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Research Article

**Evaluation of Muscle Profiles with reference to
Estradiol Valerate in Aged female Albino Rats**

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ABSTRACT

The main objective of this study was to evaluate the effect of estradiol valerate on muscle in female aged rats. In the present study estradiol valerate (Progynova) was administered to aged female rats and studied muscle profiles. In the present study estradiol valerate (progynova tablets) administered orally at the dose of 8mg/Kg body weight/day to aged female rats for one week through oral gavages method. The administration does not regain the reduced proteins and carbohydrates. Lowered muscle lipids do not altered by administration.

Key Words: Quadriceps femoris muscle, Estradiol valerate, Osteoporosis, Lipids.

INTRODUCTION

Aging is an important event in the life of mammals including human beings, during which a number of metabolic and hormonal changes take place. In post-menopausal women, having a low concentration of estradiol and progesterone, there is an increased risk of various health problems such as diabetes, cardiovascular complications, osteoporosis and others¹⁻². The physiological hallmark of menopause is the decrease in the production of endogenous sex hormones by the ovaries. Osteoporosis is considered a major public health problem and it is characterized by decrease bone density, resulting in skeletal fragility and fractures³. Estrogen replacement therapy after menopause is associated with a lower incidence of cardiovascular disease and the cardio protective effect of estrogen can be attributed to changes in plasma lipid levels. Abbey *et al.*, (1999)⁴ reported that the role of HRT in post-menopausal women is to maintain a lipid profile, which has been estimated to be 25%–50% cardio-protective and has been attributed mainly to restoration of lipoprotein profiles by estrogen.

Estrogen replacement is frequently the treatment of choice for maintaining reproductive function and bone mineral density in post-menopausal women and amenorrheic adolescents. While estrogen's effects on the reproductive system and bone are well established, less is known about how it affects other tissues⁵. Skeletal muscle is a tissue that is expected to be estrogen responsive since it has estrogen receptors

with properties similar to those in classical target organs. Estrogen may increase the maximal activity of key lipid oxidation enzymes⁶ and alter myosin heavy chain (MHC) isoform expression⁷. Estrogen also seems to attenuate skeletal muscle damage as measured by the release of cytosolic enzymes or other markers⁸⁻¹⁰. Therefore the present study was aimed to evaluate the effect of estradiol valerate on muscle profiles.

MATERIALS AND METHODS

In the present study healthy female albino rats were used. The rats were purchased from Sri Raghavendra Enterprises, Bangalore, India and divided in to three groups. First group are young rats (4 months), second group are aged rats (20 months) and third group are aged rats administered with estradiol valerate (progynova tablets) (2mg/animal/day)¹¹ orally for one week with gastric gavages method. Animals were housed in a clean polypropylene cage under hygienic conditions in well ventilated clean air conditioned room, with photoperiod of 12 hours light and 12 hours dark cycle at 25±2°C, with a relative humidity of 50±5%. The rats were fed with standard laboratory feed supplied by Hindustan Lever Ltd, Mumbai and water *ad libitum*. The usage of animals was approved by the institutional animal ethical committee, in its resolution no: 13/2012-2013(i)/a/CPCSEA/IAEC/SVU/CC - AL dt.01-07-2012. Twenty four hours after the last dose, the

animals were autopsied. The quadriceps femoris muscle isolated, chilled immediately and used for biochemical analysis. The total proteins¹², total carbohydrates¹³, total lipids¹⁴, triglycerides¹⁵ and phospholipids¹⁶ were estimated in young, aged and estradiol valerate administered aged female rats.

RESULTS AND DISCUSSION

The data represented in table 1 indicates the levels of total proteins, total carbohydrates, total lipids, triglycerides and phospholipids in muscle.

Muscle proteins were slightly reduced in aged rats over young rats while these were further reduced by administration. Skeletal muscle is a tissue that is expected to be estrogen responsive since it has estrogen receptors with properties similar to those in classical target organs. These receptors appear to be functional, demonstrating diverse effects of estrogen on skeletal muscle. Estrogen also seems to attenuate skeletal muscle damage as measured by the release of cytosolic enzymes or other markers¹⁷⁻¹⁹. Estrogen deficiency does not affect soleus muscle fiber maximal shortening velocity²⁰, the functional measure most highly correlated with myosin ATPase activity²¹. Thus EV administration does not showed any effect on muscle proteins.

In muscle, carbohydrates do not show any significant changes in aged rats but in EV administration significant reduction (-7.98%) was observed. Carbohydrates fulfill both structural and metabolic roles. Carbohydrates are major constituents of animal food and tissues. The glucose is the most important

carbohydrate in the animal biochemistry because nearly all carbohydrates in food are converted to glucose for further metabolism. Glucose is a major fuel of the tissues of animals. It is converted into other carbohydrates having highly specific function, viz., glycogen for storage, in certain complex lipids and in combinations with proteins in glycoproteins²². There were no significant changes in muscle carbohydrates in aged rats over young once, but estradiol reduces over aged rats.

Muscle lipids were lowered by age, but not altered by EV administration. Estradiol treatment reduces the expression of lipogenic genes in adipocytes from ovariectomized mice²³ and reduces lipid oxidation in skeletal muscle in ovariectomized rats⁶. These findings support the reduced muscle lipids. Muscle triglyceride content was substantially lowered in aged rats and EV administered rats.

In muscle the phospholipids were significantly decreased in aged rats but EV administration does not showed any effect. The phospholipids were lowered in aged rats due to lowered estrogens in muscle. The most abundant membrane lipids are the phospholipids. They serve primarily as structural elements of membranes and are never stored in large amounts. However, as indicated by studies on the analysis of membrane phospholipids, substantial changes occur in phospholipids profiles with age. Phospholipids such as phosphatidyl inositol and phosphatidyl serine inhibit the binding of R5020 and progesterin receptors.

Table 1
The levels of Total proteins, Total carbohydrates, Total lipids, Triglycerides and Phospholipids in muscle of young, aged and EV administered aged female rats.

S.No	Parameter	Young (1)	Aged (2)	% Change (1&2)	EV administered aged (3)	% Change (2&3)
1.	Total proteins (mg/g wet wt)	105.0 ± 9.23	97.2 ± 8.16	-7.42***	90.83 ± 3.26	-6.55***
2.	Total carbohydrates (mg/g wet wt)	2.279 ± 0.120	2.318 ± 0.190	+1.71 ^{NS}	2.133 ± 0.100	-7.98***
3.	Total Lipids (mg/g wet wt)	62.31 ± 4.73	50.96 ± 3.94	-18.21**	49.01 ± 3.26	-3.82 ^{NS}
4.	Triglycerides (mg/g wet wt)	25.71 ± 1.97	21.25 ± 1.65	-17.34**	19.87 ± 1.01	-6.49***
5.	Phospholipids (mg/g wet wt)	24.32 ± 1.98	20.98 ± 1.72	-13.73**	20.12 ± 1.65	-4.09 ^{NS}

Mean ± SD of six individual observations. * indicates P<0.001 the level of significance, **indicates P<0.01 the level of significance, ***indicates P<0.05, NS- indicates non significant changes.

The effect of phospholipids on the binding of estrogen and estrogen receptors of rat uterine cytosol was studied. Phosphatidyl choline, sphingomyelin, phosphatidyl inositol, phosphatidyl ethanolamine, cardiolipin and phosphatidic acid inhibited the binding of estradiol and estrogen receptors. This inhibitory effect of phosphatidyl inositol and cardiolipin was dose dependent. Phospholipids act as a pool for the fatty acid precursors required for uterine prostaglandin synthesis. The availability of the prostaglandin fatty acid precursors is dependent upon the availability of free fatty acids^{24, 25}. Estrogen affects free fatty acids, cholesterol and phospholipids²⁶. Phospholipids, triacylglycerols and cholesterol were identified as the main lipid components of the ovaries during the process of vitellogenesis. EV administration does not show any significant effect on muscle phospholipids.

CONCLUSION

The administration of estradiol valerate reduces muscle carbohydrates in aged rats. Muscle lipids were not altered by administration. However, muscle triglycerides were substantially lowered in aged rats and EV administered rats. Thus the administration of estradiol valerate does not show much effect on muscle.

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