Radiofrequency Electromagnetic Field Exposure is a Risk Factor for Acute Mountain Sickness: a Cross-sectional Study

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Abstract: Radiofrequency electromagnetic field (RF-EMF) can cause adverse effects in living systems. However, it is still unknown whether RF-EMF could affect the incidence of acute mountain sickness (AMS). For study, 171 RF-EMF-exposed subjects (RF-EMF group) and 188 non-RF-EMF-exposed subjects (control group) ascended rapidly from 500 to 3700 m, then further up to 4400 m after one week acclimatization. At 500 m, RF-EMF exposure was assessed and the subjects had no further exposure from the beginning of the ascent. A Lake Louise score self-report questionnaire and physiological parameter measurements were completed prior to and the next morning after arrival at high altitudes. Results showed that RF-EMF exposure of the subjects is below Chinese national standard. Compared with the control group, the incidence and severity of AMS was significantly increased in the RF-EMF group, with increased heart rate (HR), blood pressure (BP), cardiac output (CO), middle cerebral artery blood flow velocity (MCAv) at 3700 m, but lower arterial oxygen saturation (SaO_2) and hemoglobin (Hb) level. However, at 4400 m, no significant differences in the above-mentioned variables (except for MCAv, SaO_2, and Hb) were observed between two groups. Furthermore, HR (adjusted OR 1.039, CI 1.015-1.064), MCAv (adjusted OR 1.072, CI 1.039-1.106), and RF-EMF exposure (adjusted OR 2.122, CI 1.030-4.373) were positively correlated with AMS. This study suggests that RF-EMF exposure clearly increases the risk of AMS and short-term altitude acclimatization is an effective strategy for the prevention of AMS in the RF-EMF-exposed populations. Additionly, high HR and high MCAv are risk factors for AMS.

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1. Introduction

Many people ascend to high altitudes every year for all kinds of reasons (e.g., work, travel). For them, acute mountain sickness (AMS) may be the first obstacle after arrival at high altitudes. AMS is a common syndrome encountered particularly by unacclimatized troops after rapidly ascending to 3000 m or above (Basnyat and Murdoch, 2003, Imray et al., 2010). Headache is the most frequent symptom of AMS and is indispensable for final AMS diagnosis (Roach et al., 1993). Other symptoms include dizziness or lightheadedness, gastrointestinal symptoms, weakness or fatigue, and insomnia. Although often self-limiting, AMS may develop into fatal high-altitude pulmonary edema or high-altitude cerebral edema in a small number of people (Scherrer et al., 2010). Studies have shown that brain swelling occurs in every person after arrival at high altitudes (Muza et al., 1999). In addition, cerebral autoregulation is impaired in AMS subjects, possibly as a result of oxidative stress (Bailey et al., 2009) and oxidative stress may be a contributing factor to the AMS development (Lisk et al., 2013). Some factors, such as arterial oxygen saturation (SaO_2) (Koehle et al., 2010) and smoking (Wu et al., 2012b), are related to AMS incidence. However, the effects of these factors remain controversial (Richalet et al., 2012, Wagner et al., 2012). Although further investigation is needed to establish the risk factors for AMS (Wu et al., 2012a), individual susceptibility to AMS may be due to a combination of environmental and genetic factors (Hackett and Roach, 2001).

In recent years, modern society has been experiencing an obvious increase in radiofrequency electromagnetic field (RF-EMF) sources (Paniagua et al., 2009), including different kinds of radars, broadcasting or mobile phone transmission towers, magnetic resonance imaging systems for medical use, and others. Therefore, concern on the possible adverse effects of RF-EMF exposure to public health has been increasing (Jauchem, 2008, Valberg et al., 2007, Verschaeve, 2009). Studies have shown that long-term

RF-EMF exposure may increase the risk of leukemia (Ha et al., 2007, Park et al., 2004), brain (Hardell et al., 2011, Hardell et al., 2010), breast cancer (Kliukiene et al., 2003, Tynes et al., 1996), and other diseases (Mohamed et al., 2011, Redmayne et al., 2013). However, these correlations remain controversial (Ahlbom et al., 2004, Frei et al., 2011, Kundi, 2009). Electromagnetic field exposure may lead to a decrease in hemoglobin (Hb) (Ma et al., 2005, Usman et al., 2012) as well as to an increase in cerebral blood flow (CBF) (Huber et al., 2005) and glucose metabolism in the exposed regions of the brain (Volkow et al., 2011). Exposure may also cause cell and DNA damage, with oxidative damage being a major contributor (Al-Damegh, 2012, Garaj-Vrhovac et al., 2011, Xu et al., 2010).

Given the potential adverse health effects of RF-EMF exposure (particularly on oxidative stress, Hb and CBF), we hypothesize that long-term RF-EMF exposure would increase the incidence of AMS, and that this exposure may be an independent factor associated with AMS. Therefore, this study aims to explore the relationship between RF-EMF exposure and AMS using a cross-sectional design.

2. Material and Methods

Ethics Statement

The study protocol and informed consent form were approved by the Ethics Review Board of the Xinqiao Hospital, Second Affiliated Hospital of Third Military Medical University (decision number: 2012015). This investigation conforms to the Declaration of Helsinki. All subjects were informed of potential risks and were provided written informed consent before the investigation started. All subjects were told that they could withdraw from the study at any time. The trial protocol was registered in the Chinese Clinical Trial Registry (http://www.chictr.org, registration no. ChiCTR-RCS-12002232), which is a WHO International Clinical Trials Registry Platform (WHO ICTRP) Primary Register.

Subjects

The inclusion criteria were: (a) male adult aged ≥ 18 years old; (b) apparently healthy; (c) lowlander; (d) without a previous history of high-altitude exposure; and (e) willing to join the trial and sign an informed consent document. Subjects would be excluded if they: (a) were Tibetan people; (b) got airsick or bus sick; (c) had fear of blood/injection. Detailed information about the subjects in the trial was described as followings.

A total of 200 young Chinese men (RF-EMF group) who were certified to work as radio operators came from the same radio communication station. Chinese Han individuals, as well as those from Miao, Man, Buyi, and other ethnic groups, were the major subjects in the study. Tibetans were excluded. The subjects had job seniorities of 6 months to 11 years and worked in eight-hour shifts that rotated each week. On weekends, the subjects could leave the radio station for four hours to attend to personal matters by submitting a written application. One-month vacations for visiting relatives were arranged for each subject every year. Except under the two aforementioned conditions, the subjects were not allowed to leave the radio station. Thus, they were continuously exposed to RF-EMF.

For the matched control group, 200 office men from the head office of the radio communication station situated 10 kilometers away were recruited. The two study groups were matched in terms of race, age, education, height, weight, body mass index (BMI), drinking and smoking behavior, job seniority (namely the RF-EMF exposure time), and work shift.

Totally, 400 male subjects were recruited to the trial from June 16, 2012 to July 11, 2012. All subjects were lowlanders who had no previous exposure to high-altitude environments. Prior to the study, each subject had been given a routine medical examination. No one had a fever or respiratory tract infection. No one suffered from cardiopulmonary disorders. After ascending to the specified altitude, all subjects had the same daily regime and avoided vigorous exercises.

Experimental Design

In the morning all subjects in batches ascended from 500 m to 3700 m by air within 2 hours. After one week of acclimatization at 3700 m, all subjects ascended to 4400 m by car within 2 hours. Five days before ascending to 3700 m, measurements (blood pressure [BP], heart rate [HR], SaO_2, echocardiogram, middle cerebral artery blood flow velocity [MCAv], and LLS self-report questionnaire) were completed. And venous blood was drawn from each subject. The procedures were then repeated on the next morning after arrival at 3700 and 4400 m. All identifying characteristics of the subjects (e.g., name and work unit) were concealed prior to data analysis.

RF-EMF Exposure Measurement

RF-EMF exposure was analyzed at different locations: workplace, bedrooms, and entertainment areas (playground, reading room, etc.). The measuring height was set at 1.5 m. Measurements during each work shift were performed while the radio transmitter was in operating (transmitting signals) and standby mode. The operating time of the radio transmitter for each shift was approximately 2 hours. With the peak power at 125 W, the radio transmitter (type TOR220-2; Baoji, China) operated between 1.6 and 30 MHz. The signal was amplitude modulated. A NBM-550 broadband meter (Narda Safety Test Solutions GmbH, Pfullingen, Germany) with an EF-0691 probe was used in the analyses of the RF-EMF exposure levels of the subjects. No broadcast antenna or mobile phone base station was located near the study site. At the same time, the noise level was measured with a sound meter (type AWA6218, Zhejiang, China).

AMS Assessment

AMS was diagnosed in the subjects using the Lake Louise scoring system (Roach, Bärtsch, 1993). The LLS self-report questionnaire includes five items: headache, dizziness or lightheadedness, gastrointestinal upset (anorexia, nausea, vomiting), fatigue and/or weakness, and difficulty in sleeping. Each item is rated from 0 to 3 using a four-point Likert scale (0 = no event, 1 = mild, 2 = moderate, and 3 = severe). Subjects completed the LLS self-report questionnaire after waking in the morning. Subjects were initially considered to be suffering from AMS when they complained headache plus one or more of the other symptoms as well as a Lake Louise score (LLS) ≥ 3, and classified as mild (LLS = 3 or 4) or serious (LLS ≥ 5).

Physiological Measurements

After the completion of the LLS self-report questionnaire, SaO_2, HR, and BP were measured after the subjects had a 15 min rest in a comfortable chair. SaO_2 and HR were measured using finger-pulse oximetry (Onyx 9500; Nonin Medical, Inc., Plymouth, MN, USA). BP was measured with an electronic wrist sphygmomanometer (OMRON HEM-6200; Omron Health Care, Inc., Bannockburn, IL, USA). Three consecutive measurements for all parameters were recorded.

Heart function was measured using a portable Doppler echocardiogram machine (Philips CX50; Philips Ultrasound, Inc., Bothell, WA, USA) with an S5-1 cardiac probe. Ejection fraction (EF), stroke volume (SV), and CO were recorded for each subject after a 30 min rest following breakfast.

Following the measurement of heart function, MCAv was assessed using a transcranial Doppler device (Nicolet EME TC2021-III; Nicolet, Madison, WI, USA) with a 2 MHz hand-held probe. The mean MCAv in each subject was calculated from the left and right MCAv. The assessment in each subject was performed by the same examiner.

In the morning, blood samples were collected from an antecubital vein using an EDTA-anticoagulated tube. Hb in the samples was then measured using a hematology analyzer (AU400; Olympus Optical, Co., Tokyo, Japan).

Statistical Analysis

Data are shown as means ± SD unless otherwise stated. The data were analyzed using an SPSS social statistics package (version 13.0; Chicago, IL, USA). Statistical significance was considered at $P < 0.05$ (two-tailed). Frequencies were compared using Chi-squared test. Mean values were obtained using Student's *t*-test. Nonparametric test (Mann–Whitney U-test) was used for the non-normally distributed values. Spearman correlation test was used to analyze the relationships between LLS and HR, BP, SaO_2, MCAv, Hb, and cardiac function parameters. An analysis of variance for two-way repeated measures was used to determine the changes in HR, BP, SaO_2, MCAv, Hb, and cardiac function parameters. Tuckey's post hoc test was used for group comparisons. Prior to the multivariate analysis, an odds ratio (OR) with a 95% confidence interval (CI) for AMS associated with risk factors was determined using logistic regression. Factors with p values below or equal to 0.10 in the univariate analysis were analyzed using multivariate logistic regression analysis. Significant risk factors were retained by the backward stepwise likelihood ratio test.

In this study, AMS was a dichotomous dependent variable and recorded as 0 = no or 1 = yes. The independent variables were HR, SaO_2, CO, MCAv, Hb, and RF-EMF exposure duration. By referring to a previous study (Santinirl et al., 2003), we recorded RF-EMF exposure duration as 0 (no exposure), 1 (< 2 yr), 2 (2 yr to 5 yr), and 3 (> 5 yr).

3. Results

Subject Characteristics

At 3700 m, in the control group, 3 subjects withdrew because of severe headache and 2 subjects could not be reached for follow up for unknown reasons. In the RF-EMF group, 12 subjects withdrew because of severe headache, and 5 subjects were excluded for significant hypertension (SBP $\geq$ 160 mmHg and/or DBP $\geq$ 95 mmHg). In addition, 19 subjects were excluded because of missing data at 3700 and 4400 m, including 7 in the control group and 12 in the RF-EMF group. Consequently, we collected data from the remaining 359 subjects at high altitudes.

The demographic characteristics of the RF-EMF and control groups are shown in Table 1. No significant differences in age, weight, height, BMI, smoking and drinking behavior, race, education, and job seniority were observed between two groups.

Table 1. Demographic characteristic of the subjects.

Variables	RF-EMF group (n = 171)	Control group (n = 188)	P value
Age, yr	22.76 ± 4.01	22.31 ± 3.29	0.24
Weight, kg	63.76 ± 6.79	63.66 ± 6.04	0.89
Height, cm	171.70 ± 4.74	171.54 ± 4.23	0.74
BMI, kg/m^2	21.65 ± 2.02	21.60 ± 1.75	0.84
Smoking, yes	65 (38.01%)	78 (41.49%)	0.50
Drinking, yes	34 (19.88%)	30 (15.96%)	0.33
Race			0.13
Chinese Han	156 (91.23%)	162 (86.17%)	
Others	15 (8.77%)	26 (13.83%)	
Education			0.81
Junior school	59 (34.50%)	60 (31.91%)	
High school	89 (52.05%)	99 (52.66%)	
College	23 (13.45%)	29 (15.43%)	
JS, yr			0.95
< 2	54 (31.58%)	60 (31.91%)	
≤ 5	60 (35.09%)	63 (33.52%)	
> 5	57 (33.33%)	65 (34.57%)	

Abbreviations: BMI, body mass index; JS, job seniority; yr, year. Data are shown as means ± SD or n (%).

Exposure to RF-EMF

When the radio transmitter was operating, the RF-EMF exposure at the workplace was 7.88 ± 1.13 V/m, which was clearly higher than those at the bedrooms and entertainment areas (0.18 ± 0.03 V/m and 0.20 ± 0.05 V/m, respectively). During the standby mode of the radio transmitter, the exposure at the workplace dropped to 0.71 ± 0.03 V/m but remained higher than those at the bedrooms and entertainment areas (0.07 ± 0.03 V/m and 0.08 ± 0.02 V/m, respectively).

At the non-exposed locations (where the office workers living and working), the RF-EMF exposure was below the measurement threshold of the probe (0.01 V/m). The noise level was below hygienic standards, with no difference between the two groups (data not shown).

AMS

The LLS in the RF-EMF group was significantly higher than that in the control group at 3700 and 4400 m (4.01 ± 2.04 vs 3.29 ± 2.15, P < 0.01 and 2.36 ± 1.42 vs 1.86 ± 1.24, P < 0.05, respectively). At 3700 m, the incidence of AMS in the RF-EMF group was 65.50%, which was 1.24 times higher than that in the control group (65.50% vs 52.66%, P < 0.05). After one week acclimation at 3700 m and then rapidly ascending to 4400 m, the incidence of AMS in both groups clearly decreased (65.18% and 63.63% in the RF-EMF and control groups, respectively). Meanwhile, no significant difference in the AMS incidence was observed between the RF-EMF and control groups, although the former was 1.19 times higher than the latter. Notably, the severe AMS in the RF-EMF group decreased more than control group after arrival at 4400 m, because the ratio of the severe AMS incidence of the RF-EMF group to that of the control group dropped from 1.66 to 1.38. The comparison of AMS incidence in term of job seniority in both groups was shown in Table 2.

After arrival at 3700 m, the AMS symptoms in the RF-EMF group were more common compared to the control group (Figure 1). The most common symptoms of AMS in the RF-EMF group were headache (88.30%), followed by dizziness or lightheadedness (81.29%), weakness or fatigue (77.78%), difficulty sleeping (70.18%), and gastrointestinal symptoms (34.50%). At 4400 m, the further rapid ascent followed one week acclimation at 3700 m, the incidence of AMS symptoms in both groups was clearly dropped compared with 3700 m, except for gastrointestinal symptoms in the control group. Furthermore, the decrease in incidence of AMS symptoms in the RF-EMF group was a little more than control group (data not shown), and no significant difference in the incidence of AMS symptoms was observed between the two groups.

Additionally, no high altitude pulmonary or cerebral edema was observed in the present study.

Table 2. Comparison of AMS incidence in term of job seniority between the RF-EMF and control groups.

		3700 m				4400 m		
Variable		JS: < 2 (yr)	JS: 2-5 (yr)	JS: > 5 (yr)		JS: < 2 (yr)	JS: 2-5 (yr)	JS: > 5 (yr)
Mild AMS	RF-EMF group	15 (27.78%)	14 (23.33%)	15 (26.32%)		6 (11.11%)	6 (10.00%)	7 (12.28%)
	Control group	19 (31.67%)	17 (26.98%)	18 (27.69%)		7 (11.67%)	6 (9.52%)	7 (10.77%)
Severe AMS	RF-EMF group	13 (24.07%)	25 (41.67%)	30 (52.63%)		4 (7.40%)	7 (11.67%)	9 (15.79%)
	Control group	13 (21.67%)	16 (25.40%) #	16 (24.62%) *		5 (8.33%)	5 (7.94%)	6 (9.23%)

Compared with the RF-EMF group: # P = 0.056,* P = 0.001. Abbreviation: JS, job seniority. Data are shown as *n* (%). N = 171 and 188 in the RF-EMF group and the control group, respectively.

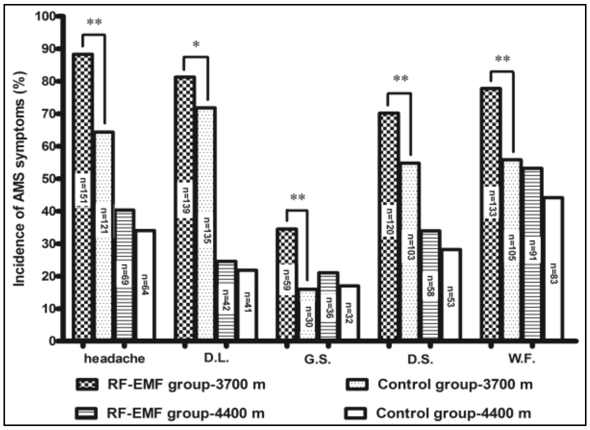

Figure 1. Comparison of incidence of AMS symptoms. Compared with the control group at the same altitude: * P < 0.05 and ** P < 0.01. Abbreviations: D.L., dizziness or lightheadedness; G.S., gastrointestinal symptoms; D.S., difficulty sleeping; W.F., weakness or fatigue.

HR, BP, and SaO_2

At 500 m, HR, BP, and SaO_2 between the RF-EMF and control groups showed no significant differences, although HR and BP in the RF-EMF group were slightly higher than those in the control group (Figure 2 a, b, and c).

Upon rapidly ascending to high altitude, HR increased in both groups and was significantly higher than the values obtained at 500 m (all P < 0.01) (Figure 2 a). Both at 3700 m and at 4400 m, HR in the RF-EMF group was significantly higher than that in the control group (both P < 0.01). At 4400 m, HR in the RF-EMF group was significantly higher as compared with the values obtained at 3700 m (P < 0.01). However, no significant change in HR in the control group was observed after the subjects ascended from 3700 to 4400 m (P = 0.06).

In the present study, a rising trend in mean blood pressure was observed with increasing altitudes. Both at 3700 m and at 4400 m, SBP and DBP in both groups were significantly higher than the values obtained at 500 m (all P < 0.01). At 4400 m, SBP in both groups showed an increasing trend compared with the values obtained at 3700 m, but neither reached statistical significance. At 4400 m, DBP in both groups was significantly higher than the values obtained at 3700 m (both P < 0.05). At 3700 and at 4400 m, both SBP and DBP were significantly higher in the RF-EMF group than in the control group (P < 0.05 or P < 0.01) (Figure 2 b).

At 3700 and 4400 m, the SaO_2 values of the two groups were significantly lower than those obtained at 500 m (all P < 0.01). At 4400 m, SaO_2 in both groups was significantly lower as compared with the values obtained at 3700 m (both P < 0.01). Statistical difference in SaO_2 was found between the two groups both at 3700 and 4400 m (both P < 0.01) (Figure 2 c).

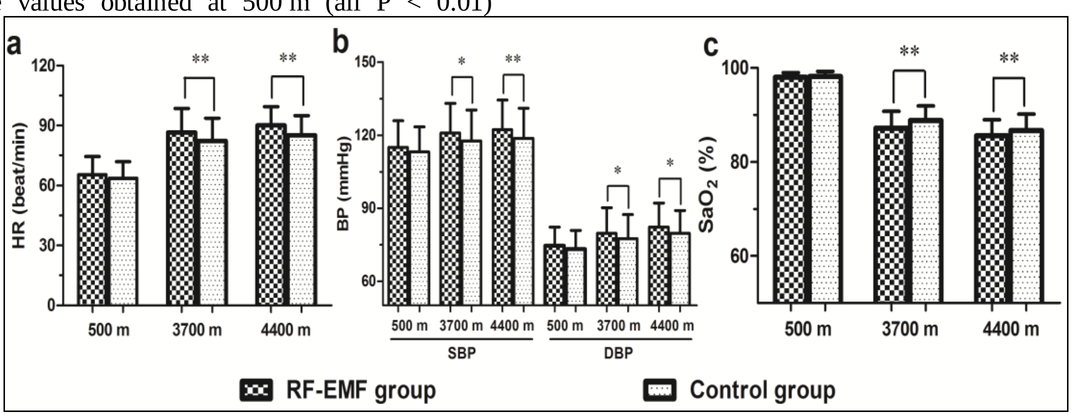

Figure 2. Comparison of physiological parameters: a) HR, b) BP, and c) SaO_2. Compared with the control group at the same altitude: * P < 0.05 and ** P < 0.01. Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; SaO_2, arterial oxygen saturation.

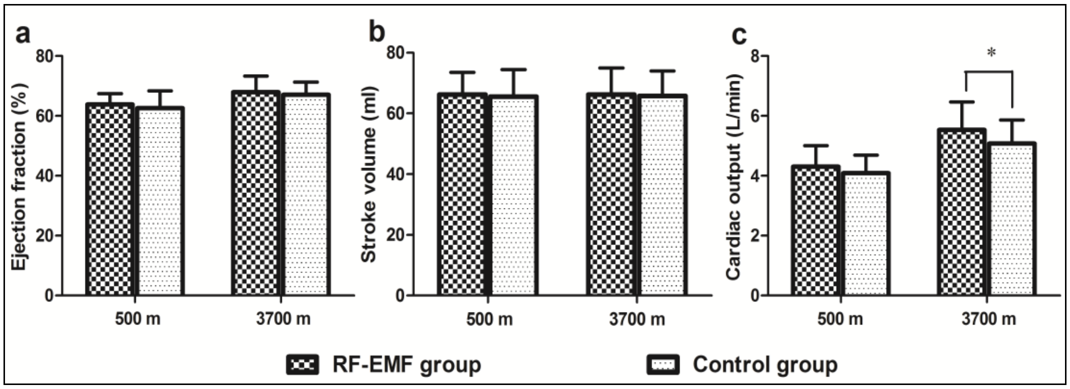

Figure 3. Comparison of cardiac function: a) EF, b) SV, and c) CO. Compared with the control group at the same altitude: * P < 0.01. Abbreviations: EF, ejection fraction; SV, stroke volume; CO, cardiac output.

Cardiac Function

At 3700 m, the EF and CO values tended to be higher than the values obtained at 500 m in both groups (Figure 3 a and c). However, there was a slight decrease in SV in both groups after arrival at 3700 m. Meanwhile, cardiac function of the subjects was not measured at 4400 m because of equipment failure.

Middle Cerebral Artery Blood Flow Velocity

In the present study, a rising trend in MCAv was observed with increasing altitudes, and MCAv in the RF-EMF group was significantly higher than the control group both at 3700 and 4400 m altitude (Figure 4). Further rapid ascent to the higher 4400 m followed one week acclimation at 3700 m, MCAv in both groups showed a decreasing trend compared with the values obtained at 3700 m, but didn't reached statistical significance in control group(P = 0.08).

Hemoglobin Concentration

After high altitudes exposure, Hb increased in both groups of subjects (Figure 5). The mean increase in Hb in the control group was 2.16% and 16.25% at 3700 and 4400 m, respectively. By contrast, no significant change in the Hb of the RF-EMF group was observed at 3700 m compared with the values obtained at 500 m. At 4400 m, the Hb of the RF-EMF group increased by 11.12% (approximately 17 g/L) compared with the values at 500 m.

Correlation Analysis

In the present study, HR, CO, and MCAv were positively correlated with LLS, whereas SaO_2 and Hb were negatively correlated with LLS (Table 3). In addition, HR, CO, MCAv, SaO_2, Hb, and LLS were correlated with RF-EMF exposure time in the RF-EMF group (Table 4). No significant correlations were found between LLS and other variables, just as well between RF-EMF exposure time and other variables.

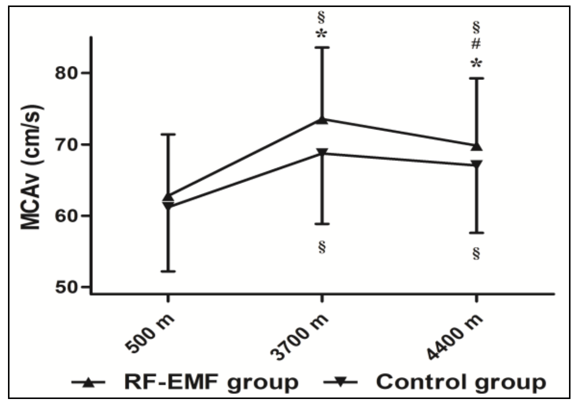

Figure 4. Comparison of MCAv. Compared to the value obtained at 500 m altitude in the same group: § P < 0.01; compared to the value obtained at 3700 m altitude in the same group: # P < 0.01; compared with the control group at the same altitude: * P < 0.01. Abbreviation: MCAv, middle cerebral artery blood flow velocity.

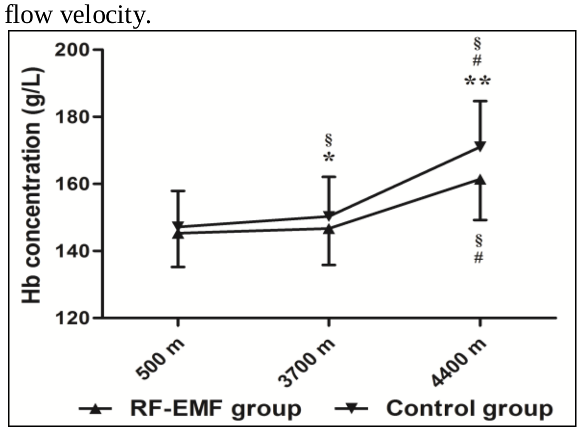

Figure 5. Comparison of Hb concentration. Compared to the value obtained at 500 m altitude in the same group: § P < 0.01; compared to the value obtained at 3700 m altitude in the same group: # P < 0.01; compared with the RF-EMF group at the same altitude: * P < 0.05 and ** P < 0.01. Abbreviation: Hb, hemoglobin.

Logistic Regression

In a univariate logistic regression analysis, AMS and non-AMS were associated with HR (OR, 1.042; 95% CI, 1.021 to 1.064; P < 0.001), CO (OR, 1.016; 95% CI, 1.007 to 1.026; P < 0.01), MCAv (OR, 1.080; 95% CI, 1.049 to 1.113; P < 0.001), Hb (OR, 0.962; 95% CI, 0.940 to 0.985; P < 0.01), and RF-EMF exposure (OR, 1.332; 95% CI, 1.105 to 1.605; P < 0.01), but not with SaO_2 and other variables (e.g., age, BMI, smoking, etc.).

A multivariate analysis that considered previous HR, CO, MCAv, Hb, and RF-EMF exposure time showed that all variables except CO and Hb were significantly associated with AMS (Table 5).

Table 3. Correlation between LLS and HR, CO, MCAv, SaO_2, and Hb.

	3700 m			4400 m	
Correlated variables	ρ	P value		ρ	P value
LLS - HR	0.260	0.000		0.232	0.007
LLS - CO	0.231	0.000		-	-
LLS - MCAv	0.224	0.000		0.191	0.012
LLS - SaO_2	-0.145	0.009		-0.168	0.022
LLS - Hb	-0.155	0.013		-0.151	0.039

Abbreviations: CO, cardiac output; Hb, haemoglobin; HR, heart rate; LLS, Lake Louise Score; MCAv, middle cerebral artery velocity; SaO_2, arterial oxygen saturation. "-" indicates no data available.

Table 4. Correlation between RF-EMF exposure and HR, CO, MCAv, SaO_2, Hb, and LLS.

		500 m			3700 m			4400 m	
Correlated variables		ρ	P value		ρ	P value		ρ	P value
RF-EMF - HR		0.116	0.034		0.201	0.000		0.181	0.002
RF-EMF - CO		0.108	0.042		0.184	0.008		-	-
RF-EMF - MCAv		0.121	0.034		0.305	0.000		0.203	0.000
RF-EMF - SaO_2		-0.096	0.089		-0.150	0.007		-0.177	0.003
RF-EMF - Hb		-0.134	0.020		-0.155	0.012		-0.329	0.000
RF-EMF - LLS		-	-		0.201	0.000		0.208	0.004

Abbreviations: CO, cardiac output; Hb, haemoglobin; HR, heart rate; MCAv, middle cerebral artery velocity; SaO_2, arterial oxygen saturation; RF-EMF, radiofrequency electromagnetic field. "-" indicates no data available.

Table 5. Multivariate logistic regression analysis.

Variables	β	SE	Wald	P value	OR (95% CI)
HR, beat/min	0.038	0.012	10.118	0.001	1.039(1.015-1.064)
MCAv, cm/s	0.069	0.016	18.738	0.000	1.072(1.039-1.106)
RF-EMF exposure time, yr					
0			7.116	0.068	1(ref)
< 2	-0.434	0.387	1.258	0.262	0.648(0.303-1.384)
2-5	0.055	0.334	0.027	0.169	1.056(0.549-2.034)
> 5	0.752	0.369	4.157	0.041	2.122(1.030-4.373)

Abbreviations: CI, confidence interval; HR, heart rate; MCAv, middle cerebral artery velocity; OR, odds ratio; RF-EMF, radiofrequency electromagnetic field. Dependent variable: AMS.

4. Discussions

To date, this study is the first to investigate the incidence of AMS in RF-EMF-exposed populations. The main finding of our study is the significantly higher incidence of AMS in the RF-EMF-exposed subjects compared with their non-exposed counterparts. A total of 65.50% of the RF-EMF group subjects that ascended to 3700 m developed AMS. This value is 12.84% higher than that in the control group. Moreover, the incidence of AMS clearly increased with prolonged RF-EMF exposure. The RF-EMF exposure time and two other risk factors (HR, and MCAv) for AMS were identified by univariate and multivariable analyses in the present study. Importantly, short-term altitude acclimatization could effectively decrease both the incidence and severity of AMS in the RF-EMF-exposed populations during further rapid ascent.

As a new environmental pollution source, the potential health effects of RF-EMF have been reported (WHO, 2007). RF-EMF exposure duration is an important factor of possible health effects (Hardell and Sage, 2008). Thus, occupational radio operators (with RF-EMF exposure times of 0.5 yr to 11 yr) were enrolled in the present study. In the present study, exposure to RF-EMF was measured at different locations (workplace, bedrooms, and entertainment areas). Our results showed that the RF-EMF exposure of the subjects was below the Chinese national standard GB 9175-88 (10 V/m).

Hypobaric hypoxia is one of the most important etiological factors of high-altitude illness. And the brain is more sensitive to hypoxia than other organs in living system due to the higher rate of O_2 utilization. Therefore, the presence of central nervous system symptoms in AMS subjects is more common. In the present study, the AMS symptoms, headache, dizziness or lightheadedness, and difficulty in sleeping, were more prevalent in the RF-EMF exposure subjects, which resulted in the higher LLS and then the higher incidence of AMS. This may be explained by the higher MCAv in the RF-EMF exposure subjects. AMS is correlated with MCAv (Baumgartner et al., 1994). Although the effect of RF-EMF on MCAv is unclear and the difference in MCAv prior to ascending between the RF-EMF and control groups did not reach statistical significance in our study, studies (Huber, Treyer, 2005, Volkow, Tomasi, 2011) have shown RF-EMF exposure may increase regional cerebral blood flow and regional cerebral metabolic activity, and then affects the brain function. Furthermore, our results showed a positive correlation between RF-EMF exposure and MCAv and LLS. Therefore, we think RF-EMF exposure may impair the autoregulation of cerebral blood flow which results in more common central nervous system symptoms in AMS subjects.

Hypobaric hypoxia results in alterations in the cardiovascular system. The present study shows an increase in HR, BP, CO, and EF in both RF-EMF and control groups, which is consistent with the literatures (O'Connor et al., 2004, Siques et al., 2009). Notably, the above mentioned parameters in the RF-EMF group changed more than in the control group. This difference may be partly caused by the RF-EMF exposure in the RF-EMF groups. Firstly, our results showed a positive correlation between RF-EMF exposure and HR and CO. This may be partially explained by the increase in sympathetic activity caused by RF-EMF exposure (Bortkiewicz et al., 2012, Vangelova et al., 2006, Vangelova and Israel, 2005). In addition, studies (Chen et al., 2008, Hainsworth et al., 2007) have suggested that sympathetic activity is increased in subjects after rapid ascent to high altitudes. Taken together, after arrival at high altitudes, overactivity of the sympathetic nervous system in the RF-EMF exposure subjects may be account for the different alterations in the cardiovascular system between the RF-EMF and control groups. Moreover, univariate and multivariable analyses indicate that HR is a risk factor for AMS in the present study. Although different results were obtained (Karinen et al., 2010, Wagner, Knott, 2012), we believe that the difference may be due to the different sample sizes and ascent profile. In addition, CO was correlated with AMS in the present study. However, this association was overcome by HR and other factors after the multivariate logistic regression analysis.

In response to hypoxia, SaO_2 was reduced significantly both in the RF-EMF and control groups after arrival at high altitudes. Moreover, mean SaO_2 in the RF-EMF group was significantly lower than that in the control group, which indicated that the degree of hypoxia in the RF-EMF group was more serious. To respond to more severe hypoxia, the compensation in the aforementioned cardiovascular system in the RF-EMF group changed more than in the control group. In addition, our results indicate an absence of correlation between SaO_2 and AMS, although SaO_2 was significantly correlated with LLS. One of the reasons may be that AMS diagnosis depends on both LLS and the occurrence of headache. This finding is also supported by other studies (Chen et al., 2012, Wagner, Knott, 2012).

An increase in erythropoietin is observed after 2 hours of hypoxia exposure (Mason, 2000), ultimately resulting in high Hb levels to improve arterial oxygen concentration (Frisancho, 2013). In addition, dehydration is a contributor to an increase in Hb. Consistent with those of previous studies (Basu et al., 2007, Choukèr et al., 2005), an increasing trend was observed in the Hb of both groups in the present study, but the increase was more significant in the control group than in the RF-EMF group. Studies (Ma, Xiong, 2005, Usman, Wan Ahmad, 2012) have shown that long-term RF-EMF exposure can cause a decrease in Hb both in humans and animals. This may be partially confirmed by the negative correlation between Hb and RF-EMF exposure time in the present study. Taken together, we think that RF-EMF exposure, hypobaric hypoxia, and dehydration all contributed to the difference in Hb between the RF-EMF group and the control group after rapid ascent to a high altitude. Meanwhile, lower Hb, in some degree, may indicate worse adaptation to hypoxic environment, and then increased the risk of AMS, which was confirmed by univariate logistic regression analysis in our study.

Our results show a significant decrease in AMS incidence in both groups when the subjects ascended from 3700 to 4400 m after one week of acclimatization at 3700 m. These findings are supported by those of previous studies (Schneider et al., 2001, Schneider et al., 2002). Most importantly, the incidence and severity of AMS in the RF-EMF group decreased a little more than in the control group, as well as the incidence of AMS symptoms (except for gastrointestinal symptoms). Furthermore, SaO_2 in the RF-EMF group decreased a little less than in the control group (the ratio of mean SaO_2 of the RF-EMF group to that of the control group increased from 0.981 to 0.986). These results suggest that short-term altitude acclimatization is effective in preventing AMS in the RF-EMF-exposed populations during further rapid ascent. This may be explained, in part, by the lower Hb level in the RF-EMF group. At altitudes, Hb level over 18g/dl will not provide anymore benefit in oxygen transport, and higher Hb level may impair oxygen transport (Villafuerte et al., 2004). On one hand, in the present study, Hb level in both groups increased significantly after one week altitude acclimatization. On the other hand, Hb level in the control group was significantly higher than in the RF-EMF group at 4400 m, as well as cases of Hb level over 180g/L (39 vs 12, $P < 0.01$). Taken together, the difference in Hb level may be one reason why the incidence and severity of AMS in the RF-EMF group decreased a little more than in the control group at 4400 m.

The present study has some limitations. First, the subgroup sample size in term of job seniority is a little small. A large sample size in a study generally provides highly stable results. However, suitable RF-EMF-exposed subjects that can participate in a high-altitude, on-site research were difficult to find. Second, the participants in this study are all male. Although the existence of a sex difference in the possible health effects of RF-EMF exposure is unclear, a sex difference does exist in AMS incidence (Imray, Wright, 2010). Therefore, further studies involving females and a large sample size should be conducted to confirm the present findings.

5. Conclusions

Our findings suggest that RF-EMF exposure is an independent risk factor for AMS, and that the RF-EMF exposure time is highly correlated with AMS incidence. Short-term (0.5 yr to 5 yr in the present study) RF-EMF exposure does not significantly affect the incidence and degree of AMS. Meanwhile, short-term altitude acclimatization can effectively reduce AMS incidence in the RF-EMF-exposed subjects during further rapid ascent. In addition, high HR and high MCAv are also independent risk factors for AMS. With the increase in RF-EMF sources (Paniagua, Rufo, 2009), an increasing number of people would be inevitably affected by RF-EMF in our modern society. A better understanding of the relationship between RF-EMF exposure and AMS could lead to a highly effective prevention of AMS. Prevention of AMS is particularly important when people need to ascend to high altitudes within a short time (e.g., during rescues after earthquakes and other disasters, urgent military deployment, etc.). Therefore, the present study may have implications for the prevention of AMS among RF-EMF-exposed populations. Further studies involving females and a large sample size should be conducted to confirm the present findings.

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