

Effects of Testosterone on Pain Threshold

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

Keywords— Testosterone, Pain, Mice.

I. INTRODUCTION

TESTOSTERONE is a steroid hormone from the androgen group and is found in mammals, reptiles [1] birds [2] and other vertebrates. In mammals, testosterone is secreted primarily in the testicles of males and the ovaries of females, although small amounts are also secreted by the adrenal glands. It is the principal male sex hormone and an anabolic steroid [1] – [3]. The threshold of pain or pain threshold is the point along a curve of increasing perception of a stimulus at which pain begins to be felt. It is an entirely subjective phenomenon. A distinction must be maintained between the stimulus (an external thing that can be directly measured, such as with a thermometer) and the person or animal's resulting pain perception (an internal, subjective thing that can be indirectly measured, such as with a visual analog scale). Also, an IASP document defines "pain threshold" as "the minimum intensity of a stimulus that is perceived as painful" [1], [5]. Recent studies indicated that there is a relation between men reproductive system and pain. The most important part of reproductive system are hormones that have important role in pain system [3]. According to recent studies we have got that

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there is a relation between pain threshold and testosterone [4]-[6]. The aim of this study was to investigate the effects of testosterone on the pain threshold in different times after testosterone administration using tail flick technique.

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 °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, male mice were randomly divided to control group, and groups receiving low, moderate and high dose of testosterone (10, 20 and 50 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 stopped and the recorded time (latency) was a measure of the pain threshold. All animal experiments were carried out in accordance with the guidelines of Institutional Animals Ethics Committee.

C. Statistical Analysis

All values are presented as mean \pm 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 testosterone injection in male mice.

The data are indicated as mean \pm SEM. P values are expressed in comparison with control group. N.S. represents non-significant difference and T indicates testosterone. T0, T1 and T2 indicate before, 30 min after and 1 hour after testosterone administration, respectively.

The results of the present study show that moderate and high dose of testosterone resulted in increased pain threshold 1 hour after administration ($P < 0.01$ and $P < 0.001$, respectively), however, low dose of testosterone could not influence pain threshold significantly and also moderate or high doses of

testosterone could not increase significantly the pain threshold 30 minutes after injection of testosterone.

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

GROUPS	Latency Time (second)	P
CONTROL	2.900±0.213	-
T0 (10mg/kg)	2.933±0.163	NS
T1 (10mg/kg)	2.916±0.204	NS
T2 (10mg/kg)	3.050±0.187	NS
T0 (20mg/kg)	2.950±0.234	NS
T1 (20mg/kg)	2.966±0.121	NS
T2 (20mg/kg)	4.033±0.136	<0.01
T0 (50mg/kg)	2.883±0.147	NS
T1 (50mg/kg)	3.116±0.147	NS
T2 (50mg/kg)	5.266±0.403	<0.001

IV. DISCUSSION

The results of the present study show that moderate and high dose of testosterone resulted in increased pain threshold 1hour after administration. In line with our findings, there are other studies indicating association between sex steroid hormones and pain [7], [8]. Recent studies also show that testosterone metabolites are potential agents for the treatment of diabetic neuropathic pain [9]. Contrary to our findings, there are reports showing that there is not a clear relation between reproductive system and pain [10], [11]. According to some studies the hormones of reproductive system may not influence pain system [12]. Some studies also have shown that there is not a clear association between testosterone and pain [13], [14]. Recent studies also show that elevated levels of gonadotrophins but not sex steroids are associated with musculoskeletal pain in middle-aged and older European men [15].

In our study, low dose of testosterone could not influence pain threshold significantly and also moderate or high doses of testosterone could not increase significantly the pain threshold 30 minutes after injection of testosterone, according to which, it should be noted that testosterone action on pain modulating is dependent on its dose. On the other hand, it takes a time for testosterone to modulate the pain system.

V. CONCLUSION

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

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