Verification of efficacy as an ergogenic aid and safety in doping of sibjeondaebo-tang

Hyun Jin Yoo¹, Geun Hoon Choi¹, Man Gyoong Lee², Chang Kyun Kang² and Hyon Park¹*¹

¹Exercise Biochemistry Laboratory, College of PE, Kyung Hee University, Global Campus, Korea
²Graduate School of Physical Education, Kyung Hee University, Global Campus, Korea

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INTRODUCTION

Ergogenic aids are dietary supplements intended to enhance athletic performance. Athletes consume diverse kinds of ergogenic aids that can give them an advantage in weight loss, boosting energy during exercise, recovery from fatigue, muscle growth, etc. [1-2]. Positive aspects of popular ergogenic aids which are widely used among most athletes are well known. However, there have been reports that the aids may also undermine physiological function of the athletes [3-4]. Due to lack of organized system to define ergogenic aids, athletes who took the aids without proper knowledge about the aids they consume may suffer serious side effects such as rise in blood pressure, respiratory distress, heart attack and even death [5-6]. Ergogenic aids are also associated with doping rules. Thus, accurate knowledge and understanding about ergogenic aids are required for those who want to benefit from them.

Among diverse ergogenic aids, oriental herb medicines are widely used among athletes in East Asian countries - Korea, China and Japan - to enhance their performance. However, they rely on these medicines merely based on old tradition without verifying the efficacy of the medicines, or checking negative side effects or possibility to violate doping regulations, etc. [7]. Among several studies that investigated the relationship between intake of herbal medicine and athletic performance, Song Soon-gi [8] reported in his study that intake of Bojoong-gikgitang resulted in significant decrease in lactate concentration after exercise. A study by Kim Dong-geon [9] reported that intake of Gyeongokgo in soccer players resulted in increase in maximum oxygen consumption and heart rate recovery after exercise, enhancing the players’ aerobic exercise capacity and recovery from fatigue. Taken together, oriental herbal medicine can be used as an effective ergogenic aids

* Corresponding author: Hyon Park, Tel. 82-31-201-2732, Fax. 82-31-204-8177, Email. hpark@khu.ac.kr

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if its safety is confirmed in doping test.

Studies that looked into safety of herbal medicine for doping test focused on the medicine most widely prescribed for athletics—Sibjeondaebo-Tang. While many athletes took it alone, many other athletes were prescribed with animal folk drugs mixed with Sibjeondaebo-Tang such as Samul-Tang, Sagunja-Tang, etc. [10].

Sibjeondaebo-Tang has been used as an energy booster to reinvigorate tired mind and body, promote appetite and treat patients with anemia [11].

Also, the medicine has been reported to have a potential to be used as a treatment for degenerative brain disorders such as dementia by protecting nerve cell line from oxidation stress and activating glutamine to rejuvenate brain cells. It is also reported to facilitate inhibition of T-cell and growth of hematopoietic stem cell, improving immunity of those who consumed Sibjeondaebo-Tang [12-13]. It has also been reported to enhance muscular endurance and general endurance in athletes [14].

However, whether intake of herbal medicine is safe in doping test has not been confirmed.

Therefore, purpose of this study is to confirm the potential of Sibjeondaebo-Tang as an ergogenic aid by monitoring VO2max, fatigue recovery and change of subjective condition of each individual who took the medicine. Also, its safety in the doping test will be tested to confirm its potential as a safe ergogenic aid. To this end, individuals were subjected to doping test in accordance with WADA protocol to see whether the intake of the herbal medicine produces banned substances.

**METHODS**

**Subjects**

Six 20-something male Taekwondo Pumsae players at K university participated in the experiment. The participants had similar life pattern and exercise volume. This study was performed with an approval of Kyung Hee University Institution Review Board (KHU IRB 2013-G15). Their physical characteristics are shown in the Table 1.

**Study design**

Since efficacy of herbal medicines varies by each individual, all six subjects were tested as one group in order to minimize gap in their exercise ability and blood lactate which were measured repeatedly during the period to see the effects of Sibjeondaebo-Tang and placebo. Also, wash-out period was placed between each measurement in order to minimize possible effects of the herbal medicine taken previously. Double-blind test was applied to all procedures of the experiment.

Before taking Sibjeondaebo-Tang and placebo, all subjects underwent a physical checkup to record their physical characteristics. Then, the subjects took bowls of Sibjeondaebo-Tang and placebo brewed from a pack of herbal medicine three times a day for five days at the same time, at the same place under the supervision of the investigator. After taking the medicine and placebo for five days, their exercise capacities were measured for the same items and they answered the questionnaire about their subjective condition.

Meanwhile, their urine specimens were taken total of five times one day and three days after they took the last dose of the medicine. The doping test was conducted pursuant to the international test standards at a lab where detection and analysis of substances proposed by WADA can be carried out. Proceedings of the overall experiment are shown in the Fig. 1.

| Table. 1. Physical characteristics of subjects |
|-----------------------------------------------|
| Subjects                                      |
|                                               |
| Subjects | 1   | 2   | 3   | 4   | 5   | 6   | Mean ± SD |
| Sex      | M   | M   | M   | M   | M   | M   | M ± 0.00  |
| Age (years) | 20  | 20  | 20  | 20  | 20  | 20  | 20 ± 0.00 |
| Height (cm)  | 175.5 | 170.7 | 172.5 | 174.8 | 184.8 | 174.5 | 175.47 ± 4.90 |
| Weight (kg)    | 74.7  | 63.4  | 69.6  | 64.6  | 78.0  | 66.4  | 69.45 ± 5.83 |
| Muscle Mass (kg) | 56.4  | 49.6  | 53.0  | 49.8  | 58.1  | 51.8  | 53.12 ± 3.49 |
| Percent Body Fat (%) | 18.7  | 15.8  | 18.0  | 17.0  | 19.6  | 16.1  | 17.53 ± 1.50 |

**Fig. 1.** Procedure of experiment
Manufacturing and supply of the herbal medicine

Sibjeondaebro-Tang used in this study was a liquid-type manufactured and supplied based on standard herbal medicine prescription and Donguibogam (Principles and Practice of Eastern Medicine). The placebo used in this study included kudzu, mugwort and small amount of eucommia bark that do not contain bioactive substance in order to embody the taste and smell of herbal medicine. Herbal ingredients of Sibjeondaebro-Tang were not included in the placebo.

Measurement items and methods

Measurement of body size and body composition

A body composition analyser (X-Scan Plus 2, Jawon Medical Co., Ltd., Korea) was used to measure subjects’ height, weight, body mass index (BMI) and total body water.

Step test

A 40 cm high bench and Panoramic Software ver. 2.4.2 metronome were used for the 5-minute step test. The metronome was set at 90 beats per minute, to indicate the stepping rate of 22.5 steps per minute. Polar Heart Rate Analyzer (Finland) was used to measure heart rate for 30 seconds before and after the exercise in order to estimate the heart rate recovery based on VO₂max estimated from the formula developed by Sharkey [15] that used post-exercise heart rate and body weight.

Blood lactate concentration test

An YSI 1500 lactate analysis system (Italy) was used to analyze blood lactate in a blood sample drawn from a finger tip. In order to investigate the effects of Sibjeondaebro-Tang on the fatigue degree of the subjects, blood lactate concentration was measured at the same time every morning. Apart from this, blood specimen were taken before, right after and 30 minutes after the exercise to measure blood lactate concentration that changed during the aerobic step exercise.

Questionnaire

The questionnaire about subjective condition of the subjects consisted of questions on their fatigue degree, digestion, bowel movement and overall conditions in 5-point Likert scale format. The subjects answered the questionnaire after taking Sibjeondaebro-Tang and placebo.

Doping test

A doping control officer approved by KADA (Korea Anti-Doping Agency) collected and transported the subjects’ urine specimen after they finished taking the medicine. All test procedures were carried out at a lab where the samples could be analyzed pursuant to the international test standards and international lab standards.

BEREG-KIT (Berlinger Special AG, Switzerland) used in real doping test was used in the doping test for this experiment. In order to secure reliability of the doping test, gas chromatography, liquid chromatography and mass spectrometer were used to identify about 250 substances banned during the game periods (S0-S9) and substances prohibited in particular sports (P1-P2) considering their chemical characteristics.

Data analysis

The SPSS statistics 21 was used to process data gained from the experiment. Both mean value and standard deviation of all measured values were recorded. Repeated measures two-way ANOVA was used to identify change in blood lactate concentration, while one-way ANOVA was used for the questionnaire on subjective condition in order to identify differences between the groups.

All values were presented via frequency analysis for each item. A p-value < .05 was considered statistically significant.

RESULTS

Change of blood lactate after the intake of Sibjeondaebro-Tang

Blood lactate concentration of the subjects was measured at the same time every morning during the period the subjects took Sibjeondaebro-Tang. However, no significant changes were identified (p < .05).

Measurement of changing blood lactate concentration during aerobic exercise showed no significant change among measurement times in all groups. However, significantly different changes was witnessed (p < .05) among groups - intervention, control and placebo groups. (p < .05). While the measurement for the control group (1.42 ± 0.31 mmol/L), placebo group (1.75 ± 0.51 mmol/L) and intervention group (1.53 ± 0.30 mmol/L) showed no significant difference before taking the medicine, blood lactate concentration in intervention group that took Sibjeondaebro-Tang showed a significant decrease (p < .05) than control group (3.50 ± 0.78 mmol/L) and placebo group (3.45 ± 0.78 mmol/L) after taking the medicine. Also, blood lactate concentration 30 minutes after the exercise showed
Efficacy and doping safety of Sibjeondaeb-Tang

Table. 2. Changes of lactate according to taking herbal medicine (mmol/L)

| Groups              | pre         | post         | post 30 min | P       |
|---------------------|-------------|--------------|-------------|---------|
| Control             | 1.42 ± 0.31 | 3.50 ± 0.78  | 1.84 ± 0.85 | T:0.224 |
| Lactate             | 1.75 ± 0.51 | 3.45 ± 0.78  | 1.97 ± 0.37 | T × G:0.676 |
| Sibjeondaeb-Tang    | 1.53 ± 0.30 | 2.45 ± 0.22  | 1.54 ± 0.41 | G:0.035 |

Mean ± SD, *p < .05, **p < .01, ***p < .001 level. Same alphabet indicates significant difference by LSD. T: time, G: group, T × G: interaction.

Table. 3. Urine specimen analysis results according to Sibjeondaeb-Tang intake

| Subject | Result |
|---------|--------|
| Anabolic agents | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Agents with anti-estrogenic activity | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Narcotics | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Beta-2 agonists | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Stimulants | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Hormone and related substances | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Diuretics and other masking agents | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Cannabinoids | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |
| Glucocorticosteroids | Subject 1 (negative) Subject 4 (negative) |
|          | Subject 2 (negative) Subject 5 (negative) |
|          | Subject 3 (negative) Subject 6 (negative) |

Table. 4. Changes of VO2max according to herbal medicine intake (ml/kg/min).

|                | Control | Placebo | Sibjeondaeb-Tang | F     | P     |
|----------------|---------|---------|------------------|-------|-------|
| VO2max         | 48.67 ± 6.80 | 48.83 ± 3.76 | 45.33 ± 3.93 | .924  | .418  |

Mean ± SD

Results of drug test after the intake of Sibjeondaeb-Tang

A doping test on those who took Sibjeondaeb-Tang gave negative results for all substances specified in the ban list. It may be a natural result given the fact that substances of each medicinal herb used in Sibjeondaeb-Tang did not contain any substance banned in the list of prohibited substances. However, since the process of brewing herbal medicine into liquid type medicine require high temperature and pressure, change in bioactive substances or creation of new substance may occur. Also, how any substance contained in each herb will work in human body through an unknown mechanism has not been pharmacologically defined yet. That’s why doping test was needed for Sibjeondaeb-Tang in order to confirm its safety. Results of the drug test through urine specimen are shown in the Table 3.

Although all urine specimen results were negative, T/E ratio - ratio of testosterone and epitestosterone concentration in the specimen - in one subject was four times higher than the normal level after the intake of both Sibjeondaeb-Tang and placebo, a result that requires additional analysis in accordance with the WADA regulations. However, the level was not as high as to violate the doping rules.

Change of VO2max after the intake of sibjeondaeb-tang

Step test results conducted to investigate the change of subjects’ VO2max after intake of Sibjeondaeb-Tang are shown in the Table 4. Intake of the herbal medicine resulted in no significant difference in VO2max between the control group (48.67 ± 6.80 ml/kg/min), placebo group (48.83 ± 3.76 ml/kg/min) and intervention group (45.33 ± 3.93 ml/kg/min) (p < .05).

Subjective condition after the intake of sibjeondaeb-tang

An analysis on subjective condition of the intervention group and the placebo group showed no statistically significant difference (p < .05). Results of the survey by the two groups are shown in the Table 5.
DISCUSSION

The purpose of this study is to investigate if the intake of Sibjeondaebo-Tang produces doping substances and results in recovery from fatigue and improvement in VO2max - an expected efficacy of the herbal medicine [14,17] - in order to confirm the safety of the oriental medicine. The doping test was conducted in accordance with the test procedures and methods specified in the WADA protocol. The test on those who took Sibjeondaebo-Tang gave negative results for substances specified to be tested during the game period. However, T/E ratio - ratio of testosterone and epitestosterone concentration in the specimen - in one subject was four times higher than the normal level after the intake of both Sibjeondaebo-Tang and placebo. It may have occurred due to several reasons: intake of herbal medicine that contains testosterone, a male hormone, may control the amount of the sex hormone via intermediary metabolic products created by several enzymes [16,18-19]; injection of hormone synthesized outside the body or injection of extracted hormone [20-23]; endocrine disorders [24-25]; race [26]; and etc. However, the result in this study may not have been derived from outside reasons since diets, life pattern, amount of exercise of the subjects have been strictly controlled and subjects were told not to drink and advised to keep existing life pattern. The fact that the T/E ratio was high after the intake of both Sibjeondaebo-Tang and placebo in one person also suggests the same. Thus, high T/E ratio in the test result is deemed to have been derived from a unique personal trait [20,27].

Results from this study are valid only when Sibjeondaebo-Tang is produced based on the standard oriental medicine prescription for Sibjeondaebo-Tang. Doping test results from other applied prescriptions or prescriptions with additional herbs may differ from results in this study, thus require more specific study.

Blood lactate concentration after the intake of Sibjeondaebo-Tang were measured at rest, before, after and 30 minutes after the exercise. Level of concentration did not show significant change at each measurement time except the level measured right after the exercise which was significantly lower than other values, suggesting that lactate created during exercise was reduced as a result of intake of Sibjeondaebo-Tang. The level measured 30 minutes after the exercise also showed some level of decrease, supporting the assumption that intake of Sibjeondaebo-Tang was somewhat effective in reducing fatigue after exercise.

Intake of Sibjeondaebo-Tang resulted in no significant difference in VO2max measured before, after and 30 minutes after the exercise. Generally, it takes at least 6 weeks to 12 weeks for any herbal medicine to produce any physiological effect [32-33]. A short period of time used in this study may explain little difference in VO2max shown in this study. Therefore, long-term study is required in the future to draw concrete conclusion on this subject.

An analysis on subjective condition of the intervention group and the placebo group showed no statistically significant difference in all question items. A short period of time used in this study may also explain little difference in subjective condition since it takes longer period of time for the medicine to produce any effect. Results from the frequency analysis are neither reliable due to the short period of time used in this study. Bitter smell and taste of the medicine may have
been repulsive to the subjects at the beginning of the experiment [34-35], producing negative effects in the subjects. Since oriental medicine combines and processes different kinds of medicinal herbs that contain various substances unlike Western medicine, it is important to consider different component composition of medicinal herbs according to their place of origin [36-38]. Also, clear labeling of ingredients and administrative management the labels are also important.

CONCLUSIONS

The purpose of this study is to confirm the potential of oriental medicine as an ergogenic aid based on effects of Sibjeondaebo-Tang. Also, a doping test pursuant to the WADA protocol was conducted to screen banned substances from urine specimen of the subjects. The test results were all negative. Blood lactate measured right after exercise was significantly lower than others. These suggest that the herbal medicine is an ergogenic aid effective in recovering from fatigue after the exercise. However, due to the method and short period of time used in this study, it would not be appropriate to say that the results are applicable in every case.

Additional studies will be needed for this subject because: it takes far longer period than the period used in this subject for any oriental medicine to produce effect; lack of information on intermediary metabolic products created during the process of the medicine brewing, digestion, absorption; many Sibjeondaebo-Tang used in clinical setting add additional medicinal herbs, etc. Since only several Asian countries consume oriental medicine, there aren’t much interest, clear background knowledge, and scientific studies on oriental medicine. Although increasing number of Western athletes pays attention to and consumes oriental medicine, potential of oriental medicine as an ergogenic aid and its safety in doping test have not been clear. This study was carried out as an initial research on this subject.

Due to short period of time and methodological limits in this study, this study cannot offer enough data for the subject. However, since potential and safety of oriental medicine have been confirmed, interdisciplinary research that involves oriental medicine, sports science, dietetics, etc. should be conducted to draw more definitive conclusions.

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