Original Article

Influences of L-DOPA and Blocking Dopamine Receptors on Aromatase Gene Expression and Serum Concentration of LH in Rat Model of Polycystic Ovary Syndrome

Haghighat Gollo Kh, Mahmoudi F*, Bayrami A, Zahri S

Faculty of Sciences, University of Mohaghegh Ardabili, Ardabil, Iran

Received: 22 Jul 2020 Accepted: 19 Aug 2020

Abstract

Background & Objective: Polycystic ovary syndrome (PCOS) is associated with higher plasma levels of androgens, LH/FSH ratio and lower activity of aromatase and dopaminergic signaling pathways. In the present study, the effects of L-DOPA and dopamine receptor antagonists were investigated on *aromatase (Cyp19)* gene expression and LH concentration in PCOS rat model.

Material & Methods: Following PCOS induction by estradiol valerate, The PCOS rats received saline, L-DOPA(100mg/kg) or simultaneous injections of sulpride (10mg/kg)/ SCH23390 (1mg/kg)/ L-DOPA (100mg/kg). Five intact estrous rats were used as a control group. Mean serum LH concentration and *aromatase* relative gene expression was evaluated by radioimmonoassay and real- time-PCR method respectively.

Results: Mean *aromatase* mRNA levels significantly decreased in the hypothalamus and ovary of PCOS model rats compared to intact ones. Mean serum LH concentration significantly increased in PCOS group in comparison with intact rats. The L-DOPA significantly increased mean hypothalamic and ovarian *aromatase* gene expression compared to PCOS rats while it significantly declined serum LH concentration compared to PCOS rats. Dopamine receptor antagonists including sulpiride and SCH23390 blocks the stimulatory or inhibitory effects of L-DOPA on hypothalamic *aromatase* or serum LH levels respectively. But the sulpride and SCH23390 did not inhibit the stimulatory influences of L-DOPA on ovarian *aromatase* gene expression.

Conclusion: L-DOPA may be involved in the controling of PCOS condition via decreasing LH secretion and increasing the *aromatase* gene expresion.

Keywords: aromatase, L-DOPA, sulpride, SCH23390, PCOS animal model

Introduction

The most important symptoms of polycystic ovary syndrome (PCOS) include infertility, insulin resistance, hyperandrogenism, increased plasma luteinizing hormone (LH) levels and abnormal increased or decreased activity of the hypothalamus-pituitary-gonad (HPG) axis. Also, PCOS patients suffer from different metabolic disorders including obesity, diabetes and cardiovascular disorders (1).

***Corresponding Author: Mahmoudi Fariba,** Faculty of Sciences, University of Mohaghegh Ardabili, Ardabil, Iran.
Email: f.mahmoudi@uma.ac.ir
https://orcid.org/0000-0001-6092-1352

Dopamine (DA) is a neurotransmitter synthesized from the amino acid tyrosine. Peripheral injection of dopamine does not directly affect the central nervous system because it lacks the ability to cross the blood-brain barrier, whereas dopamine precursors (tyrosine or L-DOPA) or synthetic dopamine agonists, such as SKF-38393 pass through the blood-brain barrier (2). In the rat brain, dopaminergic neurons are concentrated in the hypothalamus especially in the arcuate nucleus (ARC) (3). The different physiological effects of dopamine are exerted via 5 receptors which are

divided into two groups of D_1- like (D_1 and D_5 subtypes) and D_2- like receptors (D_2, D_3 and D_4 subtypes) (3). Dopamine or its receptor agonists suppress the activity of GnRH neurons and they inhibit HPG axis activity (3). Dopamine release is decreased in PCOS patients (4). Dopaminergic neurons innervate the ovaries and dopaminergic receptors are expressed in the ovaries (5,6). Ovarian D_1 receptors play an important role in the development of follicles and ovulation whereas ovarian D_2 receptors may be involved in controlling the positive feedback effect of estradiol on GnRH/LH secretion and subcutaneous injection of haloperidol (dopamine receptor antagonist) blocks the ovulation (5,6).

Aromatase, also called estrogen synthetase is a key enzyme for the synthesis of estrogen from androgens and it is encoded by the *Cyp19* gene. In fact, aromatase enzyme converts testosterone to 17β- estradiol in liver, gonads, hypothalamus and other organs (7). In addition to neural protection and other important functions, the estradiol produced by aromatization of androgens plays an important role in the regulation of GnRH/LH secretion in males and females, ovulation and follicles development of females (7). Evidence showed that *aromatase* gene expression reduces in PCOS and decreased levels of aromatase enzyme results in increasing blood androgen and LH concentration (8). Due to finding some drugs and possible mechanisms to reduce androgen levels in PCOS, in the present study, the effects of L-DOPA and dopamine receptor antagonists such as SCH23390 hydrochloride (D_1 receptor antagonist) and sulpiride (D_2 receptor antagonist) are investigated on the serum LH concentration and relative gene expression of *aromatase* in the hypothalamus and ovary of rats with estradiol valarate- induced polycystic ovary syndrome.

Materials & Methods

Animals: Twenty adult female Wistar rats, weighing 180-220g were provided by the Center of Neuroscience Research of Shahid Beheshti University of Iran. Animals were maintained under standard laboratory conditions (12h light, 12h dark cycle) with free access to food and water. All procedures for the maintenance and the use of experimental animals were executed with the Guide for the Care and Use of Laboratory Animals (National Institute of Health Publication No. 80-23, revised 1996). This research was approved by Ethics Committee of University of Mohaghegh Ardabili (code: 95:125).

Induction of polycystic ovary syndrome: The vaginal smear was performed for two consecutive weeks to select the rats with the normal estrus cycle. Estradiol Valerate (EV) and sesame oil purchased from Aburayhan Co., Iran and Barij Essence Co., Iran respectively. Then, in the estrus stage which was characterized by cornfield epithelial cells, the experimental animals received a single dose of EV (2 mg/rat, dissolved in 0.2 ml sesame oil) intramuscularly. Also, five rats in the estrus stage, received a single intramuscular injection of 0.2 ml sesame oil as an intact control group. Sixty days after the EV injection, the polycystic status was confirmed by observation of persistent cornified epithelium cells with vaginal smear.

Injections: The PCOS rats in three groups received intraperitoneal injections of saline, L-DOPA (100mg/kg) or R (+) SCH23390 hydrochloride (1mg/kg)/ sulpiride (10mg/kg)/ L-DOPA (100mg/kg) in a volume of 0.5 ml at 9:00-9:30. The doses of drugs were chosen based on previous studies (9,10). Five intact were rats used as an intact control group. R (+) SCH23390 hydrochloride, sulpiride, and L-DOPA were purchased from Sigma Co., U.S.A.

Hormone assays: Blood samples were collected in a volume of 0.5cc via tail vein. Blood samples were immediately centrifuged for 15 min at 3000 rpm and the plasma stored at –20°C until assayed for LH concentration. Mean plasma LH concentration was measured using rat LH kit and the method of the radioimmunoassay (RIA) (Institute of Isotopes Co, LT'D, Hungary).

Total RNA extraction and RNA analysis by real-time RT-PCR: Whole hypothalamus and ovary were removed. Animal was placed on its back. An incision was made through the skin and muscles of the abdominal surface of animal. After dissecting the ventral side, the ovaries were dissected above the convoluted oviducts. Then, isolated ovaries were dissected free of fat. The brains were placed ventral side up, anterior coronal slices were cut from 1 mm anterior to optic chiasm. The slices were then dissected laterally up to the hypothalamic sulci and posterior coronal slices were cut posterior to the mammillary body (11).

Following freezing in liquid nitrogen, they were stored at -80°C for determination of mRNA levels. Total RNA was isolated from samples

using the acid guanidinium thiocyanate-phenol-chloroform extraction method according to PureZol manufacturer instruction (Bio Rad Co., U.S.A.). The RNA concentration was determined by nanodrop spectrophotometer (Themo Fisher Scientific, U.S.A). For reverse transcription, 1µg of total RNA of each sample was reversely transcribed in a 20µl reaction with Strand cDNA Synthesis Kit (Vivantis Co., Malaysia) following the manufacturer's protocol. Briefly, in a sterile nuclease-free tube on ice, the following reagents were added: total RNA template (1µg), µl oligo T (dt) primer (40 µM), 1µl dNT (10mM) and nuclease-free water to 10 µl. After mixing gently, the mixture was incubated at 65°C for 5 min using MJ Mini thermal cycler (Bio Rad Co., U.S.A.). Then, it was chilled on ice, spinned down and the vial was placed back on ice to add 2 µl of 5X reaction buffer, 1µl of Ribo Lock RNase Inhibitor (10U/ µl), and 1µl of M-MuLV reverse transcriptase (200U/µl) and nuclease-free water to 20 µl. The mixture was incubated for 60 min at 42°C, followed by 5 min at 85°C. The cDNA was stored at -20°C.

Changes in gene expression levels were determined using the corbett rotor gene 6000 (Qiagen Co, Germany) real-time PCR detection system and SYBR Green I kit in a final volume of 25µl according to manufacturer instruction (Takara Bio Inc., Japan). The PCR cycling conditions were as follows: first denaturation 95 C° for 2 min, followed by 40 cycles of denaturation at 95 C° for 5 sec, annealing at 60 C° for 20 sec (aromatase or GAPDH) and extension at 60 C° for 25 sec. (Table 1)

The *aromatase* and *GAPDH* amplified products were 149 and 120 base pairs respectively. The *GAPDH* gene was used to normalize the values obtained for each sample. Calculation of relative gene expression levels of the target mRNAs were calculated by the equation $2^{-\Delta\Delta CT}$. (Table 1)

Statistical analysis: The results are presented as mean ± SEM. The data were analyzed using SPSS software (version 16) and the one- way ANOVA followed by post hoc Tukey test. In all cases, the significance level was set as $p \leq 0.05$.

Results

The mean serum LH concentration significantly increased in PCOS rats by 0.74 times compared to control group ($P \leq 0.05$, Chart1). L-DOPA significantly declined the mean serum LH levels

Table1. Specific oligo nucleotide sequences for forward and reverse primers

forward GAPDH	**5′-AAGTTCAACGGCACAGTAAG-3′**
reverse GAPDH	5′-CATACTCAGCACCAGCATAC-3′
forward aromatase	5′-CGTCATGTTGCTTCTCATCG-3′
reverse aromatase	5′-TACCGCAGGCTCTCGTTAAT-3′

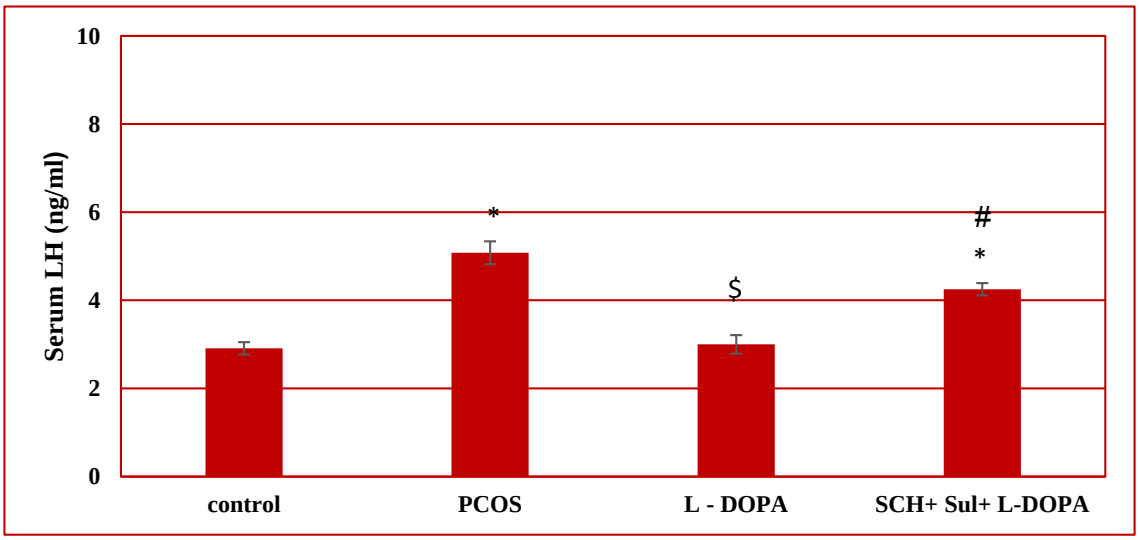

Chart 1. Effects of L-DOPA or simultaneous injections of R (+) SCH23390 hydrochloride, sulpiride and L-DOPA on serum LH hormone concentration of PCOS rats. *: compared to control; $: compared to PCOS; #: compared to L-DOPA.

by 0.41 times compared to PCOS control rats (P≤0.05, Chart1). Injections of sulpride/ SCH23390/L- DOPA significantly increased mean serum LH levels by 0.42 times compared to L- DOPA treated PCOS rats (P≤0.05, Chart1). The mean relative *Cyp19* gene expression significantly decreased in the ovary of PCOS rats by 0.91 times compared to control rats (P≤0.05, Chart2). In the ovary of PCOS rats receiving L-DOPA, the *Cyp19* gene expression levels significantly increased by 2.54 times compared to PCOS rats (P≤0.05, Chart2). Injections of sulpride/ SCH23390/L- DOPA decreased the *Cyp19* gene expression levels in the ovary by 0.17 times compared to L-DOPA group but these decreased levels of *Cyp19* gene expression were not statistically significant compared to L-DOPA group (Chart2).

The mean relative *Cyp19* gene expression significantly decreased in the hypothalamus of PCOS rats by 0.68 times compared to control rats (P≤0.05, Chart3). Injections of L-DOPA significantly increased the *Cyp19* gene expression levels by 1.42 times compared to PCOS rats (P≤0.05, Chart3). Injections of sulpride/ SCH23390/L- DOPA significantly decreased the *Cyp19* gene expression levels in the hypothalamus by 0.52 times compared to L-DOPA group (P≤0.05, Chart3).

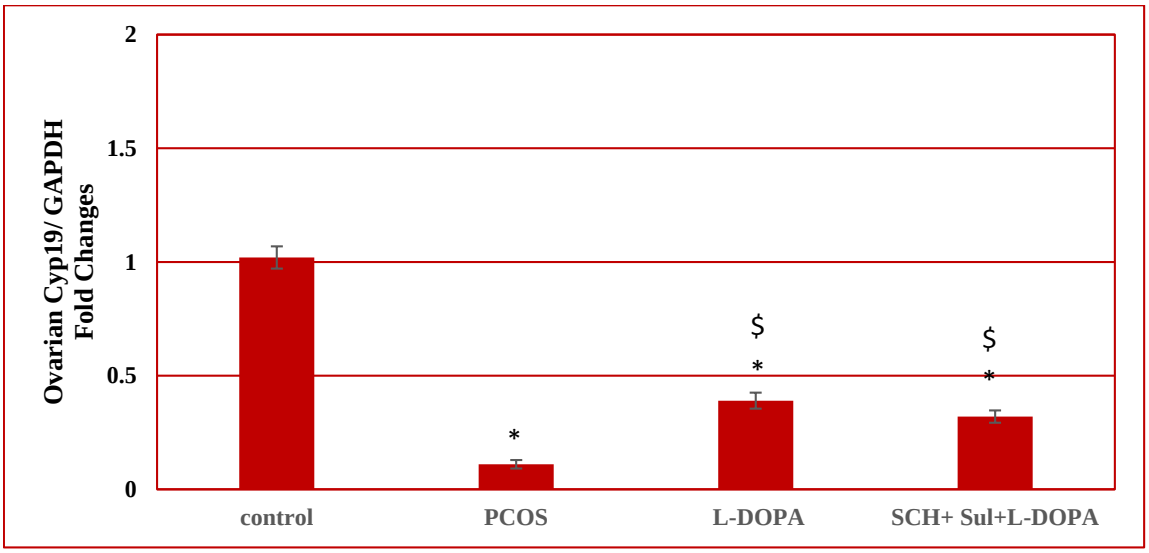

Chart 2. Effects of L-DOPA or simultaneous injections of R (+) SCH23390, sulpiride and L-DOPA on *aromatase (Cyp19)* gene expression in the ovary of PCOS rats. *: compared to control; $: compared to PCOS; #: compared to L-DOPA.

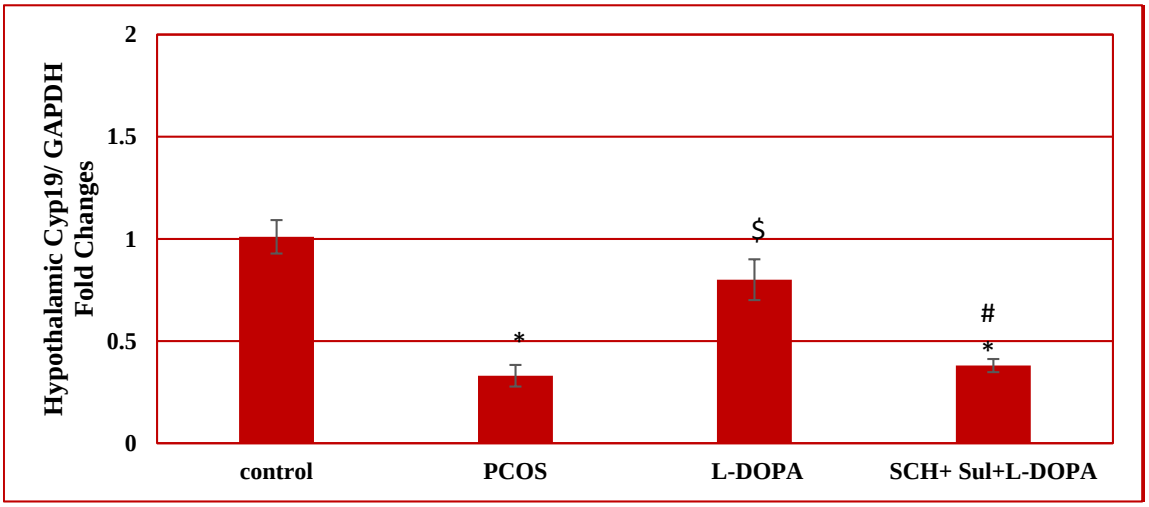

Chart 3. Effects of L-DOPA or simultaneous injections of R (+) SCH23390, sulpiride and L-DOPA on *aromatase (Cyp19)* gene expression in the hypothalamus of PCOS rats. *: compared to control; $: compared to PCOS; #: compared to L-DOPA.

Discussion

The results of the present study showed that *aromatase* gene expression significantly decreased in the ovary and hypothalamus of PCOS rats. The present results are consistent with previous studies which emphasized the key role of aromatase enzyme in the controlling of reproductive process (7). Previous studies demonstrated that level of aromatase gene expression decreases in polycystic ovary syndrome (8,12). They concluded that the disruption of aromatase synthesis level in ovarian granulosa cells results in decreasing the converting testosterone to estrogen in the ovary, disruption of the hypothalamus-pituitary-ovarian axis and following increase in the secretion of luteinizing hormone, which in turn leads to increased androgen production in the ovary (13).

Previous studies indicated that in PCOS patients, the level of dopamine release is low while plasma prolactin concentration is high compared to normal ones. They proposed that decrease in hypothalamic dopaminergic cell group activity may be partly involved in high plasma prolactin and LH levels in PCOS condition (4). Injection of dopamine significantly decreased prolactin and LH secretion in PCOS condition while infusion of metoclopramide (dopamine receptor antagonist) reversed the mentioned results (4). The present data showed the stimulatory effects of L-DOPA on aromatase gene expression in the ovary and hypothalamus of PCOS rats and the used doses of dopamine receptor antagonists blocked the stimulatory effect of L-DOPA on hypothalamic *aromatase* gene expression. The present results are consistent with previous studies which have shown the association between dopaminergic neurons and aromatase. They demonstrated that aromatase-neurons receive tyrosine hydroxylase fibers and dopaminergic compounds can modulate aromatase activity in the preoptic area of the brain (14). With regards to in vitro laboratory reports, addition of the dopamine agonist including mesulergine to the Leydig cells significantly increased the aromatase activity (15). To account for the stimulatory effects of dopaminergic pathways on aromatase gene expression in the ovary of PCOS rats, one could consider the involvement of some indirect probable mechanisms involved in mediating the stimulatory effects of dopamine on ovarian aromatase activity.

Kisspeptin is a stimulatory peptide in controlling the HPG axis. Recent studies completely established that the kisspeptin/GPR54 system plays a critical role in fertility and mutation in genes coding the kisspeptin or its receptor result in infertility (16). Evidence indicates that there is a close relationship between hypothalamic dopaminergic and kisspeptin neurons. They showed that 40% of arcuate nucleus (ARC) neuronal subpopulation contained D_2 receptors in breeding season ewes, but their levels enhanced to 80% in anestrous. Injection of kisspeptin receptor antagonists completely blocked the increase in LH pulse frequency induced by infusion of sulpiride to anestrous ewes. These results suggest that dopamine suppresses HPG axis in anestrus ewes by inhibiting the function of ARC kisspeptin neurons (17). Also, it has been shown that kisspeptin and its receptor genes are expressed in the ovary of the different species including rodents, human, primates and ruminants, and in addition to hypothalamic kisspeptin, the ovarian kisspeptin system plays a critical role in ovulation at the proestrus stage in adulthood (18). Hypothalamic *KiSS1* gene expression significantly increase in PCOS rats compared to healthy ones (19). In PCOS patient's plasma level of kisspeptin is high and its receptor antagonists (including peptide234) are one of the most important treatment strategies used for reducing LH secretion in PCOS women (20). Also, it has been demonstrated that kisspeptin neurons number in the brain of aromatase knock-out rats was higher than intact ones. Their results suggested the interaction of the dopaminergic pathway with the levels of aromatase and kisspeptin activity in the regulating the reproduction and they proposed that aromatase action may exert an inhibitory influence on *KiSSI* gene expression (20). Also, it has been shown that injections of L-dopa significantly decrease *KiSS1* gene expression in comparison with PCOS rats (19). So, based on these finding, one could expect that dopamine may be involved in increasing the expression of *aromatase* gene partly by decreasing kisspeptin synthesis in the ovary.

Previous studies demonstrated that prolactin exerts an inhibitory influence on the expression of aromatase in the luteal cells of ovarian follicles (21) and dopamine suppresses prolactin

secretion via D_2 like receptors (22). So, it is possible that dopamine may play a role in increasing the aromatase synthesis in the ovary partly via inhibiting prolactin secretion. However, to better understand the mechanisms of dopaminergic neural signaling system role upstream aromatase neural pathways, further studies are needed using higher doses of SCH23390 hydrochloride, sulpride and other different dopamine receptors agonist or antagonists than those used in the present study.

Conclusion

Estradiol valerate-induced PCOS in rats caused a significant decrease in mean relative gene expressions of hypothalamic and ovarian *aromatase* compared to intact rats. Injection of L-DOPA significantly increased the mean hypothalamic and ovarian aromatase gene expressions compared to PCOS rats. Injections of dopamine receptors antagonists, sulpiride and SCH23390 hydrochloride, blocked the stimulatory or inhibitory effects of L-DOPA on hypothalamic *aromatase* mRNA levels and LH hormone secretion respectively. Increasing the activity of dopaminergic neural pathways may be a useful treatment target for hormonal disorders caused by PCOS.

Acknowledgments

This study was supported financially by University of Mohaghegh Ardabili, Iran.

All procedures for the maintenance and the use of experimental animals were executed with the Guide for the Care and Use of Laboratory Animals (National Institute of Health Publication No. 80-23, revised 1996). This research was approved by the Ethics Committee of University of Mohaghegh Ardabili (code: 95:125).

Conflict of Interests

The authors have nothing to disclose. There is no conflict of interest in this article.

Reference

1. Polak K, Czyzyk A, Simoncini T. New markers of insulin resistance in polycystic ovary syndrome. J Endocrinol Invest. 2017; 40(1):1-8.
2. Stansley BJ, Yomamoto BK. L- dopa and brain serotonin system dysfunction. Toxics. 2015; 3(1):75-88.
3. Sadeghzadeh A, Bayrami A, Mahmoudi F, Khazali H, Asadi A. The effects of interaction of dopaminergic and kisspeptin neural pathways on ghrelin secretion in rats. J Paramed Sci. 2018; 9(1):29-35.
4. Gómez R, Ferrero H, Delgado-Rosas F, Gaytan M, Morales C, Zimmermann RC, et al. Evidences for the existence of a low dopaminergic tone in polycystic ovarian syndrome: implications for OHSS development and treatment. J Clin Endocrinol Metab. 2011; 96(8):2484-92.
5. Parillo F, Maranesi M, Mignini F, Marinelli L, Di Stefano A, Boiti C, et al. Evidence for a dopamine intrinsic direct role in the regulation of the ovary reproductive function: in vitro study on rabbit corpora lutea. PLoS One. 2014; 9(8): e104797.
6. Venegas-Meneses B, Padilla JF, Juárez CE, Morán JL, Morán C, Rosas-Murrieta NH, et al. Effects of ovarian dopaminergic receptors on ovulation. Endocrine. 2015; 50:783-96.
7. Garcia-Segura LM. Aromatase in the brain: not just for reproduction anymore. J. Neuroendocrinol. 2008; 20(6):705-12.
8. Eckmann R, Kockier D. Aromatase inhibitors for ovulation and pregnancy in polycystic ovary syndrome. Ann Pharmacother. 2009; 43(7):1338-1345.
9. Andersson K, Fuxe K, Eneroth P, Härfstrand A, Agnati LF. Involvement of D1 dopamine receptors in the nicotine-induced neuro-endocrine effects and depletion of diencephalic catecholamine stores in the male rat. Neuroendocrinology. 1988; 48(2):188-200.
10. Grierson JP, James MD, Pearson JR, Wilson CA. The effect of selective D1 and D2 dopaminergic agents on sexual receptivity in the female rat. Neuropharmacology. 1988; 27(2):181-189.
11. Khazali H, Mahmoudi F, Janahmadi M. Hypothalamic KiSS1/GPR54 gene expressions and luteinizing hormone plasma secretion in morphine treated male rats. Int J Fertil Steril. 2018; 12(3): 223-228.
12. Chen J, Shen S, Tan Y, Xia D, Xia Y, Cao Y, et al. The correlation of aromatase activity and obesity in women with or without polycystic ovary syndrome. J Ovarian Res. 2015; 8:11.
13. Pitteloud N, Dwyer AA, DeCruz S, Lee H, Boepple PA, Crowley WF Jr, et al. Inhibition

of luteinizing hormone secretion by testosterone in men requires aromatization for its pituitary but not its hypothalamic effects: evidence from the tandem study of normal and gonadotropin-releasing hormone-deficient men. J Clin Endocrinol Metab. 2008; 93(3):784-91.
14. Absil P, Baillien M, Ball GF, Panizica GC, Balthazart J. The control of preoptic aromatase activity by affirrent inputs in Japanese quail. Brain Res Beain Res Rev. 2001(1-3); 37:38-58.
15. Dirami G, Cooke BA. Effect dopamine agonist on luteinizing hormone receptors, cyclic AMP production and steroidogense in rat leydig cell. Toxicol Appl Pharmacol. 1998; 150(2):393-401.
16. Trevisan CM, Montagna E, de Oliveira R, Christofolini DM, Barbosa CP, Crandall KA, et al. Kisspeptin/GPR54 system: What do we know about its role in human reproduction? Cell Physiol Biochem . 2018; 49(4):1259-76.
17. Goodman R, Malthy M, Millar R, Hillman S. Nestor CC, Whited B, et al. Evidence that dopamine acts via kisspeptin to hold GnRH Pulse frequency in check in anestrous ewes. Endocrinology. 2012; 153(12):5918-27.
18.Yamasaki M, Kuwahara A, Iwasa T, Yamamoto Y, Taniguchi Y, Yano Y, et al. Development-related changes in the expression of the ovarian Kiss1 and Kiss1r genes and their sensitivity to human chorionic gonadotropin in prepubertal female rats. J Reprod Dev. 2017; 63(4):409-14.
19. Mahmoudi F. Synergistic effects of sulpride and SCH23390 on KiSS1 gene expressions in L-dopa treated PCOS rats. Fourth International Congress on Reproduction. 2018, Iran. ISERB04- 037.
20. EmekcinOzay O, Ozay AC, Acar B, Cagliyan E, Secil M, Kume T. Role of kisspeptin in polycystic ovary sandrome. Gynecol Endocrinol. 2016; 32(9):718-22.
21. Stocco Co, Kwintkiewicz J. Opposite effects of prolactin (Prl) on the expression of aromatase and liver receptor homolog 1 (LRH-1) in luteal cells. Biol Reprod .2009; 81(1):297.
22. Saleem M, Martin H, Coates P. Prolactin biology and laboratory measurement: An update on physiology and current analytical issues. Clin Biolchem Rev. 2018; 39(1):3-16.

مقاله پژوهشی

تاثیر ال دوپا و بلوکه کردن گیرنده های دوپامینی بر بیان ژن آروماتاز و غلظت سرمی LH در سندروم تخمدان پلی کیستیک مدل موش های صحرایی

خدیجه حقیقت گللو، فریبا محمودی*، ابوالفضل بایرامی، صابر زهری

دانشکده علوم، دانشگاه محقق اردبیلی، اردبیل، ایران

تاریخ دریافت مقاله: ۱۳۹۹/۰۳/۱۳ تاریخ پذیرش مقاله: ۱۳۹۹/۰۵/۲۱

چکیده

زمینه و هدف: سندروم تخمدان پلی کیستیک(PCOS) با سطوح بالای آندروژن‌ها، نسبت LH/FSH، فعالیت پایین آروماتاز و مسیر پیام‌رسانی دوپامینرژیکی همراه است. در تحقیق حاضر، اثرات ال‌دوپا و آنتاگونیست‌های گیرنده دوپامین بر بیان ژن *آروماتاز(Cyp19)* و غلظت سرمی LH در موش‌های صحرایی مدل PCOS بررسی شد.

مواد و روش‌ها: بعد از القای PCOS با استرادیول والرات، موش‌های صحرایی PCOS سالین، ۱۰۰mg/kg ال دوپا یا تزریق همزمان ۱۰mg/kg سولپرید، ۱ mg/kg SCH23390 و ۱۰۰ mg/kg ال دوپا را دریافت کردند. پنج موش صحرایی سالم در مرحله استروس به عنوان گروه کنترل استفاده شد. غلظت سرمی LH و بیان نسبی ژن *آروماتاز* با به ترتیب با روش رادیوایمنواسی و ریل تایم PCR اندازه‌گیری شدند.

نتایج: میانگین سطوح mRNA ی *آروماتاز* در هیپوتالاموس و تخمدان گروه PCOS در مقایسه با گروه سالم کاهش معنی‌دار و میانگین غلظت سرمی LH در گروه PCOS در مقایسه با گروه سالم افزایش معنی‌دار پیدا کرد. ال‌دوپا بیان نسبی *آروماتاز* هیپوتالاموسی و تخمدانی را در مقایسه با گروه PCOS به طور معنی‌داری افزایش و میانگین غلظت سرمی LH را در مقایسه با گروه *PCOS* به طور معنی‌داری کاهش داد. آنتاگونیست‌های گیرنده‌های دوپامین شامل سولپرید و SCH23390 اثرات تحریکی ال‌دوپا بر بیان ژن *آروماتاز* در هیپوتالاموس و اثرات مهاری آن بر غلظت سرمی هورمون LH را بلوکه کرد. ولی سولپرید و SCH23390 اثرات تحریکی ال دوپا بر بیان ژن *آروماتاز* تخمدانی را مهار نکردند.

نتیجه‌گیری: ال دوپا از طریق کاهش ترشح LH و افزایش بیان ژن *آروماتاز* ممکن است در کنترل وضعیت PCOS دخالت داشته باشد.

کلمات کلیدی: آروماتاز، ال‌دوپا، سولپرید، SCH23390، مدل حیوانی PCOS

***نویسنده مسئول: فریبا محمودی**، دانشکده علوم، دانشگاه محقق اردبیلی، اردبیل، ایران.
Email: f.mahmoudi@uma.ac.ir
https://orcid.org/0000-0001-6092-1352