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Effect of Oxymetholone medicine by mother treatment during Pregnancy and lactation period on FSH, LH and Testosterone hormones in mature newborn male rats

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Mona Khajehei, Vahid Hemayatkhah Jahromi, Samaneh Zolqhadri, Hossein kargar; Effect of Oxymetholone medicine by mother treatment during Pregnancy and lactation period on FSH, LH and Testosterone hormones in mature newborn male rats

ABSTRACT

Background and Purpose: Oxymetholone is an active nutritional anabolic steroid – androgenic that is used as energetic medicine in high doses which may result some abnormalities such as lung cancer, mineral deposits in lung, ovarian cycle irregularity, adrenal benign tumor, liver cancer and adenoma in renal tubes. The aim of this study was to investigate Oxymetholone induced complication on testosterone, LH, FSH hormones concentration levels in mature newborn male rats. Their mothers were treated by this medicine in different pregnancy and lactation period. Materials and methods: 56 female rats and 14 wistar male rats were singled out in this study. They were at the age of 110-120 days after birth and their weights were approximately 200±20 *g*r. The animals were divided into 7 groups of 8 including control, solvent 1 (pregnancy-21 days), solvent 2 (pregnancy-lactation-42days), solvent 3 (lactation–21 days), experimental 1 (pregnancy-21 days) , experimental 2 (pregnancy-lactation-42 days) and experimental 3 (lactation-21 days). Solvent groups used DMSO as Oxymetholone solvent with 99.5% purity and experimental groups used Oxymetholone with 10 *mg/kg* concentration by intra peritoneum method. The hormones concentration was measured by radio immunoassay method. Results: The LH level indicated significant decrease in experimental groups of pregnancy-lactation and lactation. FSH in experimental groups of pregnancy-lactation, lactation and also Testosterone in experimental groups of pregnancy-lactation were reduced in comparison to control group. Conclusion: Oxymetholone may results negative feedback induce to reduce LH, FSH and testosterone concentration with mentioned dose which lead to disorder in reproductive system of wistar male rats.

Key words: *Pregnancy- Lactation, Oxymetholone, LH, FSH, Testosterone, Mature Rat*

Introduction

Steroids anabolic-androgenic are pharmaceutical that affect like manly steroids such as testosterone and Dehydrotestosterone [6]. As we know about its name, these medications have two interfering effects. One of them is anabolic effect that uses anabolism (growth cell) and the other one is androgenic-effect which influences on evolution and detainer of manly features. Some of anabolic effects of this medication cause raise the production of RBC. Also in formation of muscle cells that cause increase muscle volume which lead to strength gain [13]. Steroid hormones control/qualify the evolution of generic manly features by adjoining to androgen receptor in vertebrates. It includes generic manly organ activity and secondary generic features evolution. One of Testosterone analogs is Oxymetholone which were produced by Ringold and his cooperators in 1959. It branches from 17-alpha alkylation testosterone that is a significant series of anabolic medication. Oxymetholone is an active nutritional anabolic steroid-androgenic that is generated by methylating 17-alpha carbon and saturating 5-alpha carbon. Also there is a hydroxymethyle groups in location of number 2 carbon. This medication is sold as Anadorol which is a commercial name [2]. It is used for curing different abnormalities such as hypogonadism retardation maturity and osteoporosis. Also it is used for provocation of erthropoitin and constructing hemoglobin and RBC in inherited and non-inherited anemia [16]. Consuming Oxymetholone causes blocking and reduction of constructing necrosis alpha factor in HIV patient and plays an important role in dystrophy of muscles. Thus it can be used for aiming weight gain in these patient as well as HIV patient [16]. It is effective in high infection, burnt, mental disorder and surgery,

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recovery and treatment of weight lack derived from mentioned illnesses. Athletes take advantage of this medication for muscle hypertrophy and gaining power, strength and aggression. Oxymetholone causes the muscle to become voluminous. Premature calvities, aggression, hepatic tumor, depression, annoyance and psychosis are reported as side effects [5]. Usage in adolescents may cause increasing erection time and provokes sexual maturity in adolescence [4]. Some studies have shown that it lead to testis atrophy and decrease in sperm production. Although Oxymetholone is derived from testosterone and its dangerous cellular side effect has been proved, it's worthy to do widespread studies on other different tissues such as reproductive system which survivorship of regenerating depends upon it. It results harmful effects during pregnancy and lactation period in mature newborn rats would be a good way to intercept aberrant consuming in different people. The aim of this study is to investigate phenomena originated from Oxymetholone effect on sexual hormones concentration in mature newborn rats which their mothers consume the medication during pregnancy or lactation period or both together consecutively.

Material and method

This is a completely random laboratory research. Considering ethic during working with laboratory animals has been attended. 56 female rats and 14 wistar male rats were purchased from breeding and detaining center of Shiraz medical science. They were at the age of 110-120 days after birth and their weights were approximately 200±20 *g*r. The animals were kept in Azad university animal lab for two weeks before the experiment for adaptation. The animals were fed by compact palette from Shiraz co. Temperature of ambiance was 22+_2 ^{C} and humidity was 50-55%. Also 12 hours of light and 12 hours of night/darkness was spotted. The air of room was being ventilated by two ventilation devices planted each side of animal cage. The animals were kept in specific cage. The cages were cleaned up and disinfected every day. The animals were divided into 7 groups of 8 including evidence groups 1, 2, 3 and experimental groups 1, 2, 3. Each male rat was kept with 4 female rats in a cage. Control groups were fed by standard laboratory water and food ad libitum. Evidence groups were injected DMSO as Oxymetholone with 10 mg/kg of animal weight during pregnancy, lactation period, during pregnancy and lactation period by intra peritoneum method. Newborn rats were weighted by digital scale with 0/001 accuracy (AND brand Japan). The newborn rats were from their heart by 5cc syringe two month after birth in all groups. Collected blood samples were centrifuged 3000 cycle per minute for 15 minutes. Serum of samples was separated. The serum samples were kept in 20 ^{C} refrigerators for next investigating. In the next stage, the LH level, FSH and testosterone was measured in Jahrom diagnosis laboratory by radio immunoassay method (pishtaz teb iran kit , serial number –REF IM2125, REF IM1381-IM3301). The conclusions were analyzed by SPSS software version 16 via one way ANOVA and Duncan tests. Mean and standard deviation were accounted and P</05 was contemplated as significance level. According to Duncan method [1]. Coordinated diagram was plotted by Excel software.

Results:

Obtained conclusions indicated that amount of serum LH hormone in experimental groups 2, 3 have significant reduction (P<0/05) in comparison to control groups (chart 1). Also there was a significant reduction (P<0/05) in experimental groups 2, 3 with control groups in FSH (chart 2). The experimental groups 2 have significant reduction (P<0/05) with control groups in testosterone hormone (chart 3).

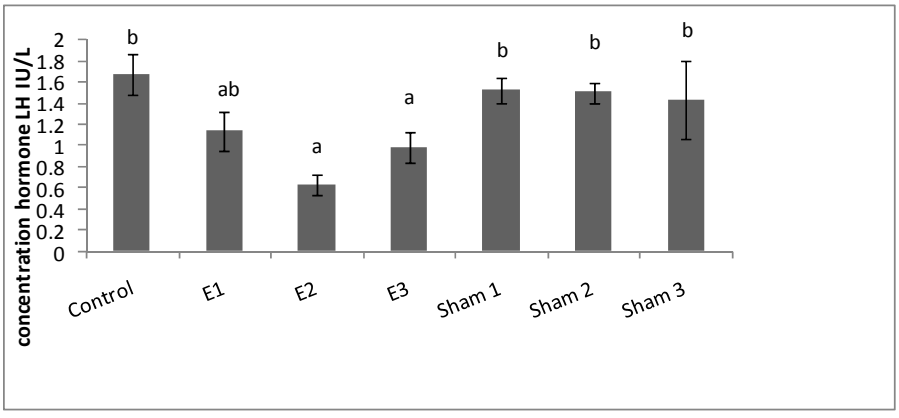

Chart 1: Oxymetholone effect on serum LH concentration in experimental, evidence, control. The groups have got at least a common letter in 5% level Duncan test.

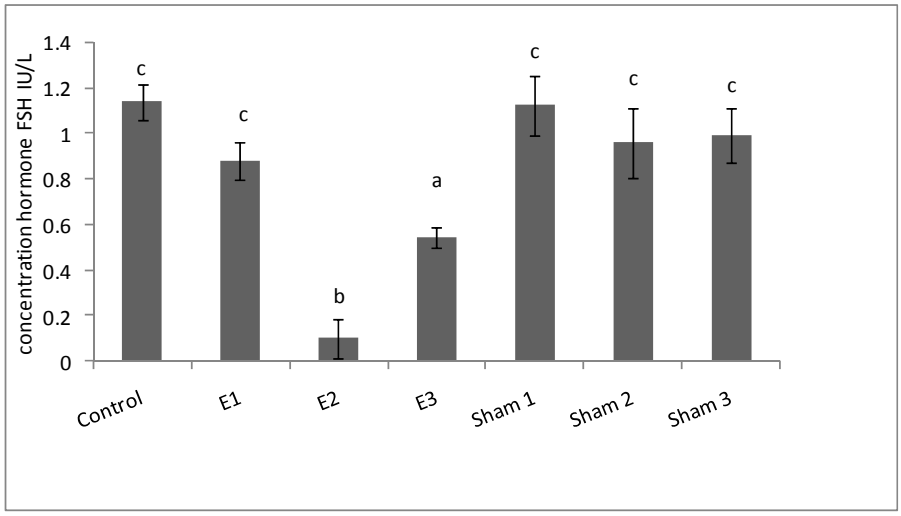

Chart 2: Oxymetholone effect on serum FSH concentration in experimental, evidence, control. The groups have got at least a common letter 5% level Duncan test.

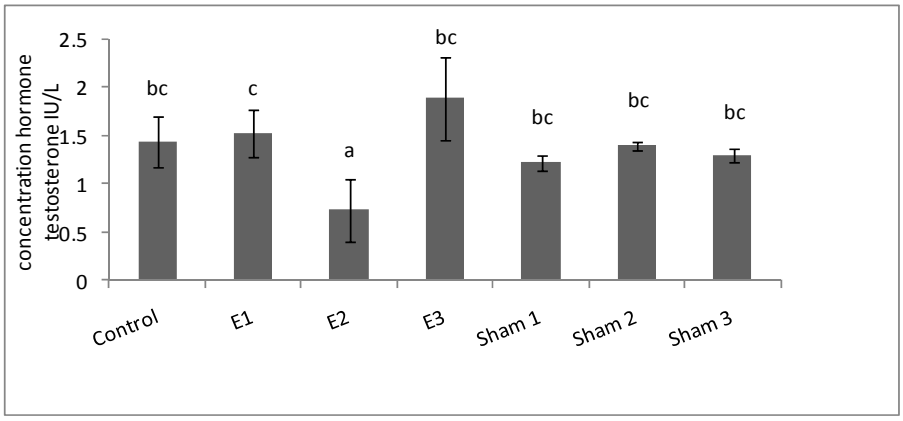

Chart 3: Oxymetholone effect on serum testosterone concentration in experimental, evidence, control. The groups have got at least a common letter in 5% level Duncan test.

Discussion:

The Oxymetholone effect was investigated on newborn rats sexual hormones during pregnancy and lactation period in this study. According to various study, Oxymetholone is an active nutritional anabolic steroid-androgen, generated by methylating 17 alpha carbons and satiating 5 alpha in testosterone. No one was noticed that anabolic steroids cause growth and reinforcement of muscle. Then anabolic steroids were used as amplifier [19]. Anabolic steroids, manufactured testosterone analogs that have been generated by making change in chemic structure in order to maximize and minimize anabolic effect and androgenic effect [17]. Changing chemic testosterone structure in order to change anabolic-androgen effect, decelerating inactive speed and changing pattern or reduction of alternation to estradiol are effective [12]. Carboxylation located in 17 beta in hydroxyl groups cause molecule more solutable in lipid environment for injection therefore nutrition steroids deal location is rather resistant versus hepatic destruction [7]. Athwart public impression, consuming androgenic-anabolic steroids as nutrition is more dangerous than injection. Steroid hormones enter cell easily because of owning lipid nucleus and do the task by direct being transformed to the cell. Intra cellar mRNA concentration increases. Increscent of mRNA concentration with increscent requirement protein cause property response to the hormones. This response along increscent protein structure. Cause adolescence of muscles and bones or make some changes in function and body Physiology [10]. Obtained results indicate that Oxymetholone

make significant reduction in LH plasma concentration mediocrity in mature experimental groups 2, 3 in comparison to control groups. Testosterone transudation is resulted of intermediate cells provocation and this hormone is LH adjustment transudation factor and by deleting the factor, cause increscent of LH transudation blood circulation. Negative feedback effect of testosterone primarily done by frequency reduction or LH wave actively. However it makes some changes in LH transudation intension. According to the obtained conclusions testosterone represents its effect on hypothalamus level. SO we can conclude that testosterone and its metabolites are adequate in negative feedback mechanism. It seems/sounded testosterone cause GnRH reduction and LH reduction of hypophysis by negative feedback wit direct effect on hypothalamic neurons. It seems that testosterone cause GnRH manufactured cell activity reduction and LH level reduction in results through activating dopaminergic neurons or by releasing dopamin from these [5]. Other studies indicates that stress existence during pregnancy like feeding or injecting medication cause ceasing/restraining cullion activity and testosterone concentration reduction and LH level reduction in male rats children. It is possible that (forenamed) stress cause LH and testosterone transudation reduction through nor epinephrine reduction in hypothalamus [3]. According to the studies, amphetamine (kind of emergizer) cause increasing releasing serotonin from neural termination. From the other side using releaser serotonin medication because releasing prolactine that exists in itself. And increasing make gonadotrop reduction [18]. Increasing FSH has halter effect on hypophysis-gonad axis and cause FSH reduction in result. Also FSH increscent enhances/raises some glycoprotein like inhibitor protein thereinafter FHS reduction will result [5]. It can be concluded according to obtained conclusion in this study and past researches that prolactin probably causes reduction.

Serum level testosterone hormone indicates significant reduction in experimental groups in comparison to control groups. Cullion function is controlled by hypophysis gland hormones in first. (FSH) adjust the spermatogenesis and LH hormone control the leydig cell function so serum level reduction FSH and LH existent in male children owning receiver Oxymetholone through oxymetholone effect on children's hypophysis gland through serum level reduction, make disorder in leydig cell function and testosterone production reduces because of leydig cell reduction in unit of leydig cells and lacking provocation Oxymetholone effect on leydig cells as well as reduction in androgen biosynthesis process by remainder active cells [11,14]. Of course a cellular result that has been done on this cullion is an explanatory of leydig cells reduction and this matter effect. Testosterone transudation decreases because of hypophysis-gonad-hypothalamus axis activity reduction through negative feedback created Oxymetholone effect.

Deduction: We can conclude that Oxymetholone causes LH and FSH significant reduction in experimental groups 2, 3 and testosterone significant reduction in experimental groups through negative feedback defeasance/inspiration in hypophysis-gonad-hypothalamus axis.

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