if this is so, the effects of acclimatization can be ruled out. Recent studies demonstrated that less experience at altitude can result in worse symptoms of AMS (Anderson et al. 2011). Similarly, the lower level of experience of mountaineers in the Eastern Alps may account for higher AMS prevalence (Marier et al. 2010). Although the reason why less experience caused greater incidence and severity of AMS at Fuji is unclear, our results may propose an important suggestion to novice climbers, indicating the importance of expert guides or colleagues. Thus, future studies are needed to elucidate the relationship between the effect of traveling with experts and incidence and/or severity of AMS.

Fluid intake and number of toilet break

Recent studies suggested that greater loss of fluid induced by urine elimination and/or hypohydration with mountain climbing, i.e., exercise develop AMS symptoms (Cumbo et al. 2002, Roach et al. 2000). In this study, no differences were observed in fluid intake between with and without AMS, whereas greater numbers of toilet break showed a higher scores of AMS, suggesting that imbalance between fluid intake and output might occur in participants with AMS. However, in this survey, fluid output such as urine discharge and sweat loss were not investigated, hence, more detailed investigations should be conducted.

Experimental study

SpO_2 and HR

It was reasonable that SpO_2 and HR responses showed a miller image in accordance with increasing altitude. Previous studies demonstrated that SpO_2 decreased to the level of 82% at 4,200 m in Mt. McKinley and resting HR increased slightly at higher altitudes (Roach et al. 1998). However, whether decrease in SpO_2 and increase in resting HR was associated with the AMS or not is inconsistent. Oliver et al (2012) reported that total AMS symptom score was associated with a lower SpO_2 and higher resting HR. However, the development of AMS was caused by elevated pulse rate not by decreased SpO_2 (O'Connor et al. 2004). In contrast, monitoring SpO_2 can help to identify AMS, but elevated resting HR did not predict impending AMS (Karinen et al. 2010). In this study, SpO_2 gradually decreased in accordance with an increasing altitude, while resting HR slightly increased. In the present study, although both SpO_2 and HR were not related to AMS scores, due to the very small sample size and small range of AMS score, we could not explain further if our results can be explained by any previous studies. Another problem is that at 3,400m altitude, measurements were performed the next morning, resulting in slight lower HR and higher SpO_2 levels. Moreover, at other altitude, SpO_2 and HR were measured during rest, however, resting time could not be controlled due to limitations on device numbers.

Fluid intake and urine output

Previous studies have demonstrated that dehydration assessed by urine pH worse altitude illness (Cumbo et al. 2002), whereas, inadequate fluid intake and dehydration were also associated with AMS (Mairer et al. 2009, Norris et al. 2012). Furthermore, Nerin et al. (2006) reported that both aggressive fluid intake and reduced urine output may play important roles in reducing and/or preventing AMS. These results suggest that both edema and dehydration may affect the incidence and severity of AMS. Fluid balance was calculated in this study, and a significant J-shaped relationship was observed between AMS score and fluid balance. Our results were partly supported by previous studies, indicating that both reduced and excessive urine output may develop AMS symptoms.

However, it might be highly speculative due to the small sample size and a lack of information about sweat loss as well as body weight changes from the 5^{th} step to the summit of Fuji.

Limitations

There were several limitations in this study. First, in the survey study, the number of questionnaire items was not enough to clarify the risk factors of AMS in detail. However, our statistical analysis clearly demonstrated several risk factors of AMS at the Fuji. Second, in the experimental study, sample size was small and sweat loss as well as body weight changes was not measured. Thus, future studies should be conducted with the aim of elucidating the mechanism of the influence of fluid balance on AMS, with careful selection of the influencing parameters such as fluid intake, urine elimination, sweat loss, body weight changes, and several related hormones.

In summary, we found that the severity of AMS in women, participants with less experience, overnight participants, and participants with greater numbers of toilet break may be risk factors in developing AMS. Moreover, fluid inbalance obtained by complementary study may also be a potential risk factor. Of them, less experience was strongly associated with incidence and severity of AMS with multiple analysis. Collectively, these preliminary data suggest that, in addition to less experience, fluid balance may also accentuate the severity of AMS.

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