

Effect of Vitamin E on Uterine Myometrium of Adult Female Albino Rats Treated With Fluoxetine

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ABSTRACT

Background: Vitamin E is well known for its antioxidant property and has potential role in treatment of infertility. Fluoxetine is an antidepressant from SSRI group having effect on reproductive organs by increasing oxidative stress.

Aim: To explore the role of vitamin E on uterine myometrium after treatment with fluoxetine

Methods: 8-12 weeks old female rats albino of wistar strain (n=10) were divided into three groups Group A (control), group B (experimental) and group C (protective) and were treated with distilled water, oral fluoxetine (80mg/kg) and oral fluoxetine along with vitamin E simultaneously (80mg/kg and 250mg/kg) respectively for 15 days. Gross and histological examination of uterine horns of all rats along with measurement of serum prolactin level was done on 15th day. Mean±SD, One-way ANOVA and fisher exact test was applied to analyze data

Results: Weight, volume of uterus, utero-somatic index, serum prolactin level and myometrial thickness was significantly increased (P value=0.001) along with presence of adenomyosis in experimental group B which was given fluoxetine alone. However it was observed that in group C which was given vitamin E along with fluoxetine, ameliorated these changes and results were comparable with control group A.

Conclusion: Vitamin E has a role in protection of reproductive organs owing to its antioxidant properties when administered along with fluoxetine which produces oxidative stress related changes serum prolactin levels and uterine myometrium.

Keywords: Vitamin E, uterine myometrium albino rats

INTRODUCTION

Multiple medical conditions are now a day's treated with use of vitamins. Vitamin E has vast use in neutralizing the harmful effects of many drugs (Rizvi et al., 2014). Vitamin E has an important role in cellular antioxidant system and present in lipid portion of cell membranes. Vitamin E decreases the Reactive Oxygen Species (ROS) levels in tissues and blood which are directly proportional to oxidative stress within body. Oxidative stress not only plays a major part in hormonal derangement but also in structural disfigurement; ultimately leading to infertility.

Fluoxetine is a widely prescribed medicine belonging to class of selective serotonin reuptake inhibitor (SSRIs) antidepressants. It was formulated at Eli Lilly and company in mid of 1970s (Wong et al., 1974). Multiple studies by researchers recorded the negative effects of fluoxetine on lungs, liver, heart and endocrine glands (Hajizada et al., 2016). It also modulates the female hormonal system by disrupting hypothalamo-pituitary gonadal (HPG) axis which brings about changes in structure of reproductive organs.

Fluoxetine use related oxidative stress is observed to be caused by an increase in ROS and other free radicals (Jalili et al., 2014; Savaskan et al., 2007). The negative effects of fluoxetine on female fertility caused by the oxidative stress were noted by Brambilla et al., 2005; Jalili et al., 2014. In a study done by Ficioglu et al. 1995 it was found that high prolactin levels are caused by chronic use of fluoxetine. Fluoxetine usage related high prolactin levels

evoke changes in uterine myometrium. Increase in prolactin levels along with endometrial stroma invading uterine myometrium was reported by Ficioglu et al. 1995 and Sengupta et al., 2013 in female rats with fluoxetine administration.

Present study is designed to observe potential antioxidant property of vitamin E in protecting rat's myometrium upon treatment with fluoxetine.

MATERIAL AND METHODS

In current study 8-12 weeks old female rats from Wistar strain were taken and divided randomly into three groups A, B, and C, each having 10 animals. These rats were kept in temperature ranging between 23±2°C along with humidity of 55±5%. 12 hours cycle of light and darkness was maintained in animal house and rats were raised on standard diet plus tap water.

Group A was categorized as control and given distilled water for 15 days orally. 80 mg/kg of fluoxetine was given orally to group B animals for 15 days. Animals of group C were treated with 80 mg/kg of fluoxetine along with 250 mg/kg of vitamin E (both orally) for 15 days.

Researches carried out by Geeta et al., 2009 and Hai-Ping et al., 2012 were the basis for dose of fluoxetine and vitamin E respectively. Vitamin E was administered after dilution in olive oil, based on study by Fariha, (2008).

Animals were sacrificed on day 15 after anesthetizing with ether. Uterus was taken after identification on gross examination in aseptic measures. For routine histology uterus was first washed with distilled water and then buffered formalin was used to fix it for 48 hours. 5µm paraffin sections were first cut and afterwards stained with

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hematoxylin and eosin for conducting histological studies and uterus was processed in automatic processor for such study.

Blood was taken by cardiac puncture and stored in plastic eppendorf tubes at -80 °C after centrifugation.

Gross examination: Weight, volume and utero-somatic index of uterus were measured. Fluid displacement method was used to measure the volume of uterus

Utero-somatic index (USI) = weight of rat' uterus in grams/ weight of the rat on whole in grams x 100

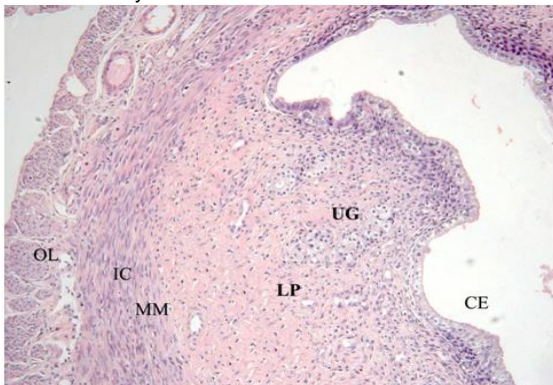
Hormonal assay: Prolactin level was measured by using specific Eliza kit.

Microscopic examination: Ocular micrometer was used to determine the thickness of uterine myometrium under light microscope by taking four slides from each animal.

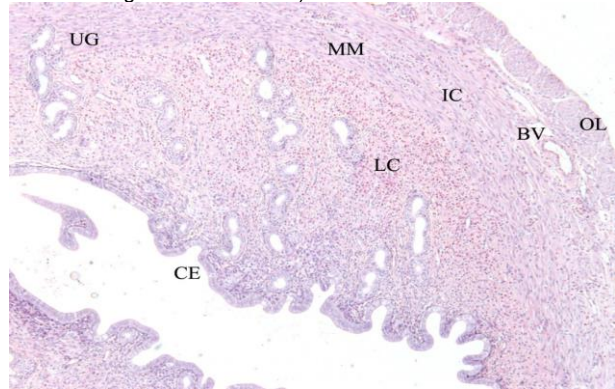
The data was analyzed on computer using SPSS version 21.0. Quantitative variable, like weight and volume of uterus, utero-somatic index, serum prolactin levels and myometrial thickness were analyzed by Mean±SD and One-way ANOVA (Analysis of Variance). A p-value ≤ 0.05 was selected statistically significant.

RESULTS

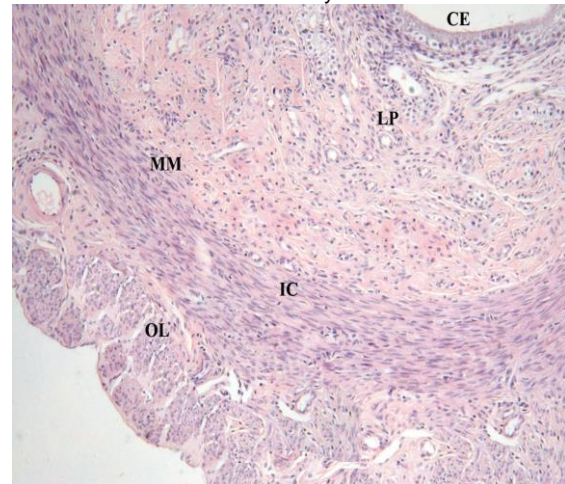
Histological micrograph from control group A showing normal thickness of myometrium.



Histological micrograph from group B showing increased thickness of myometrium and adenomyosis (invasion of myometrium by endometrial glands and stroma).



Histological micrograph from group C depicting normal thickness of myometrium and absence of adenomyosis.



Parameter	Group A	Group B	Group C	P Value
Weight of uterus (mg)	294.66±4.44	337.3±2.0	290.00±10.97	0.0001*
Volume of uterus (ml)	0.295±.002	0.336±0.002	0.298±0.003	0.0001*
Utero-somatic index (%)	0.149±.44	0.214±3.01	0.153±4.97	0.0001*
Serum prolactin (ng/ml)	11.31±1.9	61.02±2.0	12.35±1.2	0.0001*
Myometrial thickness(µm)	91.50±1.32	109.83±2.16	92.62±1.46	0.0001*

* P value ≤ 0.05 is statistically significant.

Adenomyosis

Adenomyosis	Group A	Group B	Group C	TOTAL
Absent	10(100.0%)	1(10.0%)	9(90.0%)	20(66.66%)
Present	0(0.0%)	9(90.0%)	1(10.0%)	10(33.33%)
Total	10	10	10	30

P Value= 0.0001*

* P Value ≤ 0.05 is statistically significant.

DISCUSSION

Animals of group B when given fluoxetine alone showed significant increase in weight, volume of uterus and utero-somatic index (USI) which is contributed by increase in myometrial thickness and adenomyosis.

Serum prolactin levels were also raised in group B animals supported by study done by Ficiocioglu et al.1995. A number of researches carried out have shown that with use of fluoxetine (Papakostas et al. (2006); Matuszczyk et al. (1998); Pecins-Thomsons and Betheca (1997).

Fluoxetine treated group B showed increased myometrial thickness along with hypertrophy and hyperplasia of endometrial glands which was extending

into uterine myometrium upon comparison with control group. Similar results were pointed out by Sengupta et al. (2013) and factmed.com (2015) in their studies. Fluoxetine usage leading to infertility is observed by conferring to change in histological architecture of uterine myometrium.

Female reproductive organs have a delicate relationship with hormonal levels. Savaskan et al., 2007 observed fluoxetine use related oxidative stress and commented on its role in alteration of histological structure of reproductive organs. Jan et al., 2008 reported hormonal imbalance in rats upon treated with fluoxetine. Mori et al., 1999 observed changes in ultra-structure of uterus caused by increase in serum prolactin levels.

The animals of group C when treated simultaneously with fluoxetine along with vitamin E, showed normal thickness and histological architecture of myometrium which is similar to findings in animals of control group A. Vitamin E has been reported to ameliorate the hormonal changes inflicted by raised level of oxidative stress in body (Yin et al., 2012). A study done by Jalili et al. 2014 supports the observations made in current study on protective ability of vitamin E in reproductive organs because of its antioxidant properties.

CONCLUSION

Our study has showed that vitamin E has the potential to ameliorate oxidative stress produced by fluoxetine and the consequent changes in uterine endometrium.

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