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난소절제가 체조성에 미치는 장기적 영향*

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Long-Term Effect of Ovariectomy on Body Composition

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= Abstract =

중년기 여성들에서 체중증가로 인한 여러가지 건강문제가 심각해지는데 폐경으로 인한 sex steroid hormone의 변화에 기인되는 것으로 생각된다. Sex steroid hormone의 부족은 체중, 특히 체지방의 축적을 가져오고 한편 뼈의 손실을 가져온다고 알려져 있다.

본 연구에서는 폐경기 후의 여성들과 유사한 조건을 만들기 위해 성숙한 암쥐를 이용하여 난소절제를 한 후 장기적인 체조성의 변화를 조사하였다. 난소절제한 쥐들은 체중과 체지방의 무게가 유의적으로 증가한데 반하여 근육과 뼈의 무게는 대조군과 비교할 때 커다란 변화가 없었다. 이 연구결과는 폐경기 여성들에게 일어나는 체조성 변화에 미치는 sex steroid hormone의 영향을 조사하기 위한 실용적인 animal model로 난소절제한 쥐의 사용가능성을 암시해 주고 있다.

INTRODUCTION

Obesity is the most common health problem in middle-aged women after menopause. Deprivation of sex steroid hormone may be part of the reason to increase body weight in those women. Ovariectomy has been reported to stimulate body weight gain and body fat accretion in mice[1], and rats[2-7], which is mainly due to increased food intake. Estradiol-17β injected systemically[4)7] or implanted in the area of the ventromedial hypothalamus[8)9] reverses these effects resulting in a decrease in food intake and decreased body weight.

The association between bone loss and estrogen deprivation is well documented. Loss of ovarian function at any age is followed by a loss of bone mass[10-12] which is particularly severe after an early menopause[13] and in amenorrheic women[14]. This loss of bone may be prevented by exogenous estrogens for as long as treatment is continued[15-17], yet accelerated after treatment is withdrawn[17-19]. Hence loss of ova-

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rian function is the most important factor in the development of postmenopausal osteoporosis.

However, there were very few studies that have evaluated the effects of estrogen deprivation on body composition. Therefore, in this experiment adult female rats were ovariectomized to make the similar condition as postmenopausal women and study the long-term effect on the body composition such as fat, skeletal muscle and bone.

MATERIALS AND METHODS

Experimental Animals

Six month old female Sprague-Dawley rats were purchased and housed individually in stainless steel hanging cages in a temperature(22± 1℃) and humidity(65± 2%) regulated room. The room was lighted from 0600 to 1800h. Rat chow and tap water were provided ad libitum. After three days of adaptation period, animals were randomly divided into two groups, 10 animals in each group. Ovariectomies were performed to animals in experimental group under sodium pentobarbital(30-40 mg/kg body weight) anesthesia through abdominal incision(ovariectomy) and sham ovariectomies consisted of only the abdominal incision without removal of ovaries(sham operation). After recovery from the operation rat chow and tap water were provided ad libitum for 6 months. Body weight and food intake were measured.

Sampling

Six months after surgery animals were sacrificed by ether. Four skeletal muscles, the biceps brachii from the fore limb, the plantaris from the hind limb, the soleus from the hind limb, and the psoas major from the lower back were dissected out according to the description of Green[20]. Fat and connective tissue were carefully removed and muscles were weighed. Inguinal fat pad, retroperitonial fat pad and perirenal fat pad were removed according to the method reported by Schemmel et al[21] and weighed. The femur from the hind limb and the humerus from the fore limb were removed and weighed.

Statistical Analysis

Statistically significant differences between two group means were determined by student's t-test at $P<0.05$ level[22].

RESULTS AND DISSCUSSION

Food Intake and Body Weight

Ovariectomy(ovx) resulted in a significant increase in food intake compared with sham operation(sham) (Fig. 1). Food intakes were elevated for both groups after the surgery, the magnitude of the increased food intake was larger in ovx compared with sham. Changes in body weight were shown in Fig. 1. Rats with ovariectomy gained weight markedly whereas rats with sham operation gained less weight, consequently ovariectomized rats weighed 26% more than sham-operated rats when they sacrifice.

Blaustein & Wade[2] reported that ovariectomized Sprague-Dawley rats, after 53 days, weighed 25% more than sham-operated controls and Schemmel et al.[23] ovserved similar differences in body weight of Osborne-Mendel rats. Results of this experiment are consistant with those of other reports[3,4] that ovariectomized animals developed obesity as a result of increased food intake. In addition, replacement estradiol injections suppressed food intake with a concomitant loss in body weight[1,7,23]. At present the mechanism how estrogen involves appetite control and body weight control is not clearly understood.

Weights of Fat Pads

Weights of fat pads in three different locations are

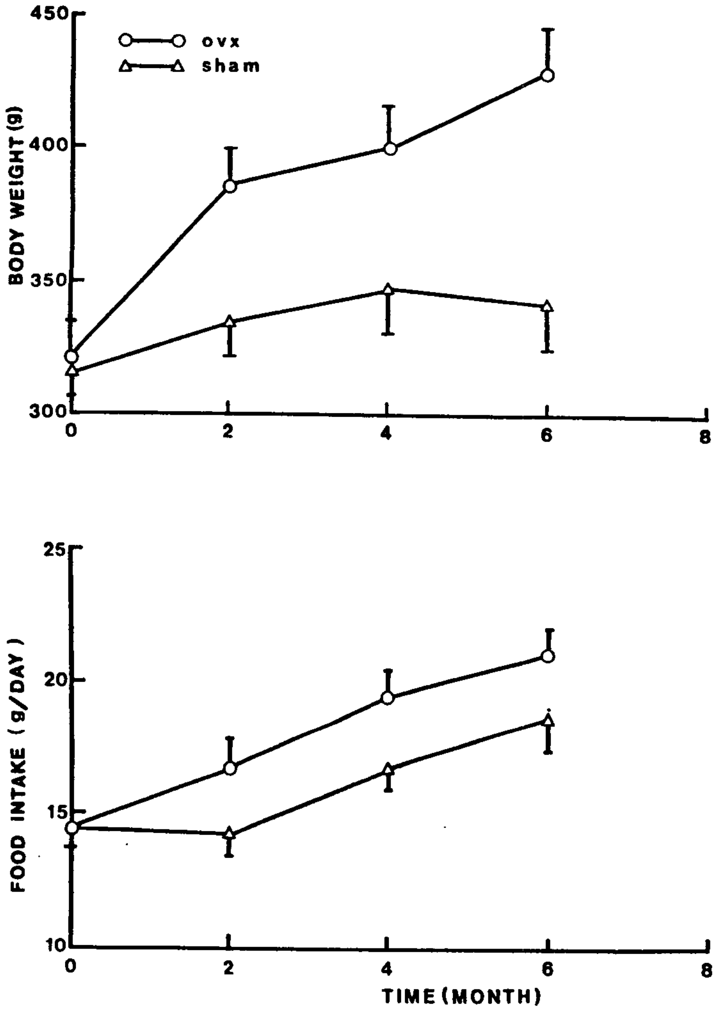

Fig. 1 Body weight and food intake following ovariectomy(ovx) or sham-operation(sham) in rats.

Table 1. Fat pad weight of rats with ovariectomy or sham operation

Fat pad	Ovx	Sham
Inguinal(g)	1.90± 0.12*	0.91± 0.10
(% body weight)	(0.44± 0.03*)	(0.24± 0.04)
Retroperitonial(g)	2.99± 0.45*	1.42± 0.25
(% body weight)	(0.68± 0.08*)	(0.41± 0.07)
Perirenal(g)	3.16± 0.43*	1.21± 0.16
(% body weight)	(0.72± 0.08*)	(0.35± 0.04)

Values are Mean ± SEM
* : Significant at $p<0.05$ by student's t-test

shown in Table 1. Compared to sham rats, fat pads were twice as heavy in ovx rats regardless of locations. To eliminate the difference of body weight between two groups fat weights were expressed as weight per 100g body weight. It indicated that ovx animals accumulated 65-100% more body fat than sham controls.

Similar gains in fat pad weights were observed by Schemmel et al.[23]. Accumulation of fat depot in ovx animals could not explained totally by increase in food intake. Wade[24] speculated the effect of estrogen

Table 2. Muscle weight of rats with ovariectomy or sham operation

Muscle	Ovx	Sham
Biceps brachii(g)	0.280± 0.008*	0.239± 0.006
(% body weight)	(0.066± 0.002)	(0.071± 0.002)
Plantaris(g)	0.336± 0.012*	0.292± 0.007
(% body weight)	(0.079± 0.002)	(0.086± 0.002)
Soleus(g)	0.141± 0.006*	0.133± 0.008
(% body weight)	(0.033± 0.002)	(0.039± 0.002)
Psoas major(g)	1.378± 0.062*	1.113± 0.059
(% body weight)	(0.322± 0.011)	(0.328± 0.016)

Values are Mean ± SEM
* : Significant at $p<0.05$ by student's t-test

on fat utilization and proposed that estradiol reduced total body lipids due to increased mobilization from fat depots. Further study is required to confirm this

Table 3. Bone weight of rats with ovariectomy or sham operation

Bone	Ovx	Sham
Humerus(g)	0.501± 0.022	0.463± 0.016
(% body weight)	(0.117± 0.005*)	(0.137± 0.005)
Femur(g)	1.001± 0.059	0.999± 0.052
(% body weight)	(0.233± 0.011*)	(0.295± 0.015)

Values are Mean ± SEM
* : Significant at $p<0.05$ by student's t-test

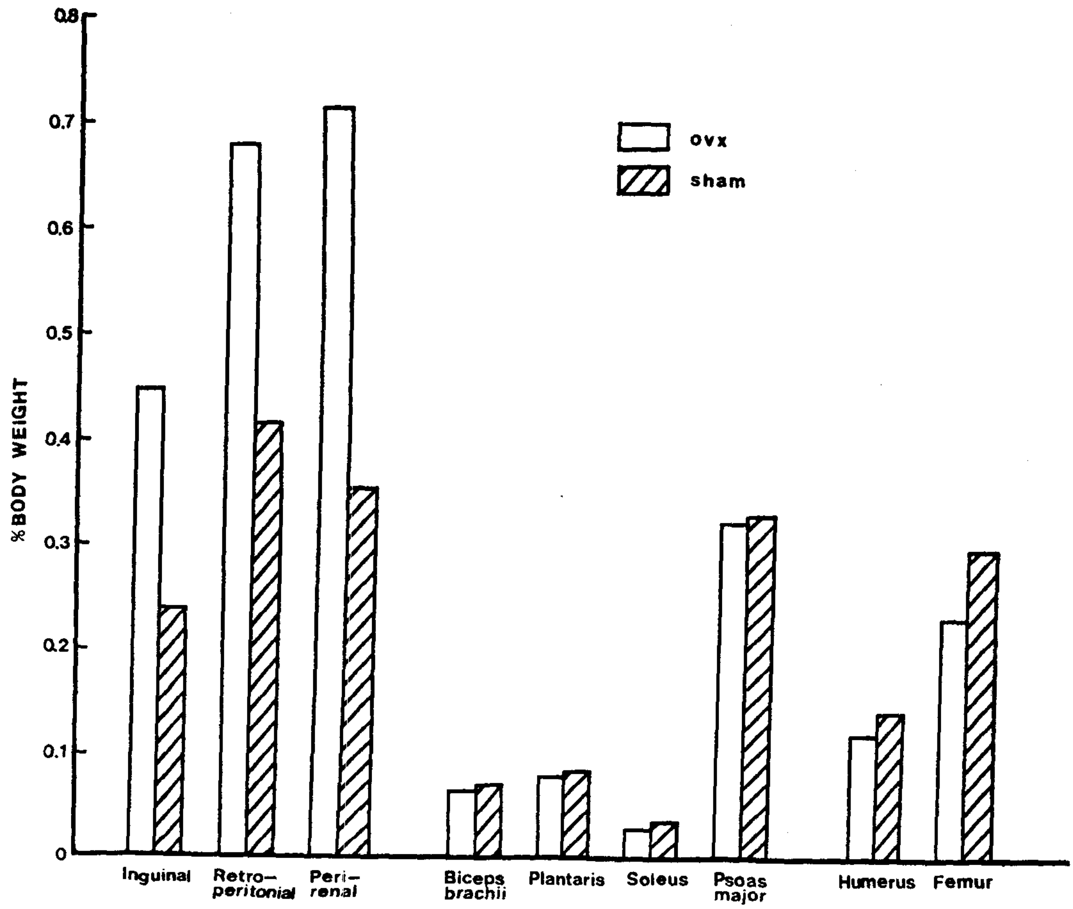

Fig. 2 Percent body weight of fat pads, muscles, and bones of rats with ovariectomy or sham operation.

explanation.

Weights of Muscles

Table 2 shows the weights of muscles in four different locations. The biceps brachii and plantaris of ovx group increased in weight about 15% more than those of sham group. These two muscles were selected as white muscle which is fast twitch muscle mainly consisted with cytoplasmic glycolytic fiber. Soleus muscle increased in weight 6% only while psoas major muscle increased in weight as much as 24%. These two muscles were selected as red muscle which is slow twitch muscle mainly consisted with mitochondrial oxidative fiber[25].

Changes in muscle weights due to ovariectomy were different among different muscles. This result suggests that the weight of the psoas major in lower back was increased when body weight was increased. Because the major function of the psoas major is maintenance of posture, whereas the function of soleus muscle is continual support of the body against gravity, hence the weight of this muscle was not necessarily increased. When the weight of muscle expressed as a percentage of body weight, the values of the ovx group were lower than those of sham group even though the differences were not statistically significant.

Weights of Bones

Bone loss was expected in ovx animals but the weights of bones were not changed by ovariectomy(Table 3). Six months may not be long enough to develop bone loss considering the life span of two years in rats. Mineral contents of bones and bone density were not determined in this experiment, so the porosity or fragility of bones could not be evaluated. When the weight of bone was expressed as a percentage of body weight, it was significantly lower in ovx group than in sham group due to the differences in body weights. Therefore, weight load of bone to support increased body weight in ovx group was much higher than those in sham group.

SUMMARY

The present experiment was performed to study whether or not ovariectomized female rats can be used as an animal model to investigate the effects of estrogen on body compositions. Six-month-old, female rats were ovariectomized and the changes in body compositions were evaluated 6 months after surgery.

As summarized in Fig. 2, body fat accretion was double in ovariectomized rats compared to sham-operated rats. Muscle weights were not different, while bone weights were lower in ovx rats than in sham rats when the values were expressed as a percentage of body weight.

Results of the present study suggest that these ovariectomized rats can be utilized as an animal model to study the body compositions of postmenopausal obese women and related health problems.

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