

Research Article

A Preliminary Study to Investigate Relaxation and Sleep-Inducing Effects of Cedrol

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Abstract. Background: Cedrol exhibits relaxation effects, and its scent may reduce stress, thereby contributing to various stressful life situation. However, cedrol has also been reported to induce sleep, which is dangerous by case. Therefore, studies are needed in order to determine whether the relaxation or sleep-inducing effects of cedrol are induced under stressful situation and also how to only attain the former. Method: A cross-over open study was conducted. Subjects were randomly divided into two groups ($n = 3$ per group). After one course of the Kraepelin test and additional dumbbell lifting before and after the test was performed, subjects entered the placebo or cedrol exposure room, and rested in a sitting position for 20 minutes. Electrocardiographic, electroencephalographic, and blood pressure measurements as well as VAS assessments were conducted. Result: In the present study, no stress response was clearly detected. However, the results of analyses with respect to individuals suggested that cedrol exhibited relaxation effects, and that it did not induce sleep under the conditions adopted in this study.

Keywords: Cedrol; relaxation; sleepiness; electrocardiography; electroencephalography

1. Introduction

The efficacy of cedrol, which is a phytoncide, a component of sesquiterpene alcohols contained in cedar and hinoki cypress scents, and an aromatic component used in aromatherapy, has been emphasized. Cedrol exhibits relaxation effects as discussed elsewhere [1–3], and its scent may reduce stress, thereby contributing to various stressful life situation. However, cedrol may induce sleep as reported by Sano et al. [4], which is dangerous by case.

Therefore, studies are needed in order to determine whether the relaxation or sleep-inducing effects of cedrol are induced under stressful situation, and also how to only attain the former.

We herein conducted a preliminary study with the aim of establishing a study system to confirm the relaxation effects of cedrol as well as presence or absence of sleep-inducing effects for its safe application to various stressful life situation. It was decided to add both psychological stress and physical stress as prone to reaction as stressor. We used

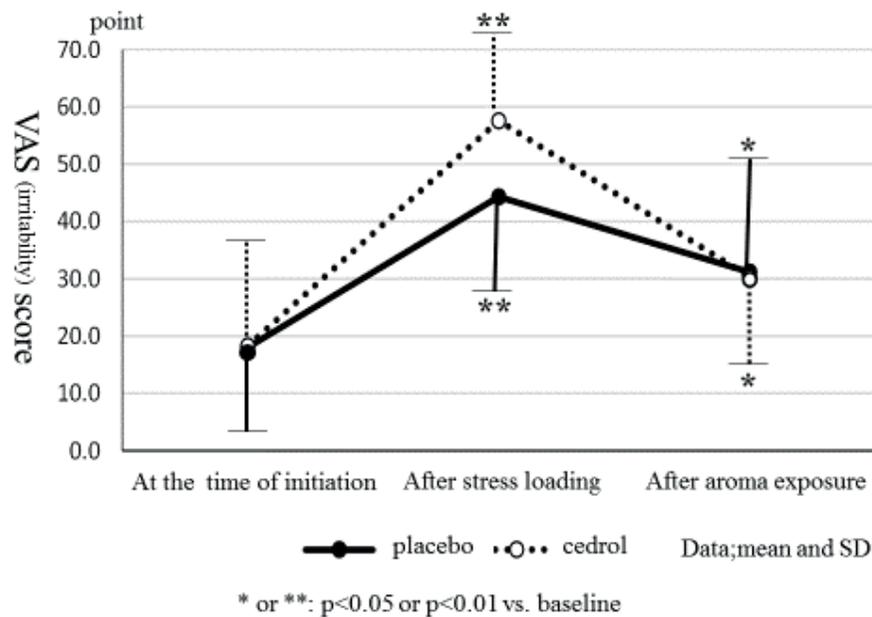


Figure 1: Changes in the VAS (irritability) score.

Kraepelin test as the former, with a dumbbell retention and sitting straight as the latter.

2. Methods

2.1. Subjects. Subjects comprised 6 healthy males aged 20 years or older (mean age: 22.7 ± 2.07 years). The aim and method of this study were explained, and informed consent was obtained from all subjects. The study protocol was approved by the Ethics Review Committee for Human Experimentation of Mie University Graduate School of Medicine.

2.2. Test substance and exposure methods. Butylcarbitol (Dow Chemical Company) was used as a placebo. As a test substance, cedrol (purity: 98.0% <, Tokyo Chemical Industry Co., Ltd.) was mixed with butylcarbitol at Dow Chemical Company. Regarding aroma exposure, an adequate volume of the placebo or cedrol was placed on a petri dish, which was then set on a hot plate (60°C). A tent room consisting of a frame measuring $1.5 \times 1.5 \times 1.9$ m and vinyl sheet was used, and room air was agitated using a small electric fan.

2.3. Study methods. A cross-over open study was conducted. Subjects were randomly divided into two groups ($n = 3$ per group) based on random numbers generated using a computer.

Subjects were instructed to wait in another room until the start of this study. They entered the test room, and were rested in a sitting position for 10 minutes. Electrocardiography

and electroencephalography were subsequently performed. Systolic/diastolic blood pressures and pulses were measured using an automated sphygmomanometer. Irritability was evaluated using the visual analogue scale (VAS). Physical and mental stressor loading was then conducted. Briefly, subjects were instructed to lift a dumbbell weighing 7.5 kg with their handedness and contralateral hand for 3 minutes in a straight sitting position. One course of the Kraepelin test (calculation for 15 minutes + rest for 5 minutes + calculation for 15 minutes) was conducted. This test requires subjects to perform continuous arithmetic addition of single-digit figures as fast and accurately as possible. This was achieved using pre-printed paper containing 15 lines of random, single-digit, horizontally aligned numbers. For each minute, the subjects were instructed to begin a new line regardless of their position on the current line. Each line contained an excess of calculations such that the subjects were not able to finish any line for a particular minute before being prompted to move on to the start of the next minute by the examiner's prompting. This test is performed for repeated 15 min of work and 5 min rest cycles. In a manner similar to that carried out immediately prior to the Krepelin test, additional dumbbell lifting was performed for 3 minutes. After further electrocardiographic, electroencephalographic, and blood pressure measurements as well as VAS assessments, subjects entered the placebo (vehicle: butylcarbitol) or cedrol (approximately $200 \mu\text{g}/\text{m}^3$) exposure room, and rested in a sitting position for 20 minutes. Electrocardiographic, electroencephalographic, and blood pressure measurements as well as VAS assessments were then conducted.

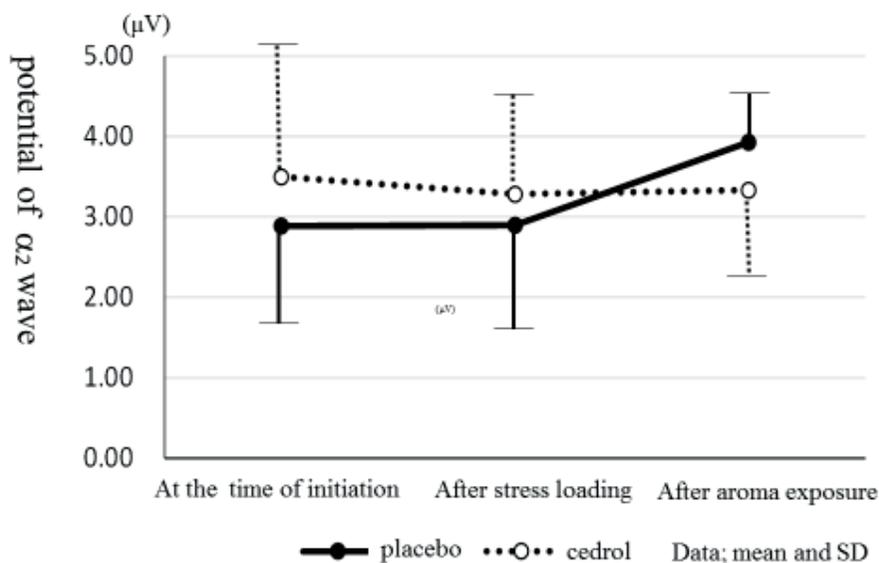


Figure 2: Changes in the mean potential of the α_2 wave.

2.4. Measurement items.

2.4.1. Electrocardiography. Using a handheld ECG recorder (Checkmyheart 3.0, Daily Care BioMedical Inc.), electrodes were attached to the medial areas of the left and right forearms, and measurements were conducted for 5 minutes. Using accessory software, HF (corrected HF), which was calculated using the AR method (Detrend), LF (corrected LF), and LF/HF were measured.

2.4.2. Electroencephalography. Using a handheld high-powered EEG (FM919, Futek Electronics Co., Ltd.), sensor bands (2 electrodes) were attached to the forehead, and electroencephalograms were recorded for 3 minutes through ear grounding. They were FFT-converted data. The mean action potentials (μV) of α , β , θ , and δ wavelength widths were calculated. Data of 20 μV or more per second at 3.0 Hz were excluded as artifacts for convenience.

2.4.3. Blood pressure and pulse. Systolic/diastolic blood pressures and pulses were measured and recorded using an automated sphygmomanometer (HEM-8731, OMRON Co., Ltd.).

2.4.4. VAS score (face scale). In order to evaluate irritability, subjects were instructed to record their emotion with an arrow on a 10-cm line, indicating “no irritability” at the left and “very irritated” at the right. The distance from the left end (mm) was regarded as the point of irritability.

2.5. Statistical analysis. A two-way variance analysis with paired factors was conducted in order to compare data between the two groups. When interactions were observed, the paired *t*-test was performed. Dunnett’s test was conducted for intra-group comparisons. SPSS 22.0 software (IBM) was used. A p-value of 0.05 was regarded as significant (two-sided test).

3. Results

3.1. Electrocardiography. No interaction in the HF component and LF/HF ratio was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence.

3.2. Blood pressure and pulse. No interaction in systolic and diastolic blood pressure and was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence.

3.3. Pulse. No interaction in the pulse rate was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence.

3.4. VAS score. Changes in the VAS score, which reflects irritability, are shown in Figure 1. No interaction was observed between the placebo and cedrol groups. A significant increase was noted after stress loading in both groups. Thereafter, the reduction in the VAS score by cedrol appears

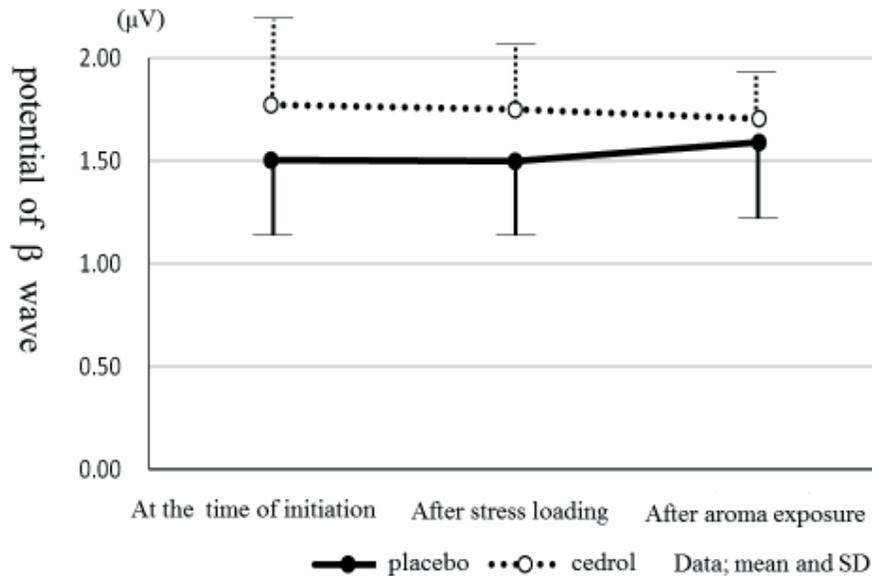


Figure 3: Changes in the mean potential of the β wave.

to be greater than that of placebo group, but significant difference between the groups was not observed. Since the VAS score is a scale of mood, it cannot always be regarded as equal to stress. However, there may have been stress responses that were not detected using other biological indices.

3.5. Electroencephalography.

3.5.1. α wave. No interaction in the mean potential of the α wave was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence.

The results obtained were analyzed with respect to the $\alpha 1$ and $\alpha 2$ waves.

$\alpha 1$ wave: 8 to <10 Hz: relaxation with low-grade awakening

$\alpha 2$ wave: 10 to <13 Hz: relaxation with high-grade awakening

Concerning the $\alpha 1$ wave, which reflects relaxation with low-grade awakening, no interaction was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence. Changes in the mean potential of the $\alpha 2$ wave are shown in Figure 2. Although interactions were observed for the $\alpha 2$ wave, which reflects relaxation with high-grade awakening, no significant differences were noted between the two groups. In the cedrol group, no relationship was observed with the concentration of cedrol used.

3.5.2. β wave. Changes in the mean potential of the β wave are shown in Figure 3. Although interactions were observed between the placebo and cedrol groups, no significant differences were found. Neither stress nor cedrol exposure had any influence.

3.5.3. θ wave. No interaction was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence.

3.5.4. δ wave. No interaction was observed between the placebo and cedrol groups. Neither stress nor cedrol exposure had any influence. In the cedrol group, the post-exposure value was lower in subjects exposed to a low concentration of cedrol.

Thus, electroencephalography did not reveal any significant influence of stress loading or aroma exposure.

4. Discussion

In the present study, the actions of the stressor were not clearly detected. No significant changes were noted, excluding the VAS score, which reflected the stress response. Marked individual differences were noted, and the number of subjects was low. Therefore, by regarding the value at the start of this study as 1, we calculated ratios, but found no marked differences. Furthermore, individuals in whom the stressor may have acted on each examination item twice were reviewed. Electrocardiography showed a stress-related decrease in the HF component and increase

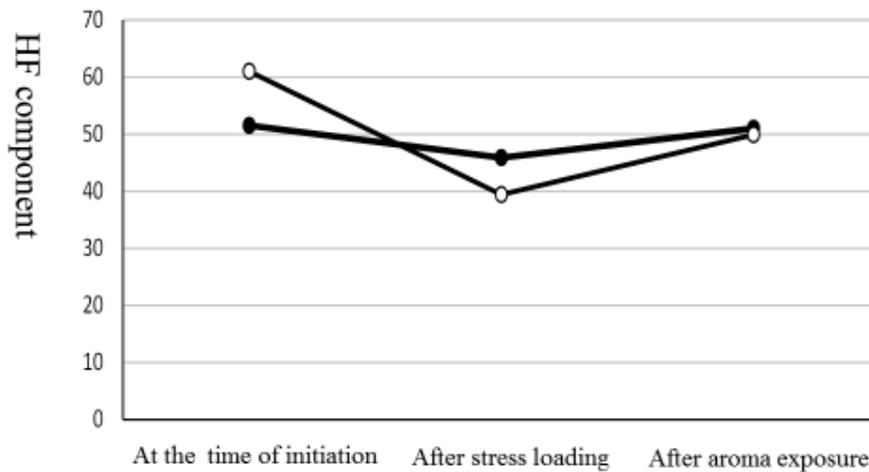


Figure 4: Changes in the HF component on Cedrol exposure in 2 subjects.

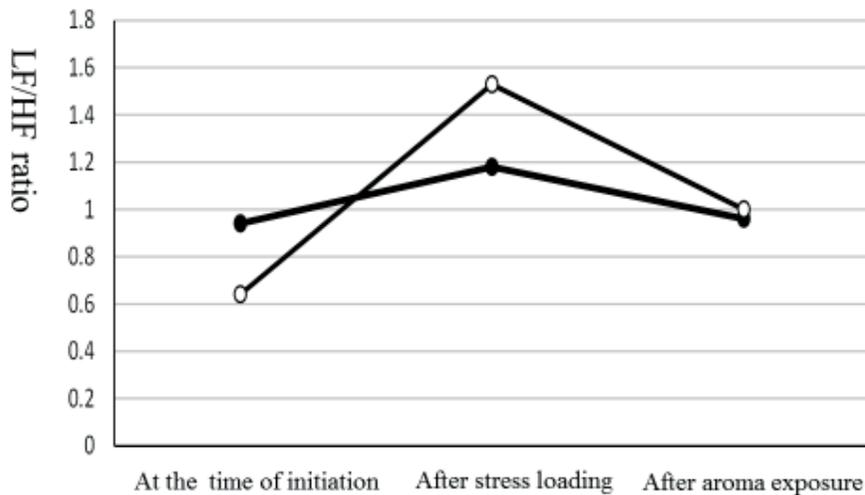


Figure 5: Changes in the LF/HF ratio on Cedrol exposure in 2 subjects.

in the LF/HF ratio in 2 subjects. After cedrol exposure, the HF component increased, while the LF/HF ratio decreased, indicating relaxation (Figures 4 and 5). In these two subjects, no increases were observed in the θ or δ wave, thereby suggesting the absence of sleep-inducing actions.

On the other hand, electroencephalography did not reveal any stress state in any subject. Neither blood pressure nor the pulse rate showed stress responses in any subject. The timing of the appearance of the stress response and its duration need to be clarified in future studies. Furthermore, since variations were observed in the values obtained in the present study,

more accurate responses may be achieved by increasing the number of subjects.

We adopted a stressor involving physical and mental stresses. With respect to mental stress, Kraepelin-test-related stress based on an increase in salivary amylase activity as reported by Yamaguchi et al. [5], a reduction in the α wave, and an increase in the β wave as reported by Mikicin & Kowalczyk [6]. Stress loading generally increases blood pressure and the pulse rate. In the present study, no stress response was clearly detected despite the physical stress of dumbbell lifting. Young people may not feel stressed by the Kraepelin test because of recent computer/portable game trends; however, this is merely speculation and has not yet been supported in the literature. On inquiry, most subjects reported satisfaction. Furthermore, each examination item was measured approximately 10 minutes after loading. This may have reduced the detection capacity. In future studies, it will be necessary to review the stressor to be established and use Holter's electrocardiography so that the timing of the appearance of the stress response and its duration can be serially measured.

On cedrol exposure, the level of the $\alpha 1$ wave, which reflects relaxation with low-grade awakening, was not high, and no increase was observed in the level of the θ wave on sleep induction (sleepiness). Furthermore, no increase was noted in the level of the δ wave on deep sleep, whereas some wavelengths were recorded due to the detection limit.

This study is a basic experiment for the application to reduce stress of driving by cedrol. In order to apply cedrol to stress relaxation of driving, it is mandatory that cedrol does not cause drowsiness. We further prepare the experimental system so as to obtain a clear result, and want to aim the application of cedrol.

5. Conclusion

In the present study, the number of subjects was low, and marked variations were observed in the results obtained. Therefore, it was impossible to reach a concrete conclusion based on comparisons between the two groups. However, the results of analyses with respect to individuals suggested that cedrol exhibited relaxation effects, and that it did not induce sleep under the conditions adopted in this study.

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