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The Effect of Physical Exercise on Ovarian Follicles of Perimenopausal Wistar Rats

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Abstract: ***Background: Aging is accompanied by a progressive loss of the functional unit of the ovary, the follicle. A decrease in the number of follicles that are the source of ovarian hormones causes irregularities of the hormonal system. Physical exercise has been recognized by society is very important and inseparable from physical and psychological health. Objective: The main purpose of this study was to examine the effect of physical exercise on the ovarian morphology of perimenopausal wistar rats. Method: This research was conducted at Biomedical Integrated Laboratory of Medical Faculty of Udayana University and Pathobiology Laboratory of Veterinary Faculty of Udayana University in June until November 2016, using 12 female Wistar rats aged 14 months divided into 2 groups, a sedentary control Group (SC) and a trained experimental group (T). The treatment group was given physical exercise to swim for 30 minutes 5 times a week for 30 days. Result: The results showed that the average number of primary follicles, secondary follicles, and tertiary follicles in the T group was significantly higher (p <0.05) than the SC group. The atresic follicle in the T group was significantly lower (p<0.05) than the mean number of atresic follicles in the SC group. Conclusion: This study demonstrates that physical exercise improves ovarian function in perimenopausal wistar rats.***

Keywords: Physical exercise, ovarian follicles, perimenopausal wistar rat

1. Introduction

The normal reproductive function of women includes the repetitive cycle of follicle development, ovulation, and endometrial preparation for implantation. This regular pattern of ovulatory cycles is achieved through good function and integration of stimulation signals and inhibition of the hypothalamus, pituitary, and ovaries [1]. The ovaries follow a different course from the other endocrine glands and organs. In the late thirties the ovaries undergo an abrupt diminution of their functional units, the follicles. A decrease in the number of follicles that are the source of ovarian hormones cause irregularities of the hormonal system and disorganization of the hypothalamic-pituitary-ovarian axis, resulting an unpredictable endocrine status followed by various clinical abnormalities [2]. As life expectancy increases beyond the eighth decade worldwide, especially in developed countries, there are an increasing the proportion of postmenopausal female population [3]. The average age of menopause is at age 51, so that more than a third of a woman's life is now spent after menopause [3]. This will certainly be a health problem that is need a serious attention and as a challenges for the world in improving the quality of life of women in the third part of their life. It has been estimated by mathematical models that the ovaries would be functioning until the age of 71 years if this rapid exhaustion of the follicles did not occurs [2].

Physical exercise has been recognized is very important and inseparable from physical and psychological health and has been supported by facts. It is important to pay attention to the physical exercise performed by women who are a large part of the world's population [4]. The problem is whether the exercise is right and enough to make the body healthy. So the purpose of exercise in relation to maintaining health should be adequate physical activity and beneficial to health but not excessive, not to cause pressure for the body [5]. The health benefits and fitness benefits associated with physical activity and endurance exercise training such as: improve physiological, metabolic and psychological parameters in the body and reduce the risk for early chronic disease and death. This evidence is generated from laboratory based studies and from population studies [6], [7].

The effects of physical exercise on female reproductive function have reported in several studies. Postmenopausal women who exercise regularly have a significant increase in estrogen levels, higher IGF-1 levels than those who do not perform physical exercise [8]. Physical exercise reported has a positive effect on the morphology and ovarian biochemical profiles in rats with Polycystic Ovary Syndrome (PCOS), regular physical exercise tends to modulate sympathetic outflow, proving that physical exercise is effective in the treatment of an ovulation and possibly preventing PCOS in humans. Accordingly, the main purpose of this study was to examine the effect of physical exercise on the ovarian morphology of perimenopausal wistar rats.

2. Research Methods

This research is an experimental research with the design of Randomized Post Test Only Control Group Design. The study was conducted at Biomedical Integrated Laboratory of Medical Faculty of Udayana University and Pathobiology Laboratory of Veterinary Faculty of Udayana University in June until November 2016, using 12 Wistar rats (Rattus norvegicus) aged 14 months

weighing 180-200 grams, divided into 2 groups randomly, (1) sedentary control group (SC) and (2) trained experimental group (T). The treatment group was given swimming exercise for 30 minutes 5 times a week for 30 days. Rats are kept on cages individually with standard food and water ad libitum. After the treatment, rats were sacrificed; the ovaries were dissected from connective tissue, fixed in formalin buffer solution. The preparations anatomical pathology of the ovaries using Hematoxylin-Eosin (HE) staining and observed with a microscope. Observed data, including the number of primary follicles, secondary follicles, tertiary follicles, and atretic follicles. Data were expressed as mean ± SD. Statistical comparisons between groups were done by Student t test. Significance was accepted at the level of $p<0.05$.

3. Results

The results showed that the average number of primary follicles (± SD) in the trained experimental group group was 10.75 ± 0.52, significantly higher ($p <0.05$) than the average number of primary follicles in the sedentary control group (2.33 ± 0.52). The average number of secondary follicles in the trained experimental group was 7.25 ± 0.52, significantly higher ($p<0.05$) than the average number of secondary follicles in the sedentary control group (1.67 ± 0.41). The average number of tertiary follicles in the trained experimental group was 2.67 ± 0.52, significantly higher ($p<0.05$) compared with the mean number of tertiary follicles of the sedentary control group (0.00) or no tertiary follicles found in control group. The atretic follicles in the trained experimental group was 5.50 ± 0.63, significantly lower ($p<0.05$) than the mean number of atretic follicles in the sedentary control group (23.75 ± 1.08).

Table 1: Mean Differences of Follicles in the Control Group and the Treatment Group

	Sedentary Control Group (Mean ± SD)	Trained Experimental Group (Mean ± SD)	t	p
Primary follicles	2.33 ± 0.52	10.75 ± 0.52	28.012	0.000
Secondary follicles	1.67 ± 0.41	7.25 ± 0.52	20.579	0.000
Tertiary follicles	0.00 ± 0.00	2.67 ± 0.52	12.649	0.000
Atretic follicles	23.75 ± 1.08	5.50 ± 0.63	35.620	0.000

4. Discussion

Our result showed that physical exercise had a positive effect on ovarian function. Several studies have reported the role of physical exercise in female reproductive function. Physical exercise improved regular ovulation rate and regular menstrual frequency [9]. In one of systematic review concluded that physical exercise improved ovulation rate, restored reproductive function through hormonal system improvement. These improvements to the hormonal environment provide an opportunity for follicle maturation thereby restoring the occurrence of ovulation [10].

Previous studies on the effect of physical exercise on ovarian morphology in aging ratswere still limited. However, some studies related to other ovarian functions can be described as follows. Postmenopausal women who exercise regularly have a significant increase in estrogen levels compared with those who do not perform physical exercise [8], [11]. This indicates that the mechanisms associated with impaired ovarian function can be enhanced by physical exercise. Physical exercise normalized the morphology and ovarian biochemical profile of PCOS rats, where regular physical exercise tends to modulate sympathetic outflow[12].In line with the recent study, reported that physical exercise normalized ovarian morphology and estrous cycles in rats with PCOS because it can decrease oxidative stress and increase antioxidants in PCOS rats[13].

Oxidative stress also has a role in the aging process because of the excess production of free radicals. In the reproductive system this causes the aging of the ovaries. Regular physical exercise is associated with decreased basal oxidant production and decreased free radical leakage in postmenopausal women. Physical exercise also alleviate frequent complaints in postmenopausal women [14].As there is a decrease in primordial follicle reserve, there is a decrease in the number of follicle recruitment in each cycle [15]. In older people, the growth of follicles becomes slower and there is a decrease in the number of granulosa cells in each follicle. The other changes in the ovaries associated with increasing age are increased mitochondrial deletions in granulosa cells and decreased expression of FSH receptors leading to infertility. The decreased of FSH receptors density leads to decreased oocyte quality with increasing abnormalities on chromosomes [16]–[18].

The number of antral follicles (tertiary follicles) selected to become dominant follicles and ovulatory follicles are highly dependent on the regulatory activity and density of the FSH receptors and LH receptors on the surface of granulosa cells [15]. As FSH levels fall, the growth of smaller follicles will decrease and only those follicles with sufficient number of FSH receptors and LH receptors will continue to grow further as they have the ability to convert and rostenedione into estrogen for growth [18]. Several factors that control the expression of the Follicle Stimulating Hormone Receptors (FSHR) gene and its receptor formation are the Follicle Stimulating Hormone (FSH) itself, a member of the transforming growth factor β family (TGF-β, activin), TGF-α and epidermal growth factor (EGF) and may modulate the expression of FSHR. Another factor that also affects is estrogen. Although estrogen alone does not have an effect on the distribution and amount of FSHR, but estrogen synergizes with exogenous FSH and cAMP to increase the amount of FSHR. This occurs because estrogen can mediate the proliferation of granulosa cells [18].

5. Conclusion

In conclusion, this study demonstrates that physical exercise increases the number of primary, secondary, and tertiary follicles and also decreases the number of atretic follicles. Thus physical exercise improves the ovarian function in perimenopausalwistar rat.

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