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Research Article

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The effects of titanium dioxide nano particles on ovarian tissue and oogenesis in mice

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ABSTRACT

Very specific properties of nanoparticles such as size, shape and high surface to volume ratio make them appropriate for medicinal and biological applications. These matters are distributed in organs and tissues rapidly after injection and are absorbed by cells highly. This study was carried out to investigate the effect of titanium dioxide nanoparticles on ovarian tissue of female mice. Forty female mice were divided into four groups: control group did not receive anything, placebo group and two experimental groups which received 10 and 100ppm of nanoparticles via gavage. At the end of period ovaries were colored using hematoxylin-eosin method and studied using light microscopy. Obtained data were analyzed using SPSS software. According to results, 10 ppm group was not significantly different from control group but 100ppm group increased graafiam follicle and corpus luteum significantly. Titanium dioxide nanoparticles can enforce ovarian tissue changes and therefore this nanoparticle can affect female reproduction potential dose dependently.

Keywords: titanium dioxide, mice, tissue, ovary

INTRODUCTION

Prior to using matters as medicinal tools, their effects on body biological environment or in other words their biocompatibility or toxicity must be studied. Harmful particles are more reactive in small sizes and have more toxicity. These particles increase the ratio of involvement per volume because of their inherent ratios [1].

Titanium dioxide nanoparticles are used frequently in various industries including industrial pigments, as photocatalysts for environmental cleanup, sunscreen creams, in water filtration and for killing cancerous cells because of their specific properties such a slight, electrical, and catalytic properties [2].

This technology is the newest technology which provides many opportunities for producing new tools and systems in atomic scale and making structures with brand new molecular order. Therefore nano biotechnology is applied highly to converge basic sciences, agriculture, food resources, biotechnology and medicine.

By converting micro particles to nanoparticles, we face with changing some physical properties such as increase in surface volume ratio, decreasing the size and changes of energy structure by entering into the realm of quantum

effects. Increase in surface to volume ratio which occurs gradually by size reduction causes dominance of surface atoms' behavior to internal atoms behavior that this phenomenon affects the physical and chemical properties of the particle. These matters are distributed in organs and tissues rapidly after injection and are absorbed by cells highly. Nowadays, different coatings such as albumin, polyethylene glycol, aspartic acid, etc. are used to increase stability of nanoparticles in biological solutions, blood cycle and tissue distribution. It also facilitates entering these substances into cells and reducing the toxic effects of them [1]. Titanium dioxide nanoparticles (TiO_2) are used widely to control microorganisms and microbial factors in sanitary products and wide range of business or applied plans[2].

Reproduction is the basis of survival in all creatures. Using nanoparticles has been considered lately around the world. These particles play important roles in curing diseases and have less harmful side effects than chemical drugs. Insufficient corpus luteum and progesterone amount is one of the important reasons of the early embryonic mortality and thus reduced fertility in animals [3]. Infertility has become a concern in recent years. It is also important in animals' reproduction [4].

The goal of this study was investigating the effects of titanium nanoparticles on ovarian tissue and oogenesis of little laboratory mice.

EXPERIMENTAL SECTION

Forty female mature mice from the age of 4-5 weeks and weight range of 25-30g were used. Samples were kept in animal nest of *Ostad Taher Research Center (Shahreza- Iran)* with free access to standard food, water and room situation. Mice were kept in 25℃ temperature and 25% to 30% humidity, for one week to adapt to environment.

Treatment groups were control group did not receive anything, placebo group, and two experimental groups which received 10 and 100ppm of nanoparticles via gavage. After separating, ovaries were kept in formalin 10% and tissue was divided into segments with 5micro meter thickness. Segments were colored using hematoxylin-eosin method and studied using light microscopy.

Obtained data were analyzed using one way analysis of variance and Duncan test (95%) was used to compare means. Mean weights of mice were compared using paired t-test. All analysis were done using SPSS program.

RESULTS AND DISCUSSION

Ovarian histologic examination

The number of graafian follicle was not affected by 10ppm of nanoparticle and first experimental group was not significantly different from control group but second experimental group (100ppm)increased graafian follicles significantly (Fig 1).

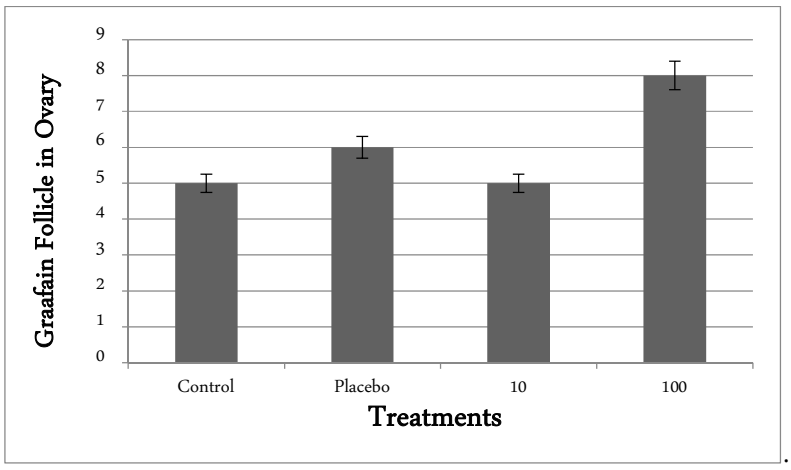

Figure 1. The number of graafian follicles in treatment groups

The number of corpus luteum showed similar result and was increased significantly in 100ppm group whereas 10ppm group was not statistically different from control group (Fig 2).

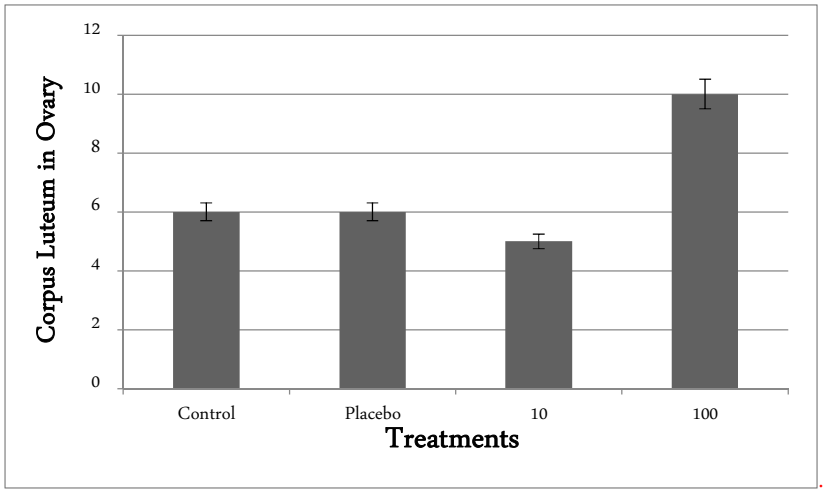

Figure 2. The number of corpus luteum in treatment groups

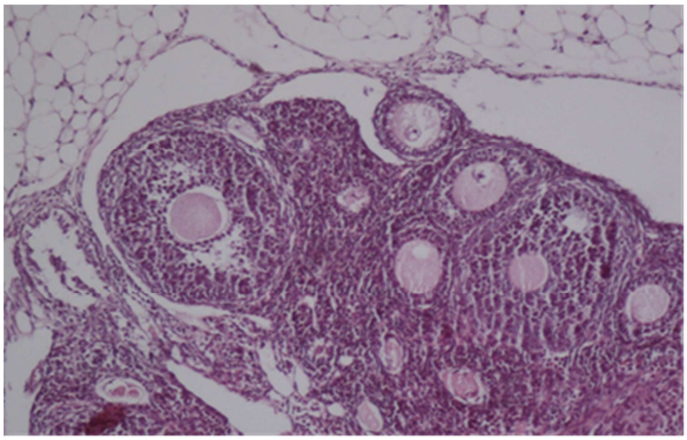

Figure 3. Photomicrograph of ovary (graafian follicles and corpus luteum) in control group

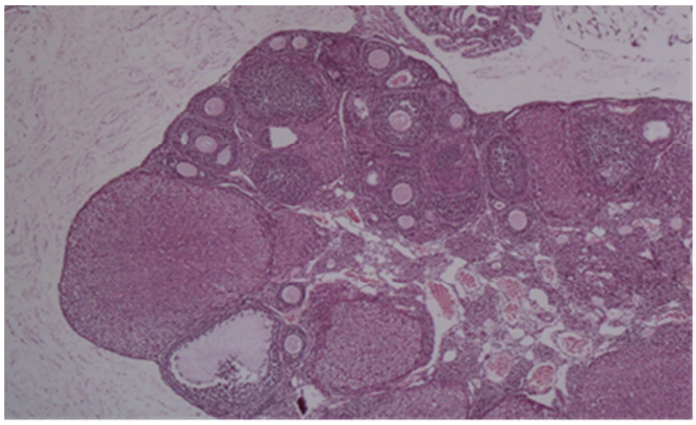

Figure 4 . Photomicrograph of ovary (graafian follicles and corpus luteum) in 100ppm group

Tio2 in 2.5,5 and 10 mg/kg doses (BW) via oral use (90 days) increases an increase in atretic follicles, intense inflammatory response and ovarian necrosis. Increased atretic follicles were highly related with premature ovarian failure caused by stimulated nano TiO2 toxicity. Furthermore, results showed that exposing to nano TiO2 reduced the number of mating, pregnancy rate, the number of infants and their growth [5].It increased the levels of sexual hormones; For example, increased R considerably and reduced serum concentrations of P4, LH, FSH and T serum concentrations highly [6]. Reduction in mating capacity of female mice after exposing to TiO2 is probably accompanied with imbalance of sexual hormones. Follicular atresia is not just the loss of ovarian follicles, it is controlled hormonal apoptosis. Therefore, reduction in FSH and LH due to exposing to TiO2 led to follicle atresia in mice ovaries. Ovarian injuries and changes in sexual hormones levels can be due to changes in existence of related genes and their proteins in ovary by nano-TiO2[6].

In mammals, the majority of ovarian follicles undergo atresia during development and only a small number will eventually reach the puberty. Apoptosis of granulose cells of ovarian follicle occurs at atresia time of most animals which is the reason of atretic start and progress [7].In current study levels of IGFBP-2 and EGF were considerably increased but IGF-1 was controlled highly in TiO2 treated ovary. It shows that follicle atresia caused by nonoTiO2 may have affected the increment of IGFBP-2, EGF and reduction of IGE-1 in ovary [7].

Granulosa cells produce estrogen which can improve self-production of FSH from LHR and aromatase activity in cells. In spite of estrogen, Androgen is able to stimulate follicular atresia. Inhibin has been also shown as an atretic factor. To create biologically active dimers associated with disulfide bond, a α subunit in combination with one of twoβ subunits make two types of inhibin. Combinations of two B subunits make three actin types. Inhibine and actin play roles in coordinating gonadotropins for regulating follicle choosing, development and atresia[8].

TNF-α induces apoptosis in various cell models and may act as a paracrine regulatory factor. GDF-9 is a growth factor which is secreted by ovule in growing ovarian follicle and is necessary for follicle natural growth. Female mice with GDF_9 deficit are infertile due to a blockage of the follicles 3B in the early follicular phase [9].

Increased levels of TNF-a, IL-1β and IL-6 are also related to inflammation in human and animals.

Previous studies showed that existence of TNF-a, IL-1β and IL-6 were increased considerably by nano-Tio2 but controlled also GDF-9 in mice ovary highly which led to inflammation and blockage of the follicle in the ovaries of mice [8].

CONCLUSION

Results of current study showed that 10 ppm group was not different from control group but 100 ppm group increased the number of graafian follicle and corpus luteum significantly. Therefore, titanium oxide nanoparticles can enforce tissue changes in ovary and is effective on female reproduction potential dose dependently.

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