

# The Study of Effect of Levofloxacin on Disorders of Female Hormones in Rats

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## ABSTRACT

**Introduction:** Levofloxacin is one of the antibiotics with wide treatment application which is often applied for treating infections of genitourinary system and lower respiratory tract. Noting that most antibiotics can affect the structure of ovary tissue, we have launched research into the effect of Levofloxacin on hormone disorder resulting from tissue damage.

**Methods:** In this survey, 40 Wistar rats with the weight of  $20 \pm 25$  gr and approximate age of 8 weeks were used. They were divided into 4 groups with 10 rats. The study groups were tube fed with 200, 500 and 750 mml of Levofloxacin for each kg of weight. The control group didn't receive anything. Duration of the survey lasted 22 days. The rats were under 12 hours light-dark cycle, 24.7-26.4 temperature and 55-66% humidity. After the termination of this term, the blood sample was taken from their hearts and the serums were sent to clinical laboratory So as the level of hormone to be measured.

**Results:** Titration of level of LH, FSH, PROG hormones revealed that there was significant decrease of the level of hormone after consuming antibiotics in comparison with that of control group.

**Conclusion:** Levofloxacin antibiotic is one of the factors which can destroy ovary tissue, and gives rise to hormone disorder. This point should be considered in case of administration of drugs.

## Key Words:

Female hormones, Rat, Levofloxacin

## 1. Introduction

It is necessary to investigate factors influencing on tissue, ovarian hormones and the number of oocytes. Different factors such as genetic factors, autoimmunity, metabolic and infection will result in premature ovarian failure. On the other hand, this complication is considered as

one of the reasons of infertility [8]. Antibiotics has important application for treatment of infectious diseases. Infectious diseases of urinary system is one of the life threatening factors of adults. Nearly 20% of females and 1% of males will suffer from some sorts of the genitourinary system diseases during their life span [11, 14]. Pyelonephritis, Leptospirosis, Cystitis, Gonorrhea, Syphilis, Lymphogranuloma as well as bacterial vaginal

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infections can be examples which cause failure in urinary system [7,15]. Antibiotics including those existing in Fluoroquinolone such as Levofloxacin are used for treatment of these diseases. This drug prevents bacterial reproduction by hindering function of DNA-gyrase (Topoisomerase) and by preventing strands of DNA from opening (DNA-Supercoiling). Levofloxacin is also effective in treating intracellular infections such as: listeria monocytogenes, Mycobacterium tuberculosis, Staphylococcus aureus [13,15], infections resulting from gram-negative bacteria in genitourinary system and infection resulting from Mycoplasma, Chlamydia and Streptococcus.

Follicle stimulating hormone (FSH) which affects the productive tissue of testicle and ovary sexual cells and another hormone which is called luteinizing hormone (LH) or corpus luteum in female and interstitial-cell stimulating hormone (ICSH) in male, is named gonadotropins. In male, FSH will complete spermatogenesis (male gamete) and ICSH will stimulate Leydig or interstitial cells and will increase testosterone secretion. The role of gonadotropins is more in female than male and puberty, monthly period, and ovarium activation is done by them. Follicle stimulating hormone will help the growth and evolution of ovarian follicles as well as ovary production. LH (corpus luteum) is also necessary for ovarian perfection and its release from follicle [3].

Increase in level of FSH & LH in individuals affected by gonadal dysfunctions indicates primary gonadal failure; it is also seen in women with polycystic ovaries or during menopause. In secondary gonadal failure, level of FSH and LH is low due to primary pituitary insufficiency or other disorders of hypothalamic-pituitary axis, stress, malnutrition or physiological delay of growth and sexual distinction. The FSH and LH is often used in order to diagnose menopause. The purpose is that we can start alternate hormone treatment as soon as possible.

The LH is also used to study testicle function disorder in males and to assess endocrine glands regarding premature puberty in children [5]. The level of FSH and LH in females change depend on phase of menstrual cycle. Daily measurement of LH during monthly period can show the peak time of LH. It is believed that the maximum fertility is in this day. Spot urine test is also useful for assessment and treating infertility. FSH & LH are often applied in order to diagnose menopause to begin hormone replacement therapy [1]. Increase in level: gonadal failure such as physiological menopause, turner syndrome (gonadal dysgenesis), testicular dys-

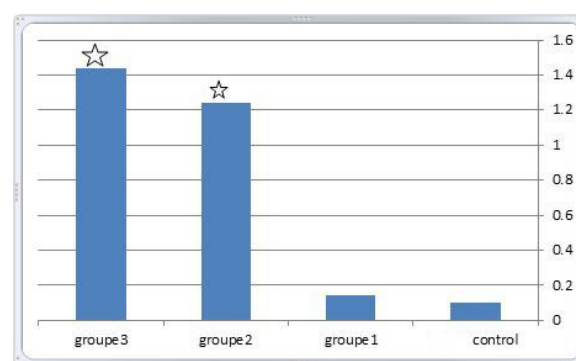
genesis (Klinefelter syndrome), castration, anorchia, hypogonadism, polycystic ovaries, Complete Testicular Disgenesis syndrome, precocious puberty, pituitary adenoma. Decrease in level: pituitary gland underactive, hypothalamic dysfunction, stress, anorexia nervosa, malnutrition [2]. Drug increasers: Cimetidine, Digitalis, Levodopa, Anticonvulsant, Clomifene, Nalaxon, Spironolactone. Drug reducers: Digoxin, Estrogens, Progesterone, Testosterone, Steroids, Oral contraceptive pill, Phenothiazines [1].

## 2. Materials & Methods

In order to conduct such experimental survey, 40 Wistar rats were used. The rats were about 8 weeks with approximate weight of  $20 \pm 25$  kg. Duration of the survey lasted 22 days, rats were maintained for 12 hours in light and 12 hours in dark. The room temperature was  $24.7-26.4$  C° and the percentage of humidity was 55-60%. The 30 rats were divided into 3 groups and received antibiotics with dilutions of 250, 500 and 750 mm/ml against each kg of body weight. 10 rats were placed at control group without care. After the completion of the said period, blood sample was taken from heart of all groups and was sent to clinical laboratory for medical test. After blood centrifuge, the serum was titrated using the Pishtaz Teb hormone and diagnostic kits by measuring light absorption rate with ELISA reader (Dana 3200).

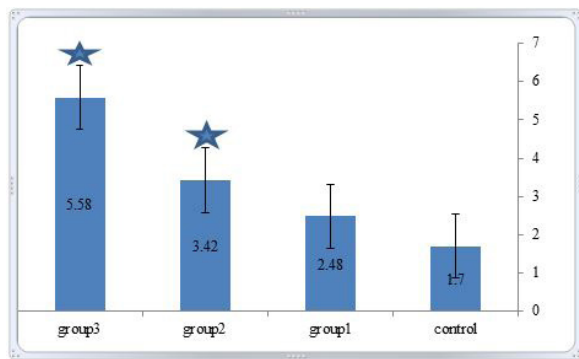
## 3. Results

The results were evaluated by using of which SPSS 16. In which  $P \leq 0.05$  is acceptable. Then, the following figures were drawn. In horizontal axis, group 1 indicate 250 dose, group 2 shows 500 dose and group 3 stands for 750 dose of Levofloxacin mg/kg. The vertical axis shows the amount of plasma hormone based on mg/dl.



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**Figure 1.** Level of LH hormone in groups receiving Levofloxacin



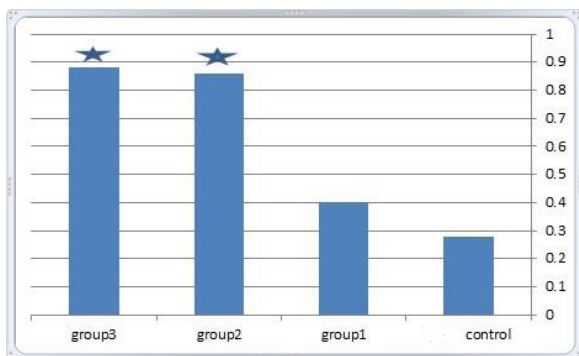
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**Figure 2.** Level of FSH hormone in groups receiving Levofloxacin.

The figure 1 shows level of LH, figure 2 indicate level of FSH and the figure 3 Points out level of PROG. All three figures revealed a significant increase the level of hormone in relation to level of control group which has been marked with asterisk.

#### 4. Discussion

Today antibiotics are widely taken in most societies. There is consensus among researchers about its probable negative repercussion. However, some studies show that after too much and long term consumption of antibiotics, the ovary will become small and damaged. In a study carried out in university of Florida, the study of medical effect of single dose of Fleroxacin which is one of Quinolones on cystitis was investigated and its effect was compared with several dosages of this drug. In this study, the decrease in number of follicles and minor damage destruction of ovarian tissue was confirmed [12]. Premature ovarian failure may be idiopathic and may happen as a result of contact with toxic matters, chromosomal abnormalities or autoimmune disorder. However, it is accompanied by changes in hypothalamus and hypophysis hormones which adjust menstua-



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**Figure 3.** Level of PROG hormone in groups receiving Levofloxacin

tion cycle, it is not considered as a central event. But it is regarded as primary ovarian insufficiency. At level of ovary, ovulatory follicular evacuation happens with most probability as a result of apoptosis. Therefore, the ovary is no more responsive to hypophysis hormones of FSH and LH and as a result, the ovarian production of estrogen and progesterone fail to function. The hypothalamic-pituitary-ovarian axis does not change during menstrual period; hence, at first the amount of FSH increases in the response to ovarian failure, and then LH in absence of negative ovary feedback [9,10].

Considering the point that Levofloxacin could cause hormone disorders, while prescribing it, its disadvantages as well as its benefits should be taken into account like other drugs. Because today hormone disorders and complications resulting from it is regarded as one of the of the medical issues.

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