Effects of Estradiol on Pain Threshold in Female Mice

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***Abstract*—** Steroid hormones have role in modulating of pain threshold. The aim of this study was to investigate the effects of estradiol on pain threshold induced by tail flick test in female mice. In this laboratory experimental study, female mice were randomly divided to control and groups receiving low, moderate and high doses of estradiol Following intraperitoneally administration of hormone, pain threshold was measured using tail flick test and data were analyzed using ANOVA. Moderate and high dose of estradiol resulted in increased pain threshold 1hour after administration ($P<0.01$ and $P<0.001$, respectively). Our findings indicate that appropriate doses of estradiol have pain reducing effects**.**

***Keywords*—** Estradiol, Pain, Mice**.**

I. INTRODUCTION

PAIN is an unpleasant feeling that is caused by a damage to a tissue or an organ. The process of pain perception begins in the periphery by activation of nociceptors. From here nociceptive signals are conveyed via the dorsal horn of the spinal cord to multiple brain regions, where pain is perceived. [1]. Evidences of gender-specific differences exist in the receiving pain [2],[3], indicating that sex steroid hormones play significant role in pain perception. Pain threshold is the threshold at which a system can detect a painful stimulus [4], followed by signaling the pathways resulting in pain perception. Estrogens are sex steroid hormones acting on many organs and particularly on reproductive organs and can modulate pain perception through various ways. Estradiol is most important estrogen acting on many organs [5] and is expected to modulate pain perception. Pain threshold which is changed through effects of various factors [1] can also be influenced by estradiol administration. The main aim of this study was to investigate the effects of different doses of estradiol in different times after administration on pain threshold induced by tail flick test in female mice.

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II. MATERIAL AND METHODS

A. Animals

Adult mice were purchased and raised in our colony from an original stock of Pasteur institute (Tehran, Iran).The temperature was at 23±2 ^{0}C and animals kept under a schedule of 12h light:12h darkness (light on at: 08: 00 a.m.) with free access to water and standard laboratory chow. Care was taken to examine the animals for general pathological symptoms. Food was withheld for 12-14h before death.

B. Protocol of Study

In this laboratory experimental study, female mice were randomly divided to control group, and groups receiving low, moderate and high dose of testosterone (100, 500 and 1000 mg/kg/body weight, respectively). Pain threshold was measured by tail flick technique before injection and 30 minutes and one hour following injection of testosterone. In tail flick test, a light beam was focused on the animal's tail and a timer started. When the animal flicked its tail, the timer stoped and the recorded time (latency) was a measure of the pain threshold. All animal experiments were carried out in accordance with the guidelines of Institutational Animals Ethics Committee.

C. Statistical Analysis

All values are presented as mean ± S.E.M. Statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS 19. Significance was measured using Fisher's least significant for the exact P values and significant differences are noted in the results. Differences with $P<0.05$ were considered significant

III. RESULTS

Table I shows recorded time (latency) before and 30 minutes and one hour after estradiol injection in female mice.

The data are indicated as mean ± SEM . P values are expressed in comparison with control group. N.S. represents non-significant difference and E indicates estradiol. T0, T1 and T2 indicate before injection, 30 minutes and 1 hour following injection of estradiol.

The results of the present study show that moderate dose of estradiol resulted in increased pain threshold 30 minutes and 1hour after administration ($P<0.01$ and $P<0.01$, respectively). High dose of estradiol also caused a significant increase in pain threshold 30 minutes and 1hour after administration

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(P<0.001). Low dose of testosterone could not influence pain threshold significantly.

TABLE I
RECORDED TIME (LATENCY) BEFORE AND 30 MINUTES AND ONE HOUR AFTER ESTRADIOL INJECTION IN FEMALE MICE.

Group	Time	Latency Time (Sec)	P
Control	-	2.75±0.08	_
E (100mg/kg)	T0	2.85±0.08	N.S
E (100mg/kg)	T1	3.06±0.04	N.S
E (100mg/kg)	T2	3.05±0.09	N.S
E (500mg/kg)	T0	3.01±0.06	N.S
E (500mg/kg)	T1	3.55±0.05	<0.01
E (500mg/kg)	T2	3.61±0.06	<0.01
E (1000mg/kg)	T0	2.90±0.10	N.S
E (1000mg/kg)	T1	3.73±0.03	<0.001
E (1000mg/kg)	T2	3.81±0.10	<0.001

IV. DISCUSSION

Our study indicated that proper doses of etsradiol can increase pain threshold in females; i.e, estradiol administration can reduce pain perception in females. In line with our findings studies show that several hormones, including sex steroid hormones, can influence pain perception [6]. Pain threshold levels are clearly linked to cycling estrogen levels in women. A variety of painful conditions have been reported to worsen with the monthly cycle [7]. In general, high estrogen results in an increase in pain-blocking neurochemicals, whereas pain-producing neurochemicals increase when estrogen falls to low levels [8] – [10]. In the mechanism of action, the rostral anterior cingulate cortex (rACC) is a key structure of pain affect. The results of studies suggest that estrogen in the rACC, as a neuromodulator, drives affective pain via facilitating NMDA receptor-mediated synaptic transmission [11]. It has also been shown that among gonadal hormones it is estradiol that has prominent role the modulation of pain sensitivity [12].

V. CONCLUSION

The findings suggest that that appropriate doses of estradiol have pain reducing effects. according to which, the role of estradiol should be considered in clinical considerations related to pain.

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