Effects of Levofloxacin on Male Reproductive System Parameters and Sperm DNA Normality in Rats

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Abstract:
Although fluoroquinolones are excessively prescribed in the therapy of genital tract infections, it can be associated with fertility problems and insufficient information concerning their effect on fertility are present. The goal of this study is to estimate the effects of levofloxacin on certain sperm function parameters (even on reproductive tissues) and to investigate whether levofloxacin can affect sperm DNA integrity or chromatin quality. Forty-eight male adult were enrolled in this study. The animals were randomly divided into 6 groups; four levofloxacin treated groups which were treated with a dose of either (37.5 mg/kg/day) or (75 mg/kg/day) of levofloxacin and two control groups, for each treatment dose the treatment continue for either 14 days or 28 days. Certain epididymal sperm function parameters, sperm motility and morphologically normal sperm percentage were analyzed. In addition to analysis of sperm DNA integrity and chromatin quality, histopathology of testes, epididymus and serum testosterone concentration. Sperm function parameters were not significantly affected when levofloxacin was administered for 14 days. While a significant reduction in sperm concentration, percentage of morphologically normal sperm and sperm motility were observed when the drug was administered for 28 days. A significant increase in the level of DNA fragmentation with a significant reduction in chromatin quality were also observed in levofloxacin treated groups. The testes of rat treated with levofloxacin showed changes in the number of spermatogonia in some seminiferous and epididymal tubules when the drug was applied in high doses and for 28 days. Serum testosterone concentration was not significantly affected by levofloxacin administration. These results indicate that levofloxacin could adversely affect fertility potential in male.

Keywords: Fertility, Levofloxacin, Male, Sperm DNA.

INTRODUCTION:
Antibiotics are usually prescribed in the treatment of several types of diseases. Whereas some patients requiring assisted fertilization, in some cases, they display evidence of the male reproductive tract infection [1]. Therefore, the use of antibacterial agents is essential in the treatment of male genital tract infections that can adversely affect fertility. The antibiotic fluoroquinolones are commonly prescribed by fertility specialists in the therapy of several types of bacterial infections when high concentration of leukocytes are displayed in the semen or prior to in vitro fertilization program, without taking consideration to the microbial evidence of infection [2]. Infertility which represent a disease of the reproductive system can be defined as failure to achieve pregnancy after 12 months or more of a regular unprotected sexual intercourse [3]. Male infertility defect represent more than 40% of infertility problems. There are a number of factors which can affect male fertility; anatomical factors like varicocele, ejaculatory disorders or ducal obstructions, represent some male infertility factors [4]. In addition, male infertility can be resulted from abnormalities in sperm parameters; it was estimated that sperm production defects represent 35-75% of male infertility problems. Other factors that associated with male infertility are sperm antibodies, infection, radiation, reactive oxygen species, heavy metals, cigarette smoking, hormonal factors, some therapeutic drugs and others. All these causes can be attributed to abnormalities in certain sperm parameters resulting in azoospermia, asthenospermia, teratozoospermia, oligozoospermia or others [5]. Levofloxacin, third generation fluoroquinolone antibacterial agent is active against most aerobic gram-positive and gram-negative organisms with moderate activity against anaerobes [6]. Treatment by levofloxacin may cause several side effects on the central nervous system, nerves, tendons, muscles, joints, and, gastrointestinal, including nausea, vomiting, and constipation [7]. In vivo and in vitro genotoxicity studies had propose that these antibiotics are safe for therapeutic use [8]. However, other studies have demonstrated that some fluoroquinolone antibiotics such as ciprofloxacin impair both testicular structure and function [9]. Therefore, this study was designed to found out the impact of levofloxacin on some aspects of male reproductive system in rat.

MATERIAL AND METHODS
Forty-eight male adult Albino-rats of the Wister strain were enrolled in this study. Their weight was in range of (200-250) gm and the age of rats was ranged between 8-9 weeks old. The rats were housed under controlled temperature around 25 °C and 13±2 hours light-dark cycles in cages. They were fed a standard commercial pellets. After adaptation, the experimental groups were equally divided into 6 groups (4 levofloxacin treated groups and 2 control groups), levofloxacin was injected intraperitoneally in a doses of (37.5 mg/kg/day) and (75 mg/kg/day) and each dose was administered in two periods, short (14 days) and long duration (28 days). After completion of each duration of treatment, rats from each group were anesthetized using diethyl ether, blood and reproductive organ were collected from each rat for following parameters measurement.

Epididymal sperm preparation:
The caudal epididymis region of each rat was dissected, and located in 1 mL of pre-warmed Hams F10 medium (37°C, 5% CO2). Gentle tearing of the tissue was done to make spermatozoa swim out into the culture medium. The dishes were placed in the incubator for 15 min.

Microscopic examination:
The microscopic observation was done for each sample. A drop of sperm sample was added on a warm slide and covered with standard cover slip. The preparation was scored under light microscope (40 X) objective.

Sperm function parameters analysis
Certain sperm function parameters were examined namely; sperm concentration, motility, and morphology. Motility was calculated as the ratio of progressive motility including Rapid spermatozoa, Grade a; Slow spermatozoa, Grade b; non-progressive spermatozoa, Grade c; and immotile spermatozoa, Grade d [10].