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Research Article

A STUDY ON OVARIAN METABOLIC PROFILES IN ESTRADIOL VALERATE ADMINISTERED AGED FEMALE RATS

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ABSTRACT

Estradiol is the most potent naturally occurring ovarian estrogen in mammals. Estradiol is effective for replacement therapy in woman and used to treat symptoms associated with menopause such as hot flashes and vaginal dryness, burning and irritation in which hormone levels are low and to prevent osteoporosis. In the present study estradiol valerate administration for old aged female rats shows some influence on the structural organization of ovary by increasing the organ weight and TSI. The treatment reduces dry matter and enhances the water content significantly in ovary. The metabolic components like total proteins are decreased less significantly by treatment. There was no significant change in ovarian carbohydrates was noticed. The lipids were significantly enhanced in ovary. Thus the estradiol treatment associated with potentially adverse changes in lipids and proteins. The decreased proteins by the estradiol treatment suggest there was no risk of ovarian cancer by the treatment. The reduced carbohydrates were coinciding with the reduced plasma glucose levels. Hence hyperglycemia is not recommended by the treatment. The increased ovarian cholesterol in old and EV treated rats suggest the accumulation of cholesterol as it is not utilized for ovarian functions like ovarian follicle dynamics. The decreased ovarian FFAs are due to lowered estrogen levels by age suggest their mobilization towards oxidative metabolism and ketogenesis.

Keywords: Ovary, Aged female albino rats, Estradiol valerate, Lipid profiles

INTRODUCTION

Aging is a syndrome of changes that are deleterious, progressive, universal and thus far irreversible. Aging damage occurs to molecules (DNA, proteins, lipids), to cells and to organs. Waste products accumulate in tissue with aging. A fatty brown pigment called lipofuscin collects in many tissues, as do other fatty substances [1]. As a woman ages, a number of changes take place in the female reproductive system. For women, the cessation of menses (menopause) is an obvious sign of aging. The menopausal transition in human females, which is driven by a cyclic ovarian function, occurs around age 50 and is thought to underlie the emergence of an array of health problems in aging women. Although mice do not undergo a true menopause, female mice exhibit ovarian failure long before death because of chronological age and subsequently develop many of the same age-associated health complications observed in postmenopausal women [2]. Changes occur in the intricate relationship between the ovarian hormones and those produced by the pituitary gland (in the brain) [1,3&4]. The causes of these changes are not well understood, majorly due to the decreased levels of estrogens produced by the ovaries. It is the primary circulating estrogen before menopause [5]. During menopause estradiol levels were decereased [6]. There are some reports on the modulating effects of estradiol and progesterone [7] on the obesity and hyperinsulinemic and hyperglycemic components of the diabetes-obesity syndrome in female mice, which includes cellular atrophy and adiposity in the reproductive tract. Hormone replacement therapy with estrogen can prevent some of these changes [8].There are several synthetic estrogens like premarin, progynova. Progynova tablets contain the active ingredient estradiol valerate which is a naturally occurring form of the main female sex hormone, oestrogen [9]. The aim of the present study was to evaluate the effect of estrdiol in the form of progynova on ovarian metabolites in aged female albino rats

MATERIALS AND METHODS

Healthy young (4 months old) and old age (20 months old) female Wistar strain albino rats were taken and divided in to three batches. First batch young rats, second batch are old age rats and third batch are old age rats administered with Estradiol valerate (progynova tablets)(2mg/animal/day) orally for one week. All animals were maintained in standard air conditioned animal house at a temperature of 25±2ºc, exposed to 12-14h day& light and fed on standard rat feed obtained from Hindustan Lever Ltd., Bombay, India. The usage of animals was approved by the Institutional Animal Ethics committee (Regd.No. 438/01/a/CPCSEA/dt.17/02/2001) in its resolution number 9/IAEC/SVU/Zool/dt.4-3-2002. Twenty four h after the last dose, the animals were autopsied, the reproductive tissue like ovary was isolated chilled immediately and used for biochemical analysis. The TSI (Tissue Somatic Index), dry matter and water content were analyzed gravimetrically. The total proteins [10], total carbohydrates [11], total lipids [12], total cholesterol [13], Phospholipids [14], Triglycerides [15] and free fatty acids were estimated in young, old age and old age +estradiol valerate administered rat tissues.

RESULT AND DISCUSSION

The data represented in table - 1 indicates the gravimetric analysis- the body weight, paired tissue weight, TSI, dry matter and water content of ovary in young, old and old treated with estradiol valerate (EV) female albino rats.

The body weight significantly increased (+24.81%) by age and the treatment does not shows any significant changes on the body weight. The paired ovaries weight decreased (-40.54%) by age and increased (+15.90%; $P<0.05$) by treatment. The dry matter increased (+49.37%) with decreased water content (-12.76%; $P<0.02$) by age. The treatment significantly decreases dry matter (-66.6%) while the percentage of water content is increased (+ 28.69%).

The administration of estradiol does not show any significant changes on body weight. The total organ weight & TSI of ovary, a primary sex organ is less in old rats than that of young due to the lowered estrogens [16]. But the treatment enhanced ovary weight as well as TSI more than young. This may be due to the accumulation of lipids [1]. The treatment reduces dry matter and enhances the water content significantly in ovary. These observations revealed that there was some influence on the structural composition of the organs by estradiol treatment.

The data represented in table - 2 indicates the proximate analysis of ovary. The metabolic components like total proteins are decreased less significantly by treatment. There was no significant change in ovarian carbohydrates. The lipids were significantly enhanced in ovary.

The decreased ovarian proteins by administration confirm the increased protease activity. Hence the protein biosynthetic

machinery seems to be slower in ovary [17]. It indicates that the estradiol valerate (EV) does not show any effect on follicular development. The reports on ovarian cancer suggest that there was an increased protein synthesis. Thus the decreased proteins by the EV treatment suggest there was no risk of ovarian cancer by the treatment.

Reduced ovarian carbohydrates (-17.07%) in old aged rats with no significant changes by treatment were observed. The carbohydrate metabolism in general and glycogen metabolic wing in particular play an important role in reproductive tissue functions and the carbohydrate metabolism was shown to be dependent on the levels of gonadotropins and gonadal hormones [18]. The estradiol treatment does not show any significant effect on ovarian carbohydrates. Hence hyperglycemia is not recommended by the treatment.

The total lipids in ovary were increased by age and also treatment. The menopause is associated with potentially adverse changes in lipids and lipoproteins, independent of any effects of ageing. These changes may in part explain the increased incidence of coronary heart disease seen in postmenopausal women [19]. In the present study lipids were elevated significantly in old aged rats. Forbes (1986) [20] suggested that estrogens increase lipid mobilization from adipose tissue to offset the negative energy balance by diverting non esterified fatty acids away from the adipose depots to serve as energy precursors of various tissues. So due to the lowered estrogens in old rats the lipids were accumulated and there by enhanced. The enhanced ovarian lipids were observed by the treatment. The lowered serum lipid profiles may causes the increased total lipids in ovary [21]. Increased ovarian lipid content in estradiol treated old female rats indicates the inactivation of lipase activity [22&23].

The data represented in table 3 indicates the levels of total cholesterol, free fatty acids, phospholipids and triglycerides.

Cholesterol levels were increased (+26.57%) in ovary by age and by the treatment (+51.90%).

Cholesterol is present in tissues and in plasma lipoproteins either as free cholesterol or as cholesteryl ester. It is synthesized in many tissues from acetyl co-A and is the precursor of all other steroids in the body such as corticosteroids, sex hormones, bile acids and vitamin D. Cholesterol and its esters are used for biosynthesis of membrane lipoprotein layers and several metabolically active compounds. The localization of cholesterol may also be attributed to the architectural and physiological functions of the tissue [24].

The increased ovarian cholesterol in old and EV treated rats suggest the accumulation of cholesterol as it is not utilized for ovarian functions like ovarian follicle dynamics. The hypothalamus produces hormones that control the other structures in the endocrine system. The amount of these regulating hormones stays about the same, but the response by the endocrine organs can change by age [18]. Hence in the present study the accumulated cholesterol indicates the ovary as an endocrine gland, the secretion of estrogens are decreased by age which is not reverted by EV treatment. The increased cholesterol also suggests the increased biosynthesis. The treatment does not show much effect on ovarian phospholipids.

The ovarian free fatty acids were lowered (-14.71 & -11.7%) by age and treatment. The decreased ovarian FFAs are due to lowered estrogen levels by age [25&26]; suggest their mobilization towards oxidative metabolism and ketogenesis.

The ovarian triglycerides were enhanced (+62.32%) in old rats and reduced (-35.21%) by treatment. They play a major role in lipid transport and storage and in various physiological conditions such as obesity, diabetes, and hyper lipoproteinemia. In the present study the ovarian triglycerides were significantly raised in old rates is due to the reduced estrogens. These accumulated ovarian triglycerides were significantly lowered by EV treatment. Thus Estradiol valerate mobilize the oxidation of triglycerides.

Table: 1 Gravimetric analysis in ovary of young, old and old + estradiol valerate treated rats.

S. No.	Parameter	Young (1)	% Change Significance (1&2)	Old (2)	% Change significance (2&3)	Old + Treatment (3)
1.	Body weight (g)	200.50±18.43	+24.81*	250.25±17.89	+0.59NS	251.75±24.23
2.	Paired ovaries weight (g)	0.074± 0.005	-40.54*	0.044± 0.001	+15.90***	0.051± 0.009
3.	T S I	0.037± 0.02	-54.05*	0.017± 0.001	+17.64**	0.020± 0.002
4.	Dry matter (mg/g wet wt.)	200.9± 17.3	+49.37*	300.1± 21.9	-66.6*	100.2± 8.3
4.	Water content (%)	80.7± 7.3	-12.76****	70.4±6.2	+28.69*	90.6± 8.4

Values are mean ± S.E.M (n = 6)

Inter- group comparison: * P < 0.001 statistically significant, ** P < 0.01 statistically significant, *** P<0.05 statistically significant, **** P<0.02 statistically significant, NS indicates Non significant changes.

Table: 2 Proximate analysis in ovary of young, old and old + estradiol valerate treated rats.

S. No.	Parameter	Young (1)	% Change Significance (1&2)	Old (2)	% Change significance (2&3)	Old + Treatment (3)
1.	Total proteins (mg/g wet wt.)	77.98± 6.78	-16.47*	65.13± 5.23	-7.79***	60.05± 3.77
2.	Total carbohydrates (mg/g wet wt.)	4.082± 0.291	-17.07*	3.385± 0.123	-2.71NS	3.293± 0.101
3.	Total lipids (mg/g wet wt.)	166.6± 10.97	+150.1*	416.5± 29.7	+50.06*	625.2± 50.9

Values are mean ± S.E.M (n = 6)

Table 3: Levels of lipid profiles in ovary of young, old and old + estradiol treated rats.

S. No.	Parameter	Young (1)	% Change Significance (1&2)	Old (2)	% Change significance (2&3)	Old + Treatment (3)
1.	Total Cholesterol (mg/g wet wt.)	2.07±0.18	+26.57*	2.62±0.19	+51.90*	3.98±0.22
2.	Phospholipids (mg/g wet wt.)	51.39±3.81	+14.88**	59.04±4.12	-5.53***	55.77±2.98
3.	Free fatty acids (mg/g wet wt.)	35.06±2.23	-14.71*	29.9±1.87	-11.7***	26.4±1.89
4.	Triglycerides (mg/g wet wt.)	2.75±0.213	+62.32*	4.464±0.372	-35.21*	2.892±0.267

Values are mean ± S.E.M (n = 6)

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