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The effect of Eight Weeks Aerobic Exercise on thyroid hormones in female Rats with Polycystic Ovary Syndrome

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Abstract

Purpose: Polycystic ovarian syndrome (PCOS), the most common endocrinopathy of women in the reproductive age group seems to be adversely affected by associated thyroid dysfunction. The purpose of this study was to examine the effect of eight weeks aerobic exercise on thyroid hormones in rats with polycystic ovary syndrome.
Materials and Methods: Forty, adult female Wistar rats (180±20g) underwent an 8-week aerobic training program. The training group was exercised on a rodent motor-driven treadmill at a 0◦ slope for 60 min/day, 5days/wk for 8 wk. During the 1st wk of training the rats ran at treadmill by speed of 10 m/min for 15 min for adaptation. During the 2nd and 3rd wk of training the speed and duration increased step by step until the animals ran for 60 min/day. Paired-sample T tests and one-way analysis of variance (ANOVA) were performed to determine the differences in a parameter among the groups. Significant level was 0.05.
Results: The results show that TSH was not significant between Low intensity group (LIG) and Medium intensity group (MIG) although it was higher in MIG group. Also MIG had significant reduction of TSH compared to CON ($P<0.00$). Also there was no observed significance in T3 between LIG and MIG although mean level of T3 was higher in MIG comparing to CON.
Conclusions: The present study showed that the aerobic training program with different intensity and duration improves thyroid hormones in rats with PCOS.

Keywords: Polycystic ovary syndrome, T3, T4, Aerobic training.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among females. PCOS is a complex, heterogeneous disorder of uncertain etiology, but there is strong evidence that it can, to a large degree, be classified as a genetic disease (Brown et al., 2009; Legro and Strauss, 2002). Insulin resistance (IR) plays a central role in PCOS as a cause or a consequence (Acién et al., 1999). Approximately 50-70% of PCOS women are insulin resistant (Dunaif, 1997).

Obesity is a risk factor for insulin resistance in PCOS women (Barber et al., 2006), and it has been also linked to endocrine disorders especially thyroid dysfunction (Reinehr, 2010). On the other hand, thyroid function even within euthyroid range has been linked to insulin resistance and metabolic syndrome (Garduno-Garcia et al., 2010; Kumar et al., 2009). In addition, increased thyroid volume and nodular gland percentage was reported in euthyroid women with IR (Rezzonico et al., 2008). PCOS is a fairly common condition that some women, particularly with hypothyroidism, can find themselves with, and the more overweight a female is, the worse the signs can be. Because of a variety of indications intercommunicate PCOS (Ganie et al., 2010).

Polycystic ovary syndrome (PCOS), the common endocrinopathy of reproductive age-group women, is a regular cause of menstrual abnormalities, insulin resistance, hyperandrogenism, an ovulation and visceral obesity in these women (Ehrmann, 2005; Franks, 1995; Homburg, 2009; Norman et al., 2007). Although, overt hypothyroidism is known to produce a reversible phenotype similar to that of polycystic ovary syndrome, there are no reports of association of hyperthyroidism with polycystic ovary syndrome. We antecedently reported

association of subclinical hypothyroidism in the full blown cases of PCOS and it did not seem to change any clinical, hormonal or biochemical describe in these subjects (Ganie et al., 2011).

Thyroid hormones have various effects on the reproductive system of the human women. Change in thyroid function, especially hypothyroidism, could be cause ovulatory dysfunction and lead to impaired female fertility (Ganie et al., 2010). Hypothyroidism and PCOS are often accompanied by increased serum free testosterone, high cholesterol and luteinizing hormone (LH). When the ovaries of hypothyroid female by PCOS are viewed with an ultrasound an increase in ovarian volume and the appearance of bilateral multicystic ovaries are often visible (Ganie et al., 2011). In adult woman, severe hypothyroidism may be associated with diminished libido and failure of ovulation. First ovarian failure could also be seen in patients with Hashimoto's thyroiditis as a part of autoimmune polyglandular syndrome.

Seldom, in primary hypothyroidism, secondary depression of pituitary function may lead to ovarian atrophy and amenorrhoea. Pregnancy complications are related to overt and subclinical hypothyroidism, while the impact has chenged among different studies (Pallotti et al., 2005). Brown et al (2009) concluded that moderate-intensity exercise without significant weight loss improved several components of the lipoprotein profiles of female with PCOS. These results protect the functional role of moderate exercise in this high-risk population. Moreover, El-Hafez et al (2013) in their studied on 40 women with PCOS and 62 healthy women matched for age and body mass index (BMI). That they were divided according to HOMA-IR into 2 subgroups: non-insulin resistant and insulin resistant PCOS, concluded that women with PCOS had changes in thyroid function and volume which are linked to a related to IR.

Obesity might be appearing a link between IR and thyroid changes in these women. Ciloglu et al (2005) was investigated the effect of different intensity levels of acute aerobic exercise on thyroid hormones in 60 male well-trained by performing bicycle ergometer at 45% (low intensity), 70% (moderate intensity), and 90% (high intensity). They found that exercise performed at the anaerobic threshold (70% of maximum heart rate, lactate level 4.59 ± 1.75 mmol/l) caused the most prominent changes in the amount of any hormone levels. However, the rate of T4, TSH and fT4 continued to rise at 90% of maximum heart rate, the rate of T3 and fT3 started to fall. Only few studies are reported suggesting a relationship between autoimmune diseases including Hashimoto's thyroiditis and PCOS (Chen et al., 2010; Goi et al., 1992; Matsuoka et al., 1986; Singh and Agrawal, 1993). Therefore, this study was to determine the effect of eight weeks aerobic exercise on thyroid hormones in rats with polycystic ovary syndrome.

Materials and Methods

Subjects and PCO protocol

40 adult Wistar females (180±20 g body weight) selected in this study. The animals had free access to pelleted rat food and water, and they were maintained ambient temperatures 23 ± 2 ° c during the day and were exposed to 12 hours light and 12 hours of darkness with relative humidity of 60-40. The rats divided into four groups: control group (HCO) (n=10), control of polycystic ovary syndrome (PCO) (n=10); polycystic ovary syndrome with low intensity exercise (LI) (n=10) and polycystic ovary syndrome with medium intensity exercise (MI) (n=10).

Animals were displaying at least 2 consecutive normal four-day estrous cycles were used in this study. Estrous cycles before and after treatment was monitored by daily examination of vaginal smears. Animals in estrus were each lightly anesanterior with ether and injected i.m. with 2 mg estradiol valerate (EV) dissolved in sesame oil. The remaining 5 animals (also in estrus) served as controls and were injected with sesame oil only (Atis et al., 2012).

In our experience, there is a period of irregular cyclicity that precedes the onset of persistent vaginal cornification (PVC) (Brawer et al., 1978). To determine whether treated animals ovulate, and if so, to what extent and for how long, we had intended to kill animals at each consecutive estrus after EV treatment so that tubal ova could be counted. As it happened, all EV-treated animals ceased cycling immediately and showed random mixed smears (i.e. diestrus- proestrus or all cell types) for the first 15-20 days, after which all animals exhibited PVC.

Exercise training protocol

The training group was exercised on a rodent motor-driven treadmill at a 0◦ slope for 60 min/day, 5days/wk for 8 wk. During the 1st wk of training the rats ran at treadmill speed of 10 m/min for 15 min for adaptation. During the 2nd and 3rd wk of training the treadmill speed and exercise duration increased step by step until the animals ran for 60 min/day. The treadmill speed and exercise duration were then held constant for the remainder of the training period. We kept training frequency (5d/wk) and duration (60 min/d) constant and modified training intensity since we were interested in whether increased training stress brought about by aerobic exercise

training affected fasting blood glucose and insulin(Garekani, et al., 2011). The exercise plan started with short-duration and light movements and gradually increased in intensity.

Blood collection and tissue preparation

To derogate the effect of acute exercise, the rats were eventually anesthetized with diethyl ether and sodium pentobarbital (50 mg/kg, intraperitioneal injection) after a 12-h fast and 32 h after the last training session and their blood was gleaned from the abdominal aorta. Tubes containing plasma sample aliquots were kept frozen at −80 ◦C until being analyzed.

Measurements

From the blood samples, T4 (Diatech Diagnostic enzyme immunoassay test kit), T3 (Diatech Diagnostic enzyme immunoassay test kit) values were measured. Duplicate measurements were made for each sample, and the mean of the duplicate measurements was assigned as the sample value. Blind duplicates were used for determining coefficients of variation (CV).

Statistical analyzing

A Shapiro-Wilk test was applied to determine of normality of distribution of measures which were found to be unmorally distributed. Kruskal-Wallis Test was performed to determine the differences in a parameter among the groups.

Significant differences were identified using a least significant difference (Bonfferoni) post-hoc test. All data were expressed as mean ± SD and significance was established at the alpha level $p<0.05$. All statistical analysis was done by SPSS version 16.

Results

The results show that TSH was not significant between Low intensity group (LIG) and Medium intensity group (MIG) although it was higher in MIG group (table1). TSH level was significantly difference in LIG comparing to Control (CON) group ($P<0.00$). Also MIG had significant reduction of TSH compared to CON ($P<0.00$) as are clear in figure1. Also there was no observed significance in T3 between LIG and MIG although mean level of T3 was higher in MIG comparing to CON or LIG and no observation of significance in CON and other experimental groups (Figure 3).

There is no significant difference between LIG and MIG in T4 variable but MIG T4 level was higher than LIG. Also no significance considered between CON and LIG or MIG (Figure 2).

Table 1: Variables of all groups

variables	TSH µIU/ml	T3 ng/ml	T4 ng/ml
MIG	2.13±0.35	1.93±0.48	94.62±0.29
LIG	1.95±0.47	1.38±0.36	81.55±0.19
CON	4.7±12.5	1.45±18.4	77.43±16.59

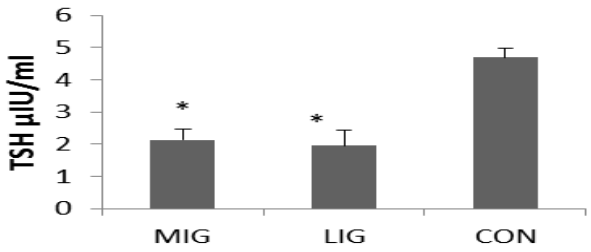

Figure 1: TSH Level after 8 week exercise training

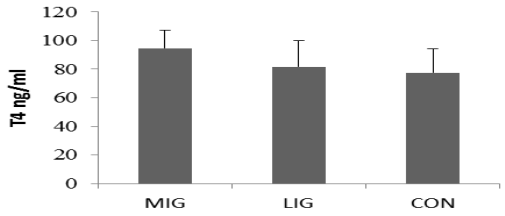

Figure 2: T4 Level after 8 week exercise training

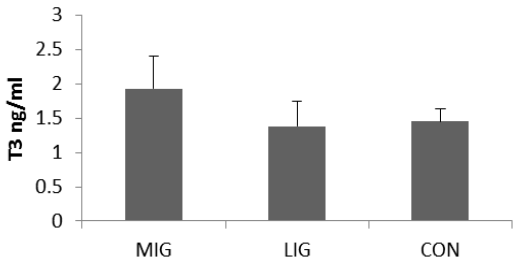

Figure 3: T3 Level after 8 week exercise training

Discussion and Conclusion

Limited data are available regarding the relation of insulin resistance with thyroid function and volume in PCOS women. In the current study, TSH was not significant between Low intensity group (LIG) and Medium intensity group (MIG) although it was higher in MIG group. TSH level was significantly difference in LIG comparing to Control (CON) group. Previous studies tried to explore thyroid changes in PCOS. Mostly the results of these studies showed elevated TSH and higher autoimmune thyroiditis in PCOS women as compared to control women without PCOS (Janssen et al., 2004; Sinha et al., 2013).

Janssen et al (2004) showed higher incidence of elevated TSH levels and four times higher prevalence of autoimmune thyroiditis in PCOS subjects. Kachuei et al (2012) from Iran has also shown significantly higher prevalence of autoimmune thyroiditis and goiter in PCOS patients than that in control subjects. Ozdemir et al (2011) observed that thyroid nodule prevalence and volume did not differ between PCOS patients with and without IR. However, previous studies reported larger thyroid volume and increased nodule prevalence in subjects with IR (Ayturk et al., 2009; Rezzonico et al., 2008) this together with our results support that thyroid changes are linked to insulin resistance in PCOS, so that PCOS only might not related to thyroid function or volume changes. In addition to that, there was no observed significance in T3 between LIG and MIG although mean level of T3 was higher in MIG comparing to CON or LIG and no observation of significance in CON and other experimental groups. Thus, these findings correspond with findings from Lucia et al (2001) and Beyleroglu (2011).

Lucia et al (2001) examined the thyroid hormone levels of professional cyclists during a 3-week stage competition, they concluded that serum T4, FT4 and FT3 levels showed a significant increase by the last week of competition while concentrations of TSH and T3 remained unchanged. Beyleroglu (2011) showed that there were no statistically significant differences among three measurements in the serum levels of TSH and thyroid hormones. However, both fT3 and TSH were significantly decreased in one hour later after exercise, whereas no change was observed in fT4. Koistinen et al (1996) on unacclimatized top class skiers showed that training at moderate altitude for 12 days resulted in a significant decrease in serum total T3 levels and an increase in fT3 levels with no significant change in TSH, T4, fT4 and reverse T3 (rT3). Physical exercise has been reported to stimulate the peripheral deiodination of T4 and an increased uptake of T4 in the liver during exercise (Opstad et al., 1984). Increased conversion of T4 to T3 by peripheral tissues during training is improbable since there were no significant changes in serum fT3 concentrations after immediately exercise in the present study.

Our results demonstrate there is no significant difference between LIG and MIG in T4 variable but MIG T4 level was higher than LIG. Also no significance considered between CON and LIG or MIG. There is a discrepancy in the results of studies on effect of exercise on thyroid hormone levels. In a study conducted by Pakerinen et. al. study on the effects of one week of very intense strength training on the thyroid hormones of male weight lifters showed a significant decrease in TSH, T3 and T4 with unchanged fT4, rT3 and thyroid binding globulin (TBG). Another study done by Deligiannis et al (1993) investigated the response of thyroid hormone to swimming for 30 minutes at varying water temperatures showed that TSH and fT4 levels were significantly increased at 20°C as compared to 32°C but no significant effect was seen on triiodothyronine. In an

previously study, Krotkiewski et al (1984) measured thyroid hormones before, during and after acute exercise (60 min) or physical training (3 months) in obese women; thyroid stimulating hormone concentration increased during acute work and decreased as soon as possible after. No variations were seen during the two following days. Thyroxine concentrations displayed no changes. Triiodothyronine decreased slightly immediately after acute exercise.

In a study carried out by Fortunato et al (2008), in their studied they classified rats into five groups to elucidate the effects of a session of acute exercise on the treadmill at 75% of maximum oxygen consumption on thyroid function of rats: Control (without exercise), and killed just after (0 min) or 30, 60, and 120 min after the end of the exercise session. They reported that a significant increase in T3 occurred just after the exercise; with a gradual decrease thereafter so that 120 min after the end of the exercise, serum T3 was significantly lower than that of controls. Total thyroxin, T4 increased progressively reaching values significantly higher than the control group at 120 min. T3/T4 ratio was significantly decreased 60 and 120 min after exercise, indicating impaired T4-to-T3 conversion. It has been reported that the type, intensity and duration of the training regimes, as well as the training background of the subjects, play a role in the changes taking place in serum T4 and fT4 levels have suggested that training may slightly impair thyroid function (Pakarinen et al., 1988).

In summary, the intensity and duration of the exercise program are important and an increase in accessible energy would result in a change in thyroid hormones levels. Therefore, we can conclude that exercise can change hormonal concentration of TSH, T3 and T4 in rats with polycystic ovary syndrome.

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