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Effectiveness of Centrifuge-induced Artificial Gravity with Ergometric Exercise as a Countermeasure during Simulated Microgravity Exposure in Humans

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Abstract: To test the effectiveness of centrifuge-induced artificial gravity with ergometric exercise, 12 healthy young men (20.7 ± 1.9 yrs) were exposed to simulated microgravity for 14 days of –6° head-down bedrest. Half the subjects were randomly selected and loaded 1.2 G artificial gravity with 60 W (four out of six subjects) or 40 W (two out of six subjects) of ergometric workload on days 1, 2, 3, 5, 7, 9, 11. 12, 13, 14 (CM group). The rest of the subjects served as the control. Anti-G score, defined as the G-load × running time to the endpoint, was significantly elongated by the load of the centrifuge-ergometer. Plasma volume loss was suppressed (–5.0 ± 2.4 vs –16.4 ± 1.9%), and fluid volume shift was prevented by the countermeasure load. Elevated heart rate and muscle sympathetic nerve activity after bedrest were counteracted, and exaggerated response to head-up tilt was also suppressed. Centrifuge-induced artificial gravity with exercise is effective in preventing cardiovascular deconditioning due to microgravity exposure, however, an effective and appropriate regimen (magnitude of G-load and exercise workload) should be determined in future studies.

Key words: Artificial gravity, ergometric exercise, deconditioning, microneurography, sympathetic nerve activity

Alterations in cardiovascular, muscular, bone and mineral functions following exposure to microgravity cause inappropriate reactions after return to 1G gravity condition on earth (Bromqvist et al. 1983; Buckey et al. 1996; Convertino et al. 1994). To minimize the reactions, several countermeasures have been proposed, e.g. exercising treadmill and cycle ergometer for myatrophy, and lower body negative pressure (LBNP) and fluid loading for cardiovascular deconditioning (NASA Task force on Countermeasures, Final Report, May 1997).

While the above countermeasures provide a certain load to human skeletomuscular and cardiovascular systems under microgravity, artificial gravity approaches the solution of deconditioning in a different manner because all systems are challenged by natural 1G gravity. Therefore, it has the possibility to provide a multisystem countermeasure. If humans do not need gravity 24 hr/day and intermittent gravity is sufficient to remain healthy, onboard human short-arm centrifuge presents a realistic near-term opportunity for providing this artificial gravity (Kotovskaya et al. 1981; Sulzman and Wolfe 1991; Young 1997). However, this artificial gravity by short-radius centrifuge is not completely sufficient to improve the multisystem hypofunction in humans.

To overcome the demerit of short-radius centrifuge, we have manufactured a centrifuge-induced artificial gravity device with ergometric exercise, and reported on the cardiovascular function during centrifugation (Iwase et al. 2002). Applying the device to a bedrest study, we examined the effect of the device on simulated microgravity exposure by bedrest.

Methods

1) Subjects

Subjects were 12 young men aged 20.7 ± 1.9 years, height 170 ± 5 cm, weight 65.8 ± 1.5 kg participating in a 14-day –6° head-down bedrest (HDBR) study, taking identical meals of 2000 *kcal*/day. Fluid was provided ad libitum but the subjects were encouraged to take 1.5 *l*/day. Urination and defecation were allowed only on the bed. This study protocol was approved by The Ethical Committee on Human Studies, Research Institute of Environmental Medicine, Nagoya University.

2) Schedule

Six subjects were exposed to artificial gravity of 1.2 G at

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heart level for 30 min with ergometric exercise of 60W as a countermeasure on day 1, 2, 3, 5, 7, 9, 11, 12, 13, 14, during HDBR (CM group), and the rest of them were treated as the control.

3) Anti-G Score

Subjects were requested to lie down in the Centrifuge-Ergometer, and have a rest for10 min to obtain a control reading. Without ergometric exercise, they were loaded artificial gravity of 1.0G for 10 min, 1.2G for 5 min, 1.4G for 5 min, 1.6G for 5 min, 1.8G for 5 min, and 2.0G for 5 min at heart level in order to determine the anti-G score. The anti-G score was calculated as the total sum of the magnitude of gravity vector toward the leg (+Gz) × time (sec) for the load to the endpoint of the centrifuge.

4) Measurements

Before and after the 14-day HDBR, the anti-G score, was determined in each subject. Heart rate (HR) by electrocardiogram, blood pressure (BP) waves with Finapres (Ohmeda Finapres 2300), and chest and leg impedance by impedancemetry (Nihon Kohden AI601G) were continuously monitored and recorded in a digital audio tape recorder (Sony Precision Technology PC-2 1 6Ax) during the graded G load by the centrifuge device. Body weight and percent plasma volume change according to the Van Beaumont formula: $\%\Delta PV = [100/(100\text{-}Hct_B)] \times [100(Hct_B\text{-}Hct_A)/Hct_A]$ where %ΔPV: percent change in plasma volume, Hct: hematocrit, A: after. B: before the bedrest (Van Beaumont, 1972) were measured before and after bedrest. Plasma angiotensin II, HR and muscle sympathetic nerve activity (MSNA) by microneurography with a tungsten microelectrode were also measured in the supine and 30° head-up tilt position before and after bedrest. MSNA was evaluated by burst number per min (burst rate) and the total sum of the integrated MSNA burst (total MSNA)

5) Suspension of the centrifuge

The rotation was suspended if one of the following occurred; 1) onset of presyncopal symptoms *e.g*, nausea, sweating, grayout or dizziness, including a drop in systolic BP > 15 *mmHg* and/or sudden drop of HR >15 *bpm*; 2) progressive reduction in systolic BP to < 80 *mmHg*, 3) the subject requested the termination. The subjects held a shutdown switch that brakes the rotation when released by the subjects. To rotate, the subjects have to continuously press the switch. This switch enables the centrifuge to stop automatically when the subjects lose consciousness. By this endpoint, we determined the anti-G score in each subject (without exercise) in the pre- and post bedrest measurement. During the bedrest we used this device as the countermeasure for microgravity exposure, and 1.2 G was loaded on the subjects with 40/60W of workload for 30 min. The suspension criteria for a break was used in both centrifuges. If the centrifuge with exercise was suspended by a request by subjects, the total countermeasure period was summed up to 30 min.

6) Statistics

HR, mean arterial BP (MAP), intrathoracic blood volume (TFI, thoracic fluid index, a reciprocal value of %change in an impedance value), leg fluid volume (LFI, leg fluid index, also the reciprocal of leg impedance) stored in DAT recorder were transferred to the hard disk with PC scan software (Sony Precision Technology, Tokyo), averaged on personal computers (Windows 2000), and expressed as mean ± SE. The variables were analyzed by a two-way repeated-measures ANOVA. Tests for simple effects were performed with the Bonferroni-Dunn comparison procedure when the interaction term was found to be significant. For simple comparison, the paired t-test was employed with significant levels of $p<0.05$.

Results

Four subjects successfully completed 60W exercise under 1.2G artificial gravity while two out of six complained of 60W being too hard so their workloads were reduced to 40W. A stand test of 15 min upright standing revealed that 2/6 were intolerant in both groups, however, two fainters in the CM group were the two subjects whose workload was reduced from 60W to 40W.

1) Changes in body weight, and plasma volume (Fig. 1)

Body weight was reduced from 68.8 ± 3.1 kg to 65.3 ± 3.1 kg in the CM group, and from 61.8 ± 1.8 to 60.1 ± 2.0 kg in the control group, both of which showed no significant difference before and after the bedrest. Plasma volume change was –5.0 ± 2.4% in the CM group while –16.4 ± 1.9% in the control, which exhibited a significant difference ($p<0.05$).

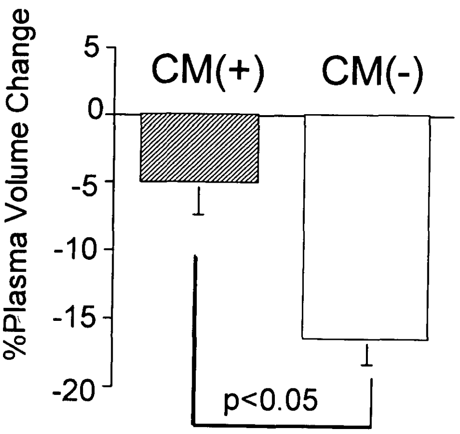

Fig. 1 Changes in percent plasma volume after bedrest. The countermeasure of centrifuge-ergometer significantly suppressed the plasma volume loss.

2) Changes in anti-G score with or without the countermeasure (Fig. 2)

In the CM group, the anti-G score was significantly increased from 973 ± 140 to 1,308 ± 144 ($p<0.05$) while that of the control group showed no significant changes between pre- (753 ± 92) and post- (843 ± 81) bedrest values.

3) Changes in cardiovascular parameters and muscle sympathetic nerve activity

HR was elevated in both groups, but the increase was significantly less in the CM group (61.0 ± 1.8 to 66.7 ± 2.5 in CM, 63.8 ± 2.6 to 72.8 ± 2.6 in the control, $p<0.05$). Systolic and diastolic BP (110.3 ±1.5 / 71.6 ± 1.2 to 114.5 ± 3.1 / 73.5 ± 2.8 *mmHg* in CM, 114.5 ± 4.3 / 74.1 ± 2.4 to 118.0 ± 2.5 / 75.0 ± 1.8 *mmHg* in the control) showed no significant change

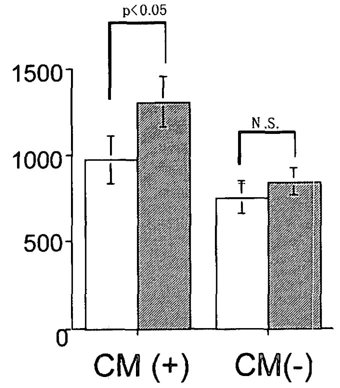

Fig. 2 Changes in anti-G score before (open bars) and after (shaded bars) bedrest with (left) or without (right) the countermeasure of the centrifuge-ergometer. There was a significant increase in the score with the countermeasure, however, no significant changes were observed in the control.

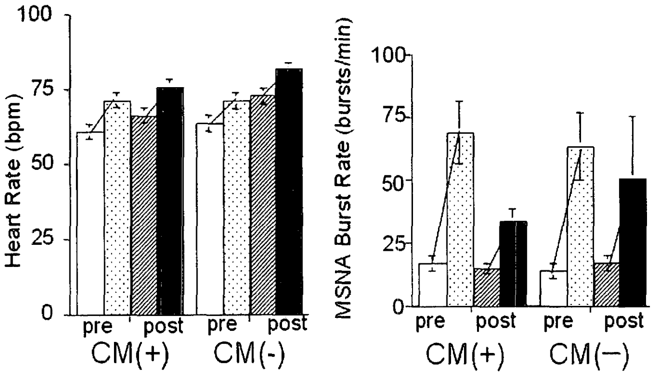

Fig. 3 Changes in heart rate (left) and MSNA burst rate (right) before and after the bedrest (pre and post) with or without the countermeasure (CM) in the supine and 30° head-up tilt position. Increased resting HR and resting MSNA by bedrest were suppressed by the countermeasure. Tilt-induced increases in HR and MSNA were also suppressed by the centrifuge-ergometer.

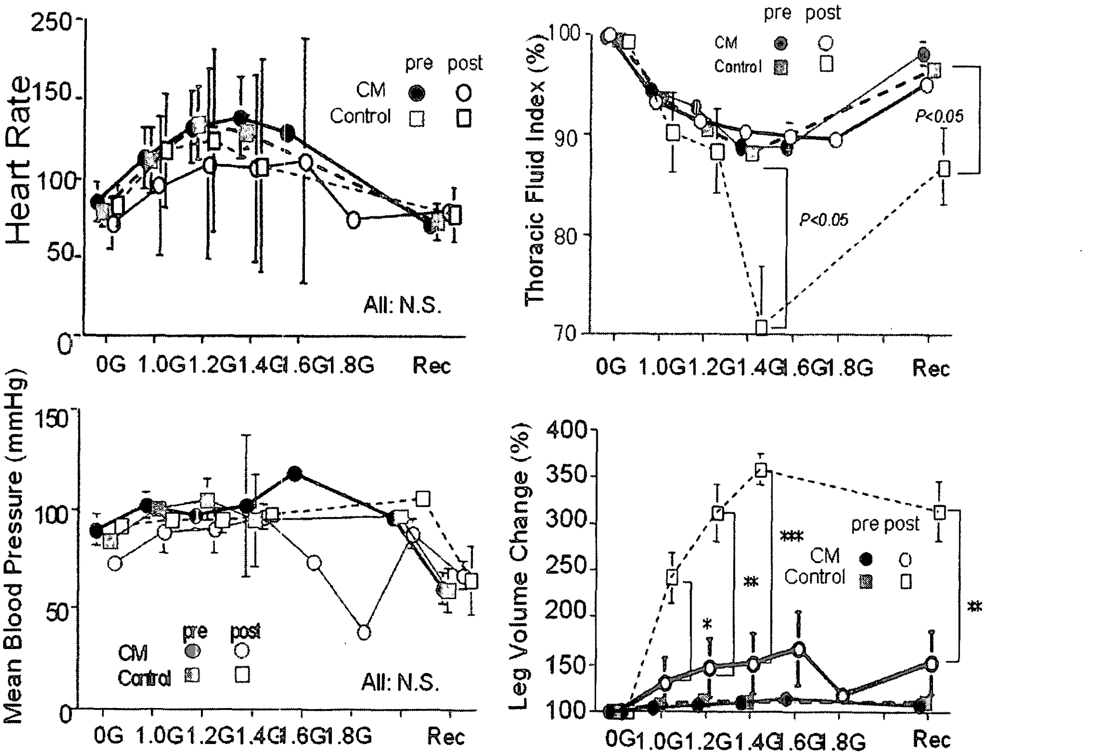

Fig. 4 Changes in heart rate (left upper), mean arterial pressure (left lower), thoracic fluid volume (right upper), leg fluid volume (right lower) in accordance with the +Gz increase before and after the bedrest with and without the countermeasure. The countermeasure of the centrifuge-ergometer significantly suppressed the fluid shift from the thorax to the leg.

between the groups. Stroke volume was reduced in both groups (78.2 ± 3.0 to 70.0 ± 2.5 in the CM, 78.4 ± 1.2 to 72.1 ± 2.5 in the control), but the changes were not significantly different between the groups. Plasma angiotensin II levels were significantly increased in the control (6.0 ± 1.5 to 14.6 ± 3.0 *pg/ml*), but not in the CM group (6.6 ± 0.8 to 6.3 ± 1.4 *pg/ml*). MSNA burst rate was suppressed in the CM group (17 ± 3 to 15 ± 2 *bursts/min*), while it was enhanced in the control (14 ± 3 to 17 ± 5 *bursts/min*).

4) *Effect of 30° head-up tilt before and after bedrest (Fig. 3)*

By head-up tilt to 30°, MSNA was enhanced, increasing the peripheral vascular resistance. Total MSNA at the 30° tilted position taking the supine as 100 before bedrest was enhanced to 405.1 ± 41.7 (arbitrary unit) in the CM group and to 454.2 ± 45.5 in the control. After bedrest, it was suppressed to 223.7± 25.3 in CM, and 298.4 ± 49.4 in the control, and both changes were not significantly different between the two groups. HR increase by the tilt was small before bedrest (61.0 ± 1.8 to 71.6 ± 2.6 *bpm* in CM, 63.8 ± 2.6 to 71.4 ± 2.8 *bpm* in the control), while it was enhanced after bedrest (66.7 ± 2.5 to 76.2 ± 2.0 in CM, 72.8 ± 2.6 to 81.8 ± 2.4 in the control), and these changes were significantly different, *i.e.* the HR increase by 30° head-up tilt after bedrest was suppressed in the CM group.

A change was also found in the plasma angiotensin II level. In the 30° tilted position, it was 7.8 ± 1.6 in CM, while 15.0 ± 4.5 *pg/ml* in the control.

5) *Change in HR, MBP, thoracic fluid volume, and leg volume change during graded G-level change (Fig. 4)*

During the graded G-load from 1.0 to 2.0G, HR and MBP did not show any significant changes during graded G-load. As for the fluid shift, thoracic blood volume reduction and leg volume increase according to the G-load were significantly suppressed in the CM group.

Discussion

We have designed and manufactured a centrifuge-ergometer, and reported that ergometric exercise under artificial gravity is beneficial for orthostatic tolerance as a countermeasure. The next step was to test the device against microgravity exposure simulated by bedrest.

The present study revealed that the centrifuge-produced artificial gravity could effectively suppress the plasma volume reduction, and fluid shift from the chest to the leg. After bedrest, 2/6 subjects fainted in both groups, however, the fainters in the CM group were the two subjects whose workloads were reduced to 40W. The MSNA enhancement caused by bedrest was suppressed in the CM group compared with the control.

There are four hypotheses for cardiovascular deconditioning after microgravity exposure, 1) hypovolemia due to centralization of body fluid and diuresis, 2) reduced responsiveness of resistant vessels to sympathetic stimulation due to lack of shear stress, 3) cardiac hypofunction or 4) alterations in the baroreflex. The present study revealed that this centrifuge-ergometer can prevent hypovolemia, suspend the attenuated vascular response, and prevent the effect of cardiac hypofunction, because the suppression of increased resting HR and accelerated HR when the position was tilted up to 30° indicated the prevention of cardiac hypofunction, although the stroke volume and cardiac output were not significantly different between the groups.

The present results have shown that centrifuge-induced artificial gravity with ergometric exercise seems to be effective in suppressing cardiovascular deconditioning. As for the exercise workload, 40W for 30 min per day might be too light to suppress cardiovascular deconditioning since the two subjects who requested to reduce a load reduction from 60W to 40W for 30 min per day suffered from orthostatic intolerance after bedrest.

In Neurolab missions in 1998, the European Space Agency tested an off-axis rotator (Clément et al. 2000) with $+G_z$ of 0.5 to 1G for 7 min, and verified the effect of artificial gravity, resulting in well preserved orthostatic tolerance and highly responsive sympathetically-mediated vasoconstriction (Moore et al. 2000). The present study verified the effectiveness even in simulated microgravity by preventing circulatory plasma loss, fluid shift, and sympathetic vasoconstriction.

Some side-effects of centrifuge training were reported, among which head movements during the centrifuge training induced illusory sensations, vestibule-ocular reflexes, and/or motion sickness (Young et al. 2001). In our device, some subjects complained of such sensations especially during the accelerating and decelerating stages, however, the episodes were short enough to be tolerated.

In conclusion, centrifuge-induced artificial gravity with exercise is effective in preventing cardiovascular deconditioning due to microgravity exposure, however, an effective and appropriate regimen (magnitude of G-load and exercise workload) should be determined in future studies.

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