International Journal of Astrobiology 15 (2): 147–153 (2016)
doi:10.1017/S1473550415000245

No effect of artificial gravity on lung function with exercise training during head-down bed rest

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Abstract: The aim of this study is to explore the effectiveness of microgravity simulated by head-down bed rest (HDBR) and artificial gravity (AG) with exercise on lung function. Twenty-four volunteers were randomly divided into control and exercise countermeasure (CM) groups for 96 h of 6° HDBR. Comparisons of pulse rate, pulse oxygen saturation (SpO_2) and lung function were made between these two groups at 0, 24, 48, 72, 96 h. Compared with the sitting position, inspiratory capacity and respiratory reserve volume were significantly higher than before HDBR (0° position) ($P < 0.05$). Vital capacity, expiratory reserve volume, forced vital capacity, forced expiratory volume in 1 s, forced inspiratory vital capacity, forced inspiratory volume in 1 s, forced expiratory flow at 25, 50, and 75%, maximal mid-expiratory flow and peak expiratory flow were all significantly lower than those before HDBR ($P < 0.05$). Neither control nor CM groups showed significant differences in pulse rate, SpO_2, pulmonary volume and pulmonary ventilation function over the HDBR observation time. Postural changes can lead to variation in lung volume and ventilation function, but a HDBR model induced no changes in pulmonary function and therefore should not be used to study AG countermeasures.

Received 1 May 2015, accepted 8 July 2015, first published online 11 August 2015

Key words: artificial gravity, ergometric exercise, head-down bed rest, lung function

Introduction

Weightlessness is an important environmental factor in space and may affect the human body's physiological function or even cause damage to the body during and after spaceflight (Fowler 1991; Grigoriev & Egorov 1992; Astakhov *et al.* 2012). Due to the unique physiology of the lungs, they are especially affected by microgravity (Prisk 2005). The influence of weightlessness on the lungs depends on the following: (1) hydrostatic disappearance and fluid metastasis to the head result in pulmonary blood over-filling; (2) diaphragm position shift causes a decrease in chest volume; and (3) redistribution of airflow and blood flow in the lung leads to ventilation-perfusion ratio (VA/Q) imbalance (Sieck 2000; Prisk 2005). Pulmonary oedema and lung injuries in rats have been observed on histopathology examinations after the Cosmos 2044 mission (Grindeland *et al.* 1992). In addition, the studies of the Spacelab Life Sciences (SLS)-1 and SLS-2 Shuttle Missions conducted by the National Aeronautics and Space Administration (NASA) in the early 1990s revealed that pulmonary perfusion, pulmonary gas exchange, lung volumes and ventilation are significantly changed under weightlessness (Elliott *et al.* 1994, 1996; Prisk *et al.* 1994, 1995; West *et al.* 1997). Because of this, preventing lung dysfunction under weightlessness is critical to the safety and health of astronauts. Our previous study did not support the hypothesis that physiological effects of microgravity , simulated by head-down bed rest (HDBR), influenced the lung function, but exercise training with artificial gravity (AG) did improve lung function (Guo *et al.* 2013). In the present study, we included more volunteers and increased the exercise load with intensive AG to further explore and test the above hypothesis.

* Longxiang Su and Yinghua Guo contributed equally to this work.

Materials and methods

Study subjects

This study was approved by the Ethics Committee of the Fourth Military Medical University (Xi'an, China). All participants were recruited from the local university in Xi'an, China (No.LL-2013163). They were fully informed of the study details and the potential risks associated with AG conditions and gave their informed consent. Volunteers were excluded if they had any abnormalities in physical checkups and lab examinations. Finally, 24 male volunteers were selected and randomly divided into the control group and AG countermeasure (CM) group based on a random number table. The experiment was divided into three batches, which included eight participants in each batch. Each batch experiment time is 1 week, including the preparation before the experiment and data collection after the experiment.

Test procedure

All volunteers were instructed to undergo 6° HDBR for 96 h. A short-arm centrifuge (radius 2 m) with a detachable cycle ergometer was employed to induce AG and sports load. During the 96 h period of HDBR, the CM group volunteers were exposed to +2.0 G (foot level) for 30 min each in the morning (10:00 am) and afternoon (15:30 pm), respectively (60 min total). At the same time, exercise training was used in the CM group. They cycled during the centrifugation. The detachable cycle ergometer was set as follows: 50 W 1 min, 75 W 2 min; 3 rounds: 80 W 2 min, 85 W 2 min, 90 W 2 min, 95 W 2 min; 75 W 2 min, 50 W 1 min. The participants of CM group were transported to the centrifuge by four people using transport bed with 6° HDBR. During the experiment, they kept their head not move. So the small vestibular stimulation did not produce the adverse reactions. The control group volunteers stayed at 6° HDBR with no intervention. When pulmonary function testing was performed in the afternoon everyday (17:00 pm), all the participants were lying in bed with 6° HDBR. That is to say, they were required to remain in a non-weight-bearing position at all times, except during once-daily defecation break. All participants complied with the work and rest regime (rest at 10:00 pm and work at 7:00 am). During the work regime, participants were allowed to eat, drink, talk, access the internet, read and listen to the music. Dietary intake was strictly controlled according to the criteria for nutrition in astronauts and the Dietary Guidelines for Chinese People.

Data measurements

Pulse rate, pulse oxygen saturation (SpO_2) and lung function were measured in the seated position and 0, 24, 48, 72 and 96 h after the start of HDBR. The Nonin 9500 Onyx Finger Pulse Oximeter (Nonin Medical Inc., Plymouth, MN, USA) was used to measure pulse rate and oxygen saturation. All measures of lung function were determined by a pulmonary function analyzer (model: H801; Chest M.I. Inc., Tokyo, Japan). The parameters measured were as follows: lung volume included vital capacity (VC), inspiratory capacity (IC), tidal volume (TV), expiratory reserve volume (ERV), inspiratory reserve volume (IRV) and minute ventilation (MV); pulmonary ventilatory function included forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FEV1/FVC, forced inspiratory vital capacity (FIVC), forced inspiratory volume in 1 s (FIV1), FIV1/FIVC, forced expiratory flow 25% (FEF25), forced expiratory flow 50% (FEF50), forced expiratory flow 75% (FEF75), peak expiratory flow (PEF), maximal mid-expiratory flow (MMEF) and maximal voluntary ventilation (MVV). To avoid errors, all parameters were measured three times and then averaged. All lung function testing was performed by the same person.

Statistics

The statistical analysis was performed with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Baseline characteristics were compared by independent samples *t*-test. Repeated measure analysis of variance (ANOVA) was used to describe the dynamic changes in lung function between CM and control groups at different time points in the study observation period (0, 24, 48, 72 and 96 h). Values of $P < 0.05$ were considered statistically significant.

Table 1. *Baseline characteristics of volunteers*

Characteristic	AG CON group ($n = 12$)	CM group ($n = 12$)	*P* value
Age (years)	21.42 ± 2.35	21.76 ± 2.61	0.807
Height (cm)	171.5 ± 2.28	172.33 ± 1.72	0.323
Weight (kg)	64.17 ± 7.37	64.75 ± 6.93	0.844
BMI	21.80 ± 2.26	21.81 ± 2.35	0.992
SpO_2 (%)	97.33 ± 0.89	97.08 ± 1.00	0.523
Pulse rate (beats min^{-1})	68.58 ± 8.27	76.00 ± 5.46	0.017
Pulmonary volume			
VC (L)	4.81 ± 0.47	4.94 ± 0.41	0.458
IC (L)	2.95 ± 0.39	3.15 ± 0.43	0.244
TV (L)	0.7 ± 0.35	1.01 ± 0.46	0.08
ERV (L)	1.85 ± 0.40	1.79 ± 0.44	0.736
IRV (L)	2.25 ± 0.35	2.14 ± 0.59	0.601
MV (L)	12.22 ± 5.11	14.90 ± 6.43	0.27
Pulmonary ventilation function			
FVC (L)	4.6 ± 0.32	4.57 ± 0.53	0.875
FEV1 (L)	4.14 ± 0.32	4.10 ± 0.30	0.786
FEV1/FVC (%)	90.15 ± 6.33	90.37 ± 0.48	0.937
FIVC (L)	4.53 ± 0.36	4.51 ± 0.52	0.924
FIV1 (L)	4.31 ± 0.51	4.41 ± 0.51	0.64
FIV1/FIVC (%)	95.15 ± 7.98	97.78 ± 3.35	0.303
FEF25 (L s^{-1})	7.80 ± 1.55	8.01 ± 1.37	0.727
FEF50 (L s^{-1})	5.58 ± 1.08	5.27 ± 0.78	0.44
FEF75 (L s^{-1})	2.85 ± 0.81	2.83 ± 0.87	0.954
MMEF (L s^{-1})	4.99 ± 0.99	4.82 ± 0.86	0.658
PEF (L s^{-1})	8.23 ± 1.34	8.63 ± 1.50	0.49
MVV (L min^{-1})	121.27 ± 24.82	141.16 ± 23.44	0.056

All data are presented as the mean ± standard deviation and were compared between groups by independent two sample *t*-test.

Results

Except for pulse rate, the CM and control groups were similar in all parameters measured in this study (Table 1). The pulse rate of the CM group was significantly higher than that of the control group ($P = 0.018$).

We compared the differences in pulse rate, SpO_2, pulmonary volume and pulmonary ventilation function between normal sitting position and −6° HDBR in supine position at 0 h. As shown in Table 2 and Fig. 1, we found that the IC and IRV of HDBR were significantly higher than the same parameters before HDBR ($P < 0.05$). The VC, ERV, FVC, FEV1, FIVC, FIV1, FEF25, FEF50, FEF75, MMEF and PEF of HDBR were all significantly lower than those before HDBR ($P < 0.05$). Although the TV, FEV1/FVC, FIV1/FIVC and MVV were lower with HDBR, there was no statistical significance between HDBR and before HDBR.

Repeated measure ANOVA was employed to explore the difference between the two groups, the difference in each group at different time points and the interaction between group and time. The data showed that there were no prominent

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Table 2. *The differences in pulse rate, SpO2, pulmonary volume and pulmonary ventilation function among all the volunteers between HDBR and before HDBR*

Characteristic	Before HDBR ($n = 24$)	HDBR ($n = 24$)	P value
SpO_2 (%)	97.21 ± 0.93	97.17 ± 1.17	0.892
Pulse rate (beats min^{-1})	72.29 ± 7.83	68.71 ± 8.17	0.128
Pulmonary volume			
VC (L)	4.88 ± 0.44	4.53 ± 0.39	0.006
IC (L)	3.05 ± 0.41	3.62 ± 0.43	<0.001
TV (L)	0.86 ± 0.43	0.79 ± 0.39	0.585
ERV (L)	1.82 ± 0.42	0.91 ± 0.38	<0.001
IRV (L)	2.20 ± 0.48	2.83 ± 0.50	0.001
MV (L)	15.56 ± 5.84	13.60 ± 8.48	0.986
Pulmonary ventilation function			
FVC (L)	4.58 ± 0.43	4.20 ± 0.43	0.003
FEV1 (L)	4.12 ± 0.31	3.66 ± 0.29	<0.001
FEV1/FVC (%)	90.26 ± 6.45	87.46 ± 6.55	0.142
FIVC (L)	4.52 ± 0.43	4.19 ± 0.47	0.018
FIV1 (L)	4.36 ± 0.50	4.03 ± 0.49	0.026
FIV1/FIVC (%)	96.47 ± 6.13	96.13 ± 6.24	0.849
FEF25 (L s^{-1})	7.91 ± 1.44	6.72 ± 1.38	0.006
FEF50 (L s^{-1})	5.42 ± 0.93	4.54 ± 1.01	0.003
FEF75 (L s^{-1})	2.84 ± 0.83	2.37 ± 0.73	0.042
MMEF (L s^{-1})	4.91 ± 0.91	4.12 ± 0.79	0.003
PEF (L s^{-1})	8.43 ± 1.40	7.24 ± 1.66	0.01
MVV (L min^{-1})	131.22 ± 25.70	121.40 ± 26.62	0.2

Before HDBR means sitting position.
HDBR means the angle of bedside was −6° in supine position at 0 h time point.

changes in pulse rate, SpO_2 (Fig. 2), pulmonary volume (Fig. 3) and pulmonary ventilation function (Fig. 4) within or between the control and CM groups over the observation time (Table 3).

Discussions

This study revealed that postural changes can lead to variations in lung volume and ventilation function. However, we found no significant changes in indicators of pulmonary volume or pulmonary ventilation function during the HDBR process. Meanwhile, we did not find any positive role of AG with exercise training on the lungs in spite of increased exercise load with intensive AG. This study confirmed the conclusion we drew from similar human trials in 2009 that microgravity simulated by HDBR and exercise training with AG do not affect lung function (Guo *et al.* 2013).

HDBR has been widely used as an analog of weightlessness, which mimics the effect of gravity on the lungs and the pulmonary vasculature (Prisk 2005; Trappe *et al.* 2006). Many previous studies have proven that this analog of microgravity could be used to explore the changes in the lung under microgravity conditions (Montmerle *et al.* 2002; Koloteva *et al.* 2004; Wood *et al.* 2009). In this study, some parameters of lung volume and pulmonary ventilation were changed after head-down tilt. The VC, ERV, FVC, FEV1, FIVC, FIV1, FEF25, FEF50, FEF75, MMEF and PEF of HDBR were all significantly lower than those before HDBR. This may be due to a thoracoabdominal configuration that leads to the weakening or elimination of external forces, resulting in elevated diaphragm, increased airway resistance and reduced activity of the chest (Paiva *et al.* 1989). Bettinelli *et al.* also demonstrated that this could be attributed to a decrease in lung and chest wall recoil pressures (Bettinelli *et al.* 2002). It is interesting to note that the IC and IRV of HDBR were significantly higher than the same parameters before HDBR. Lung physiology results in an intrathoracic hydrostatic pressure gradient in erect posture. That is to say, the negative pressure of the upper thoracic cavity is much larger than that of the lower cavity due to Earth's gravity. As a result, the alveoli located in the apex of the lung demonstrate a larger degree of expansion and a lower alveolar compliance. Thus the inspiratory flow has less volume in the upper lung alveoli. We assume that this characteristic of gas distribution disappears with a head-down tilt, which results in increased inspiratory volume.

Previous studies have shown that lung volume and pulmonary ventilation function are reduced when astronauts perform a short-term space mission (Elliott *et al.* 1994, 1996; West *et al.* 1997). This phenomenon was confirmed by the 180 day European-Russian EuroMir'95 space mission (Venturoli *et al.* 1998). HDBR is one of the most important methods used to explore changes in lung function on the ground. Montmerle *et al.* found that PEF changed slightly and MMEF (FEF(25–75%)) dropped dramatically (Montmerle *et al.* 2002). However, some studies did not find that microgravity could influence pulmonary function (Prisk *et al.* 2006), and some even suggested that the respiratory system seemed to be less affected (Riviere 2009). Our study found no difference in lung volume and pulmonary ventilation in either the CM or control group at any time after HDBR compared with before HDBR. Although increased exercise load with intensive AG was used in this study, we still did not find that any AG with exercise changed lung function when microgravity was simulated by HDBR. Our findings used larger sample and increased exercise load, but the conclusion was negative. It is consistent with the study conducted by Prisk *et al.* (2008). Wood *et al.* also demonstrated that HDBR had no effect on the ventilatory responses to exercise and hypercapnia (Wood *et al.* 2009). Therefore, we may infer that the HDBR model induced no changes in pulmonary function and therefore should not be used to study AG countermeasures.

Although the sample size remained small, 24 participants represent a large sample size for a HDBR trial. We cannot deny the value of HDBR simulated weightlessness on the cardiovascular and musculoskeletal systems. We need, however, to re-evaluate the feasibility of using HDBR and its relevant countermeasures to study the impact of simulated weightlessness on the lungs. Prisk *et al.* previously demonstrated that HDBR was a poor model of the effects of microgravity on pulmonary ventilation and gas exchange (Prisk *et al.* 2002). While it has been reported that respiratory muscle training would be beneficial to the lung (Yang *et al.* 2007), we need further studies to find efficient countermeasures to the biological effects of microgravity.

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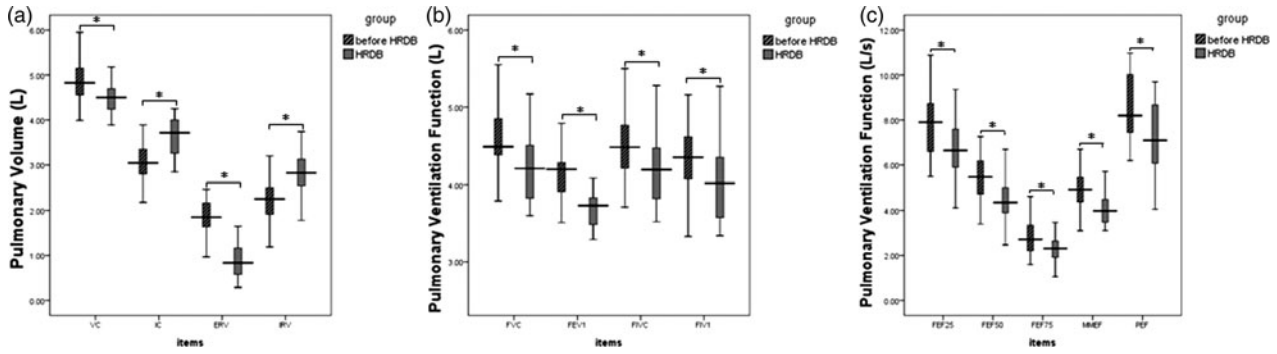

Fig. 1. Differences in pulse rate, SpO_2, pulmonary volume and pulmonary ventilation function between HDBR and before HDBR. $^*P < 0.05$.

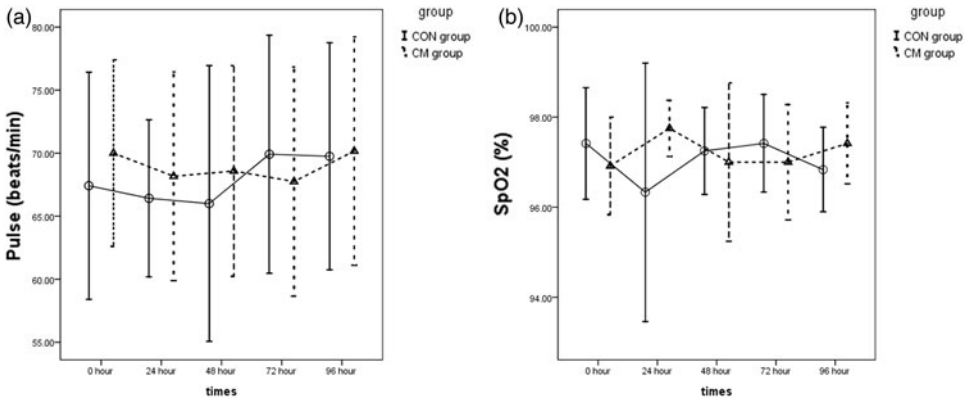

Fig. 2. Dynamic changes in pulse rate and SpO_2 between the AG CON and CM groups at different time points of the 96 h study observation.

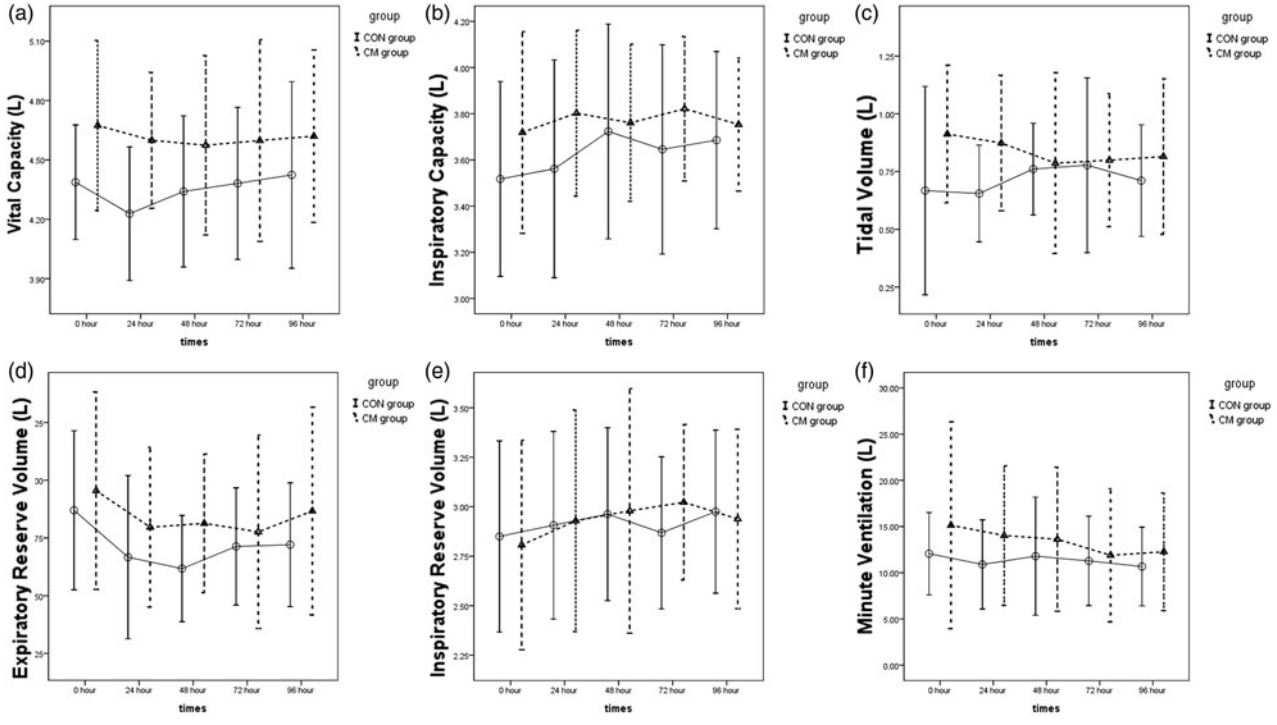

Fig. 3. Dynamic changes in pulmonary volume between the AG CON and CM groups at different time points of the 96 h study observation.

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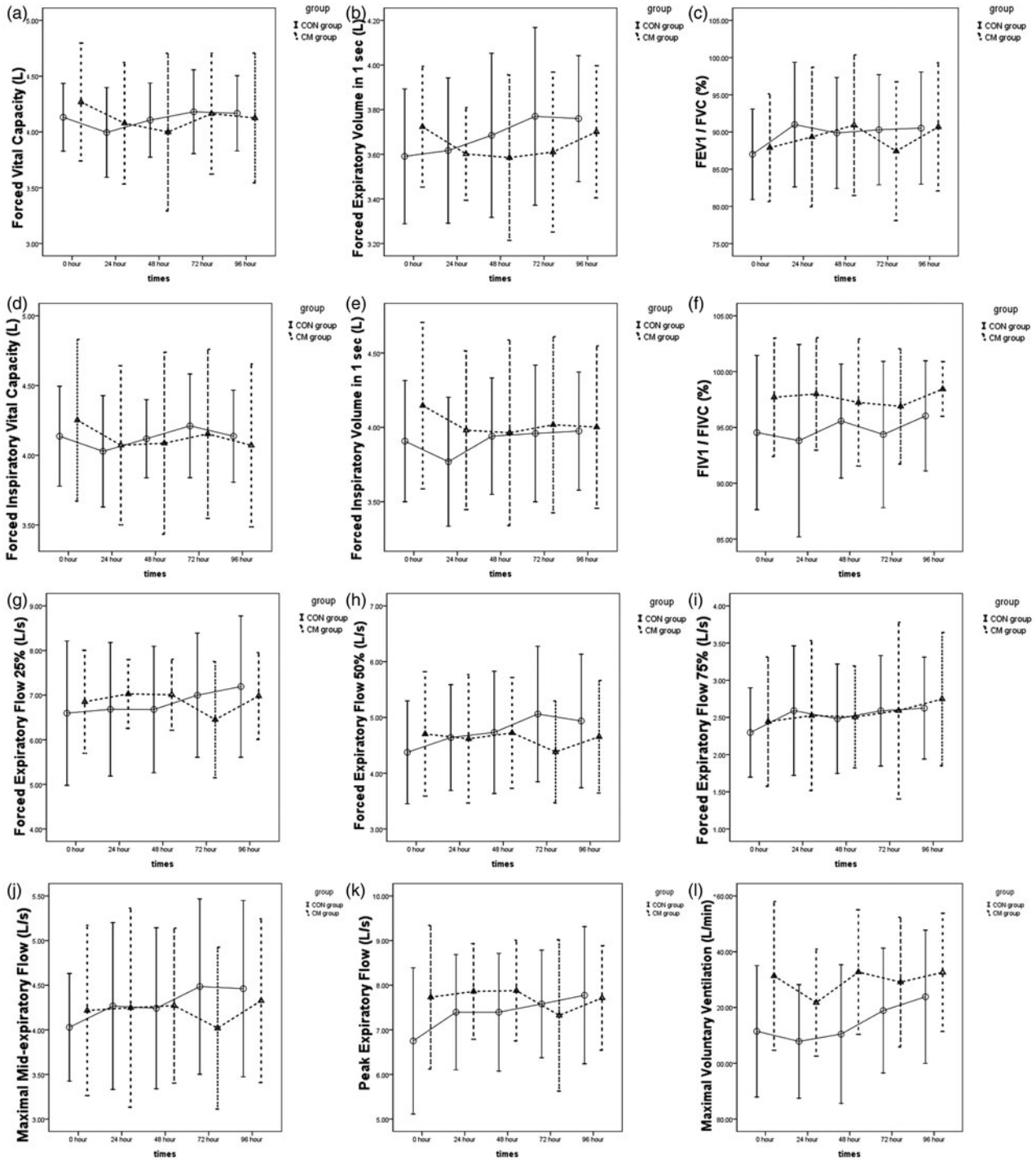

Fig. 4. Dynamic changes in pulmonary ventilation function between the AG CON and CM groups at different time points of the 96 h study observation.

Conclusions

In conclusion, our findings indicate that postural changes may affect lung volume and pulmonary ventilation. However, we found no differences in lung volume and pulmonary ventilation in either CM or control groups at any time after HDBR. The effects of microgravity on lung function may require alternative models to HDBR for clarification. While the value of adopting countermeasures to solve the influence of microgravity on lung function is debatable, further studies and new models are needed to more fully explore the effects of microgravity on the lungs.

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Table 3. *Dynamic changes in pulse rate, SpO_2, pulmonary volume and pulmonary ventilation function between the AG CON and CM* groups at different time points of the 96 *h study observation*

Parameters	0 h	24 h	48 h	72 h	96 h
Pulse rate (beats min^{-1})					
CON group	67.42 ± 9.01	66.42 ± 6.23	66.00 ± 10.94	69.92 ± 9.44	69.75 ± 9.00
CM group	70.00 ± 7.40	68.17 ± 8.28	68.58 ± 8.35	67.75 ± 9.09	70.17 ± 9.05
SpO_2 (%)					
CON group	97.42 ± 1.24	96.33 ± 2.87	97.25 ± 0.97	97.42 ± 1.08	96.83 ± 0.94
CM group	96.92 ± 1.08	97.75 ± 0.62	97.00 ± 1.76	97.00 ± 1.30	97.42 ± 0.90
VC (L)					
CON group	4.39 ± 0.29	4.23 ± 0.34	4.34 ± 0.38	4.38 ± 0.38	4.42 ± 0.47
CM group	4.67 ± 0.43	4.60 ± 0.34	4.57 ± 0.45	4.60 ± 0.51	4.62 ± 0.44
IC (L)					
CON group	3.52 ± 0.42	3.56 ± 0.47	3.72 ± 0.47	3.65 ± 0.45	3.69 ± 0.38
CM group	3.72 ± 0.44	3.80 ± 0.36	3.76 ± 0.34	3.82 ± 0.31	3.75 ± 0.29
TV (L)					
CON group	0.67 ± 0.45	0.66 ± 0.21	0.76 ± 0.20	0.78 ± 0.38	0.71 ± 0.24
CM group	0.91 ± 0.30	0.87 ± 0.29	0.78 ± 0.39	0.80 ± 0.29	0.82 ± 0.34
ERV (L)					
CON group	0.87 ± 0.34	0.67 ± 0.35	0.62 ± 0.23	0.71 ± 0.25	0.72 ± 0.27
CM group	0.96 ± 0.43	0.80 ± 0.35	0.81 ± 0.30	0.78 ± 0.42	0.87 ± 0.45
IRV (L)					
CON group	2.85 ± 0.48	2.91 ± 0.47	2.96 ± 0.44	2.87 ± 0.38	2.98 ± 0.41
CM group	2.81 ± 0.53	2.93 ± 0.56	2.98 ± 0.62	3.02 ± 0.39	2.94 ± 0.45
MV (L)					
CON group	12.06 ± 4.46	10.89 ± 4.83	11.79 ± 6.39	11.28 ± 4.84	10.68 ± 4.26
CM group	15.14 ± 11.19	14.03 ± 7.55	13.62 ± 7.80	11.89 ± 7.19	12.27 ± 6.37
FVC (L)					
CON group	4.13 ± 0.30	4.00 ± 0.40	4.11 ± 0.33	4.18 ± 0.38	4.17 ± 0.34
CM group	4.27 ± 0.53	4.08 ± 0.54	4.00 ± 0.71	4.16 ± 0.54	4.13 ± 0.58
FEV1 (L)					
CON group	3.59 ± 0.30	3.62 ± 0.33	3.69 ± 0.37	3.77 ± 0.40	3.76 ± 0.28
CM group	3.72 ± 0.27	3.60 ± 0.21	3.59 ± 0.37	3.61 ± 0.36	3.70 ± 0.30
FEV1/FVC (%)					
CON group	87.01 ± 6.08	91.00 ± 8.38	89.88 ± 7.45	90.31 ± 7.40	90.53 ± 7.53
CM group	87.90 ± 7.24	89.34 ± 9.37	90.37 ± 9.45	87.42 ± 9.32	90.69 ± 8.62
FIVC (L)					
CON group	4.14 ± 0.36	4.03 ± 0.40	4.12 ± 0.28	4.21 ± 0.37	4.14 ± 0.33
CM group	4.25 ± 0.58	4.07 ± 0.57	4.09 ± 0.65	4.15 ± 0.61	4.07 ± 0.58
FIV1 (L)					
CON group	3.91 ± 0.41	3.77 ± 0.43	3.94 ± 0.39	3.96 ± 0.46	3.98 ± 0.40
CM group	4.15 ± 0.56	3.98 ± 0.53	3.96 ± 0.62	4.02 ± 0.59	4.00 ± 0.55
FIV1/FIVC (%)					
CON group	94.54 ± 6.91	93.82 ± 8.61	95.58 ± 5.11	94.37 ± 6.55	96.03 ± 4.93
CM group	97.71 ± 5.30	98.00 ± 5.04	97.23 ± 5.70	96.89 ± 5.16	98.44 ± 2.44
FEF25 (L s^{-1})					
CON group	6.6 ± 1.62	6.68 ± 1.5	6.68 ± 1.42	7.00 ± 1.39	7.19 ± 1.58
CM group	6.85 ± 1.15	7.03 ± 0.77	7.01 ± 0.80	6.45 ± 1.30	6.98 ± 0.97
FEF50 (L s^{-1})					
CON group	4.38 ± 0.92	4.64 ± 0.95	4.73 ± 1.10	5.06 ± 1.21	4.94 ± 1.20
CM group	4.70 ± 1.11	4.62 ± 1.15	4.72 ± 0.99	4.38 ± 0.91	4.65 ± 1.01
FEF75 (L s^{-1})					
CON group	2.30 ± 0.60	2.59 ± 0.87	2.48 ± 0.74	2.59 ± 0.74	2.63 ± 0.69
CM group	2.44 ± 0.87	2.53 ± 1.01	2.51 ± 0.69	2.59 ± 0.74	2.75 ± 0.90
MMEF(L s^{-1})					
CON group	4.03 ± 0.60	4.27 ± 0.93	4.24 ± 0.90	4.49 ± 0.98	4.46 ± 0.99
CM group	4.22 ± 0.95	4.25 ± 1.12	4.27 ± 0.87	4.02 ± 0.91	4.33 ± 0.92
PEF (L s^{-1})					
CON group	6.75 ± 1.64	7.40 ± 1.29	7.39 ± 1.32	7.58 ± 1.21	7.76 ± 1.54
CM group	7.73 ± 1.61	7.86 ± 1.07	7.88 ± 1.13	7.32 ± 1.70	7.72 ± 1.17
MVV (L min^{-1})					
CON group	111.47 ± 23.56	107.86 ± 20.36	110.48 ± 24.84	118.90 ± 22.38	123.84 ± 23.89
CM group	131.34 ± 26.66	121.76 ± 19.16	132.73 ± 22.32	129.10 ± 23.22	132.61 ± 21.15

https://doi.org/10.1017/S1473550415000245 Published online by Cambridge University Press

Acknowledgements

The authors are very grateful to Professor Dan Feng of the Department of Medical Statistics, Chinese PLA General Hospital, who contributed to the data statistical analysis. This study was funded by the National Basic Research Program of China (973 program) No. 2014CB744400; Key Program of Medical Research in the Military '12th 5-year Plan,' China No. BWS12J046; Key Pre-Research Foundation of Military Equipment of China No. 9140A26040312JB10078; Beijing Novel Program, No. Z131107000413105; and the program of Manned Spaceflight NO.040203.

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