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The effect of altitude difference on gastrointestinal bleeding in the chronic period

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ABSTRACT

Aim: The susceptibility to gastrointestinal bleeding is observed with an increase in altitude. There is no recommendation regarding altitude in terms of drug selection and dose to be used in diseases requiring antiaggregant and anticoagulant use. In this study, we aimed to determine whether there is a difference between gastrointestinal bleeding requiring hospitalization due to the use of antiaggregant and/or anticoagulant therapy between two populations living at different altitudes.

Material and Method: This retrospective study was performed in two secondary care hospitals. Patients from Group B living in villages with an altitude of 9842 ft and above and Group F patients living in an area with an altitude of 30 ft were included. Patient's demographic data, co-morbid diseases, antiaggregant and anticoagulant use, hemoglobin, hematocrit, MCV values and platelet count were noted.

Results: The study included a total of 118 patients with gastrointestinal bleeding. There was no statistically significant difference between the groups in terms of the drugs used by the patients, the types and numbers of drugs.

Conclusion: We found that there was no significant difference between the groups with different altitudes in terms of drugs used by patients with gastrointestinal bleeding, drug types and numbers.

Keywords: Gastrointestinal bleeding, high altitude, antiaggregant, anticoagulant.

INTRODUCTION

With increasing life expectancy, the prevalence of coronary artery disease, atrial fibrillation and cerebrovascular disease and accordingly the frequency of single or multiple antiaggregant and anticoagulant treatment has been increasing (1-3). While recommending antiaggregant or anticoagulant therapy for these diseases, the guidelines recommend that we choose drugs according to the patient's angiographic presence, weight, GFR, age, and other co-morbidities criteria (4,5). However, there are no recommendations in the guidelines regarding the altitude at which patients live.

In studies conducted on people who need to work at high altitudes such as workers, mountaineers and soldiers, it has been observed that acute mountain sickness (AMS), high altitude pulmonary edema (HAPE) and high altitude cerebral edema (HACE) develop more frequently as altitude increases (6-9). It is known that gastrointestinal symptoms are common findings in AMS that occurs after hypoxia and hypobaric environment (10,11). It was observed that gastrointestinal symptoms and gastrointestinal bleeding (GIB) increased with increasing altitude (12,13).

As the altitude increases, the increase in hemoglobin value and the amount of platelet increases to adapt to the developing hypoxia due to elevation (14,15). Earlier studies have shown that polycythemia, which is seen as high altitude, is a risk of gastrointestinal bleeding (7,16,17).

In this study, we investigated whether there was a difference between gastrointestinal bleeding that lived at two different altitudes and requiring hospitalization and gastrointestinal bleeding due to antiaggregant and/or anticoagulant treatment.

MATERIAL AND METHOD

The study was carried out with the permission of Muğla Sıtkı Koçman University Health Sciences Ethics Committee (Date: 19.10.2020, Decision No: 15). The study was carried out in accordance with the principles of the Declaration of Helsinki and the ethical rules.

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Study Design and Settings

The study was planned as a retrospective. Group B is a center with 3050 ft. The patients included in this center were from the villages with an altitude of 9842 ft and above. Group F has at 30 ft altitude. Data of patients were examined from both state hospitals between 30 June 2015 and 30 June 2020.

Selection of the Participants

Patients aged 18 years and older who were hospitalized with the diagnosis of gastrointestinal bleeding were included in the study. Hematemesis, melena, hematochezia, and presence of the fecal occult blood were accepted as gastrointestinal bleeding symptoms.

The patients with known cancer, hepatic diseases, and whose INR above the therapeutic value (INR>3,5) were excluded from the study. The patients who have not enough data also have been excluded. In accordance with the power analysis, each group included 59 patients.

Measurements and Outcomes

The demographic data, chronic diseases, and the drugs were examined in each group.

Statistical Analysis

Descriptive statistics were given as mean±standard deviation and median with minimum-maximum values for continuous variables depending on their distribution. Numbers and percentages were used for categorical variables. The normal distribution of the numerical variables was analyzed by the Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests.

In comparing two independent groups, the Independent Samples t-test was used where numerical variables had a normal distribution. For variables without normal distribution, the Mann-Whitney U test was applied. The Pearson Chi-Square and Fisher's Exact tests were used in 2x2 tables to compare categorical variables.

For statistical analysis, "Jamovi project (2020), Jamovi (Version 1.6.22.0) [Computer Software] and JASP (Version 0.14.1) were used. The significance level (p-value) was set at 0.05 in all statistical analyses.

RESULTS

In this study, each group included 59 patients. Demographic and clinical characteristics of the patients in Group B and Group F are summarized in Table 1. The mean age and sex distribution of the patients were similar in both groups (p>0.05). Group B and Group F had at least one co-existing disease (62.7% vs 69,5%)(p=0.437). Hypertension was the most common co-morbid disease seen in both groups. There were 35(59.3%) patients with hypertension in group B and 37(62.7%) patients in group F. Distribution of the co-existing diseases was similar between two groups except for coronary artery disease. There were significantly more patients with coronary heart disease in Group B than Group F (n=15, 40.7% vs. n=9, 25.4%, p=0.013) (**Table 1**).

Table 1. Demographic and clinical characteristics of the patients

	Group B (n=59)	Group F (n=59)	p
Age (year) †, ‡			0.855**
	66.1±17.9	66.1±19.1	
	70.0 [31.0-93.0]	72.0 [26.0-91.0]	
Sex §			0.999*
Female	26 (44.1)	27 (45.8)	
Male	33 (55.9)	32 (54.2)	
Coexisting diseases, yes §	37 (62.7)	41 (69.5)	0.437*
Coronary artery disease	24 (64.9)	15 (36.6)	0.013*
Heart failure	11 (29.7)	8 (19.5)	0.294*
Diabetes mellitus	14 (37.8)	17 (41.5)	0.744*
Hypertension	35 (94.6)	37 (90.2)	0.678*
Cerebrovascular accident	6 (16.2)	5 (12.2)	0.610*
Dysrhythmia	10 (27)	12 (29.3)	0.826*
Peripheral artery disease	2 (5.4)	0 (0)	0.222*
Medications, yes §	31 (52.5)	27 (45.8)	0.461*
Anti-aggregant drugs			
Acetylsalicylic acid	22 (71)	13 (48.1)	0.076*
Clopidogrel	10 (32.3)	9 (33.3)	0.931*
Ticagrelor	0 (0)	0 (0)	-
Prasugrel	0 (0)	0 (0)	-
Anti-coagulant drugs §			
Warfarin	5 (16.1)	7 (25.9)	0.358*
Rivaroxaban	3 (9.7)	2 (7.4)	0.999*
Dabigatran	0 (0)	1 (3.7)	0.466*
Apixaban	2 (6.5)	1 (3.7)	0.999*
Edoxaban	0 (0)	1 (3.7)	0.466*
Enoxaparin	1 (3.2)	0 (0)	0.999*
Number of drugs ‡	1.0 [1.0-3.0]	1.0 [1.0-2.0]	0.510**
Number of patients using §			0.646*
No medication	28 (47.5)	32 (54.2)	
One drug	21 (35.6)	20 (33.9)	
Two drugs	8 (13.6)	7 (11.9)	
Three drugs	2 (3.4)	0 (0)	

†: mean±standard deviation, ‡: median [min-max], §: n (%), *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton tests. **. Mann-Whitney U test, ***. Independent Samples T-Test

The groups had similar rates in terms of the drugs used by the patients, types and numbers of drugs (p>0.05) (**Table 1**). Acetylsalicylic acid and clopidogrel were the most frequently used antiaggregant drugs in both groups (**Table 1**). As anticoagulant, warfarin and rivaroxaban were common drugs in both groups.

Table 2 presents the laboratory findings. Although the mean hemoglobin value was lower in Group F than Group B, the difference between the groups was not statistically significant (p=0.085). The median platelet count was significantly lower in Group B than Group F (205.0 vs. 263.0, p=0.002).

Table 2. Laboratory findings of the patients.

	Group B (n=59)	Group F (n=59)	p
Laboratory findings			
Hemoglobin (g/dL) †	10.3±2.9	9.4±2.6	0.085***
Hematocrit (%) †	31.4±8.6	29.2±7.5	0.136***
MCV (fL) ‡	87.0 [59.0-102.0]	88.3 [66.0-103.8]	0.617**
Platelet count (103/µL) ‡	205.0 [80.0-664.0]	263.0 [48.0-496.0]	0.002**

†: mean±standard deviation, ‡: median [min-max], §: n (%), MCV: mean corpuscular volume.

DISCUSSION

In our study, we examined the epidemiology of patients with gastrointestinal bleeding at different altitudes; we did not find a significant difference between altitude and the number of drugs that cause bleeding, and the type of drug. The most common chronic disease was hypertension in both groups. A statistical difference was observed in high altitude in terms of coronary artery disease distribution in patients. Hemoglobin values were lower in the low altitude region, but there was no statistically significant difference. Platelet count was lower in the high-altitude region.

In both groups, GI bleeding was observed in almost half of the patients, despite the fact that no medication was used. We hypothesize that this is due to the relatively advanced age of the patient population in the study. Because we know that the incidence of GIB increases with age and patients particularly over 60 year of age are prone to bleeding (18,19).

According to the studies on high altitude related gastrointestinal bleeding, there prevelance of bleeding were more common in males (7,20). However, in our study, no difference was found between males and females in terms of bleeding in both groups. This may be due to the relatively small number of the population in the study or that the studies on high altitude are related to workers dominated by male workers.

It is known that an increase in the number of erythrocytes occurs as a result of erythropoietin release and polycythemia occurs to increase the oxygen-carrying capacity of the blood in terms of adaptation to hypoxia at high altitudes (9,21). There are many studies showing that the hemoglobin value increases after stimulation of erythropiesis, which occurs as a result of erythropoietin release in people at high altitudes (6,8,14,22-24). In our study, the hemoglobin value of the patients was higher in the high altitude region; but no statistically significant difference. The reason may be that the patients included in the study were patients who had blood loss due to active gastrointestinal bleeding.

The frequency of gastrointestinal bleeding is higher, especially in the first 3 weeks, in those who travel temporarily to these areas rather than living in high-altitude areas (25,26). The main reason why there was no difference in the rates of GI bleeding due to altitude difference in the patients in this study is that they live in those regions constantly.

Peptic ulcer disease, alcohol consumption and non-steroidal antiinflamatory drug use are main predisposing factors for gastrointestinal bleeding (12,27,28). Additionally, the use of antiaggregant and anticoagulant increases the frequency of GIB (29,30). In our study, it was observed that the most frequently used antiaggregants were acetylsalicylic acid and clopidogrel among the drug users, but there was no statistical difference. The reason why the use of prasugrel and ticagrelor as antiaggregants was not detected in patients with GIB may be the administration of clopidogrel together with fibrinolytic therapy to acute myocardial infarctions, and afterwards continue, since there was no angiography unit in both center.

There are several reasons why there is no difference in gastrointestinal bleeding between people living at both altitudes. First, hematological changes required for gastrointestinal bleeding to occur generally begin after 3500 meters. In an investigation, Wu et al. (7) showed that GIB rarely found below 3500 meters. In our study, patients living at an altitude of 9842 ft (3000 meters) and above were taken as the high altitude group. Second, the rate of coronary artery disease is high in the population living at high altitudes, and proton pump inhibitors, which are frequently used while using antiaggregants, may have affected the bleeding rate in that group. Third, since the awareness of drug use is relatively weak in populations living in rural areas, and due to the irregular use of drugs, bleeding rates may have been relatively lower.

The limitation of this study is relatively small size of patient population. Another limitation is patients with high risk potential for bleeding (cancer, hepatic disease, high INR) were not included in the study due to the exclusions criters that would increase bleeding susceptibility.

CONCLUSION

Altitude has an effect on the frequency and risk of GI bleeding. However, this effect is closely related to the degree of altitude, whether there is an acute exposure to altitude difference, the drugs used and age. Since these criteria were not completely present in our study, no significant difference was found. Larger studies are needed to obtain more accurate information on this subject.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Muğla Sıtkı Koçman University Health Sciences Ethics Committee (Date: 19.10.2020, Decision No: 15).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J 2021; 42: 373-498.
2. Caprio FZ, Sorond FA. Cerebrovascular disease: primary and secondary stroke prevention. Med Clin North Am 2019; 103: 295-308.
3. Gremmel T, Michelson AD, Frelinger III AL, Bhatt DL. Novel aspects of antiplatelet therapy in cardiovascular disease. Res Pract Thromb Haemost 2018; 2 : 439-49.
4. Buckley LF, Rybak E, Aldemerdash A, Cheng JW, Fanikos J. Direct oral anticoagulants in patients with atrial fibrillation and renal impairment, extremes in weight, or advanced age. Clin Cardiol 2017; 40: 46-52.
5. Villain C, Liabeuf S, Metzger M, et al. Impact of age on cardiovascular drug use in patients with chronic kidney disease. Clin Kidney J 2020; 13: 199-207.
6. Fruehauf H, Vavricka SR, Lutz TA, et al. Evaluation of acute mountain sickness by unsedated transnasal esophagogastroduodenoscopy at high altitude. Clin Gastroenterol Hepatol 2020; 18: 2218-25.
7. Wu TY, Ding SQ, Liu JL, et al. High-altitude gastrointestinal bleeding: an observation in Qinghai-Tibetan railroad construction workers on Mountain Tanggula. World J Gastroenterol 2007; 13: 774-80.
8. Waeber B, Kayser B, Dumont L, Lysakowski C, Tramer MR, Elia N. Impact of study design on reported incidences of acute mountain sickness: a systematic review. High Alt Med Biol 2015; 16: 204-15.
9. Cerit M, Erdoğan M. Yüksek irtifa fizyolojisi ve adaptasyonun askeri fiziksel hazırlık seviyesine etkilerinin değerlendirilmesi. Kara Harp Okulu Bilim Dergisi 2019; 1: 1-15.
10. Wang SH, Chen YC, Kao WF, et al. Epidemiology of acute mountain sickness on Jade Mountain, Taiwan: an annual prospective observational study. High Alt Med Biol 2010; 11: 43-49.
11. Richalet JP, Julia C, Lhuissier FJ. Evaluation of the Lake Louise Score for acute mountain sickness and its 2018 Version in a cohort of 484 trekkers at high altitude 2021; 22: 353-61.
12. Wu TY, Ding SQ, Liu JL, et al. Who should not go high: chronic disease and work at altitude during construction of the Qinghai-Tibet railroad 2007; 8: 88-107.
13. Khanna K, Mishra KP, Ganju L, Kumar B, Singh SB. High-altitude-induced alterations in gut-immune axis: a review. Int Rev Immunol 2018; 37: 119-26.
14. Gassmann M, Mairbäurl H, Livshits L, et al. The increase in hemoglobin concentration with altitude varies among human populations. Ann N Y Acad Sci 2019; 1450: 204-20.
15. Hudson JG, Bowen AL, Navia P, et al. The effect of high altitude on platelet counts, thrombopoietin and erythropoietin levels in young Bolivian airmen visiting the Andes. Int J Biometeorol 1999; 43: 85-90.
16. Li K, Gesang L, He C. Mechanism of apoptosis involved in gastric mucosal lesions in Tibetans with high-altitude polycythemia. Exp Ther Med 2017; 14: 3780- 3787.
17. Aksel G, Çorbacıoğlu ŞK, Özen C. High-altitude illness: Management approach. Turk J Emerg Med 2019; 19: 121-6.
18. Aktaş HŞ. The role and importance of antiagregan, anticoagulant drugs in the etiology of upper gastrointestinal system bleeding in elderly. Haydarpaşa Numune Med J 2019; 59: 250-255.
19. Lenti MV, Pasina L, Cococcia S, et al. Mortality and risk factors for gastrointestinal bleeding in elderly patients. Eur J Intern Med 2019; 61: 54-61.
20. Mahajan P, Chandail VS. Etiological and endoscopic profile of middle aged and elderly patients with upper gastrointestinal bleeding in a tertiary care hospital in North India: a retrospective analysis. J Midlife Health 2017; 8: 137-41.
21. Heikura IA, Burke LM, Bergland D, Uusitalo ALT, Mero AA, Stellingwerff. Impact of energy availability, health, and sex on hemoglobin-mass responses following live-high-train-high altitude training in elite female and male distance athletes. Int J Sports Physiol Perform 2018; 13: 1090-6.
22. Akunov A, Sydykov A, Toktash T, Doolotova A, Sarybaev A. Hemoglobin changes after long-term intermittent work at high altitude. Front Physiol 2018; 9: 1152.
23. Moore LG. Measuring high-altitude adaptation. J Appl Physiol 2017; 123: 1371-85.
24. Storz JF, Cheviron ZA. Physiological genomics of adaptation to high-altitude hypoxia. Annu Rev Anim Biosci 2021; 9: 149-71.
25. Mieske K, Flaherty G, O'Brein T. Journeys to high altitude-risks and recommendations for travelers with preexisting medical conditions. J Travel Med 2010; 17: 48-62.
26. Amatya B, Lakhey PJ, Pandey P. Perforation peritonitis at high altitude. JNMA J Nepal Med Assoc 2018; 56: 625-8.
27. Vearrier D, Greenberg MI. Occupational health of miners at altitude: adverse health effects, toxic exposures, pre-placement screening, acclimatization, and worker surveillance. Clin Toxicol (Phila) 2011; 49: 629-40.
28. Agarwal A, Benias P, Gutierrez OIB, et al. Endoscopic suturing for management of peptic ulcer-related upper gastrointestinal bleeding: a preliminary experience. Endosc Int Open 2018; 6: 1439-44.
29. Lv M, Zheng X, Wu T, et al. A new score for predicting acute gastrointestinal bleeding in patients administered oral antiplatelet drugs. Front Pharmacol 2021; 11: 2245.
30. Solakoğlu T, Köseoğlu H, Atalay R, et al. Impact of anti-aggregant, anti-coagulant and non-steroidal anti-inflammatory drugs on hospital outcomes in patients with peptic ulcer bleeding. Saudi J Gastroenterol 2014; 20: 113-9.