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Hormonal and Immunological Study in Serum of Pregnant albino rats Treated with Nickel Oxide Nanoparticles

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Abstract

The present study was aimed to elucidate the effect of Nickel oxide nanoparticle (100mg /kg b.wt) on some parameters in pregnant Albino rats which including serum reproductive hormonal level, Leutinlizing Hormone (LH), Follicle stimulating Hormone (FSH) and Testosterone (Test), and some Immunoglobulin levels (IgA, IgG, IgM) for different period of pregnancy (12 and 14 days). The hormonal results showed significant ($P \leq 0.05$) increased of treatment groups as compared with control groups. Immunological results showed significant decreases in treated groups as compared with control groups, It could be concluded that increasing concentrations of NIO- NPs and durations of exposure leads to negative effects on the pregnant albino rat.

Key words: *NIO, nanoparticles, albino rats, hormones, immunoglobulin.*

Introduction

Nickel is a silver-white metallic chemical element that is naturally present in the Earth's crust [1]. Because of its unique physical and chemical properties, being tough, harder than iron, ferromagnetic, having good plasticity and highly resistant to rusting and corrosion, nickel and its compounds are widely used in industry [2]. Nickel is an essential element for at least several animal species. These animal studies associate nickel deprivation with depressed growth, reduced reproductive rates, and alterations of serum lipids and glucose [3] . Nickel is known as a potentially harmful element for humans. Its concentration in the environment can rise due to industrial activities [4]. Human exposure to nickel or its compounds has the potential to produce a variety of pathological effects, which may include cutaneous inflammations such as swelling, reddening, eczema and itching on skins, and may also include allergy reactions and teratogenicity in the human body. Nickel is capable of evoking dual responses in the human immune system [5]. Experiments conducted in humans and in rodents have shown that nickel exhibits both immune modulatory and immune toxic effects, Number of immunological and lymphoreticular effects have been reported in humans and animals exposed to nickel. In 38 production workers exposed to nickel (compound not specified), significant increases in levels of immunoglobulin G (IgG), IgA, and IgM and a significant decrease in IgE levels were observed [6]. Significant increases in other serum proteins, which may be involved in cell-mediated immunity (including α1-antitrypsin,α2-macroglobulin, ceruloplasmin) were also noticed. Nickel and chromium significantly depressed the circulating antibody response of rats immunized with a viral antigen ,with the greatest decrease in antibody titers noted in animals receiving the metal two weeks before the initial antigen dose [7] Several studies have examined the relationship between nickel exposures and acquired immune function. Exogenous chemicals can interfere with the normal functioning of the HPG axis, resulting in reduced fertility or even infertility in both females and males. Ni NPs effect the serum sex hormone levels (FSH, LH, E2 or T) in female and male rats. Some study demonstrate that Ni NPs increased significantly the level of serum FSH and LH, and decreased E2 this effect associated with dose-dependent in females. The results indicate the effects of Ni NPs on the female rat ovarian reserve. It is probably an indication of the decreased level of serum E2 and ovarian hormone secretion following ovarian damage with Ni NPs, which increased the level of serum FSH and LH by negative feedback. Meanwhile, the male

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rat serum FSH, LH and T content analysis showed the levels of FSH and T were decreased significantly by Ni NPs treatment [8].

Materials and Method

Animals

Animals with weight of 195- 280 gm and aged of 2.5-3 months were obtained from the animal house of the Biology Department/College of Science at University of Babylon.Animals were put inside special cages for breeding with length of 25 cm, 18 cm width and 19.5 cm height and stayed about 30 days. The cages were covered with sawdust, which replaced three times weekly with the care of hygiene and sterilization. The animals were provided with food and water *ad libitum*. The animals were housed in special rooms with controlled conditions of temperature (24± 10C°) and natural light periods (12 hours light/dark) [9]. Each two females were put with one male (for mating) in special plastic cages and strung metal caps with dimensions of 40 cm length, 25 cm width and 19.5 cm height. After ensuring the pregnancy by observing vaginal plug and vaginal smear(9).this day regarded as 0th day of gestations (GD=0) Pregnant rats divided in five groups (n=4). Each two females were put with one male (for mating) in special plastic cages and strung metal caps with dimensions of 40 cm length, 25 cm width and 19.5 cm height.

Nanoparticles Dose Preparation

Determination of Nickel oxide doses were depended on the animals body weight. 25- PPM doses of nanoparticle suspension was prepared and mixed with distilled water[10].

Animals Anesthesia

The pregnant rats were anesthetized with chloroform in 12 and 14 days of pregnancy. Pregnant rats were put after anesthesia on dissection bowl, the fore and hind limbs were fixed by fine pins, the pregnant's abdomen was opened by a sharp scissors and take blood sample by heart puncture .

Blood collection: Blood samples were collected via the left ventricular cardiac puncture into sterilized EDTA tubes and gel tube to separate the serum quickly and then centrifuged at 3000 rps for 5 minutes. The serum samples were stored frozen until used.

Hormonal Assay: Serum Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH) and Estradiol were measured by using ELISA (Monobind Company, USA) for both control and treatment animals.

Results

Effect of Nickel Oxide nanoparticles on Luteinizing Hormone in Pregnant Albino Rats for 12, 14 Days of Pregnancy.

The result of the present study showed that the LH hormone means increases significantly (P≤0.05) in treated group (12, 14 days) with NIO (100 mg / kg b.wt) (1.1 ±0.010, 1.28 ± 0.043) (pg/ ml) respectively, as compared with control group (0.8263 ± 0.02512, 0.836 ± 0.0251) for 12, 14 days respectively (Figure-1) .

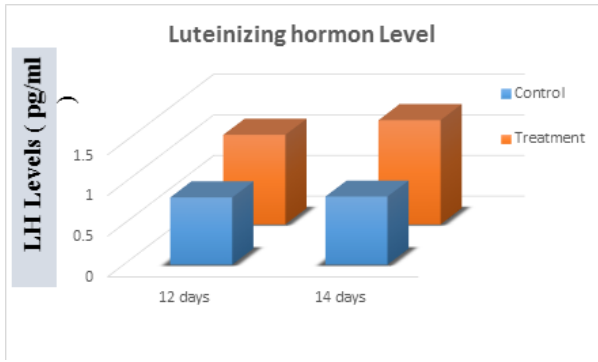

Figure (1): Effect of Nickel Oxide Nanoparticles on Luteinizing Hormone in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

Effect of Nickel Oxide Nanoparticles on Follicle Stimulating Hormone in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

FSH means in present study increases significantly (P≤0.05) in treated group with NIO (100 mg / kg b.wt) (1.023 ±0.032, 1.16 ± 0.051) (pg/ml) as comperd with control group (0.8 ± 0.004 , 0.8 ± 0.003 pg/ ml) 12 and 14 days respectively (Fig.2)

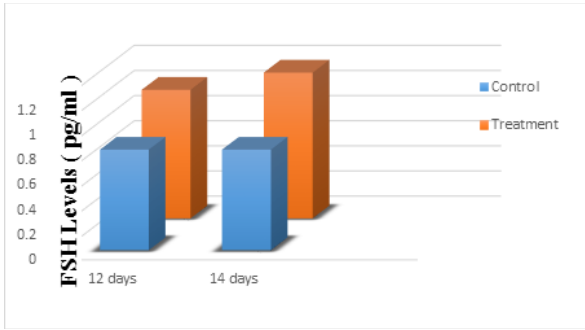

Figure (2): Effect of Nickel Oxide Nanoparticles on Follicle Stimulating Hormones in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

Effect of Nickel Oxide nanoparticles on Testosterone Hormone in Pregnant Albino Rats for 12 and14 Days of Pregnancy.

The present study showed significant increases (P≤0.05) of Testosterone in treated group with NIO (100 mg / kg b.wt) (0.61 ±0.001 , 0.63 ±0.001pg/ml), as compared with control group (0.541 ±0.013 , 0.52 ±0.08 pg/ml) for 12 and 14 days respectively (Figure-3).

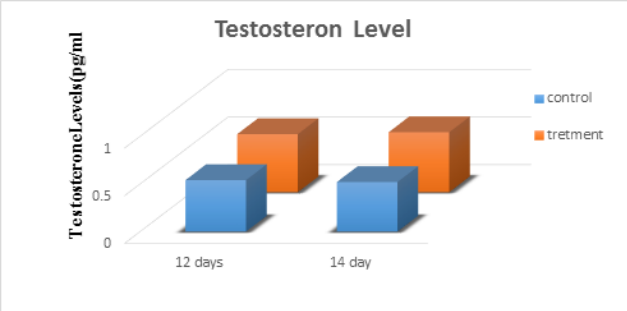

Figure (3): Effect of Nickel Oxide nanoparticles on Testosterone Hormon in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

Effect of Nickel Oxide nanoparticles on Immunoglobulin A in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

The result in the (Figure-4) revealed that the IgA, showed significant (P≤0.05) decreases in the treated group with NIO (100 mg / kg b.wt) (16.29 ± 0.292, 14.3± 0.22 pg/ml) as compared with control group (19 ± 0.386, 18.63± 0.52 pg/ml) for 12 and 14 days respectively.

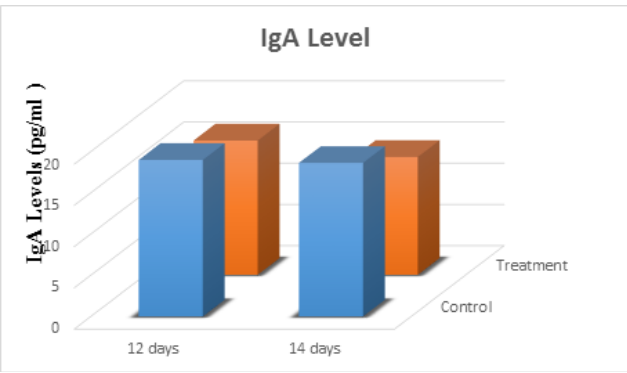

Figure (4): Effect of Nickel Oxide Nanoparticles on Immunoglobulin A in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

Effect of Nickel Oxide Nanoparticles on Immunoglobulin G in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

The result in the (Figure-5) revealed that the IgG, showed decreases significant (P≤0.05) in the treated group with NIO (100 mg / kg b.wt) (95 ± 1 , 82.66± 1.52 pg/ml) respectively, as compared with control group (119 ± 1 , 118.3± 1.52 pg/ml) for 12 and 14 days respectively.

Figure (5): **Effect of Nickel Oxide Nanoparticles on Immunoglobulin G in Pregnant Albino Rats for 12 and 14 Days of Pregnancy**.

Effect of Nickel Oxide Nanoparticles on Immunoglobulin M in Pregnant Albino Rats for 12and 14 Days of Pregnancy.

The result in the (Figure-6) revealed that the IgM showed significant (P≤0.05) decreases in the treated group with NIO (100 mg / kg b.wt) (16.35 ± 0.19 , 14.46± 0.21 pg/ml) respectively, as compared with control group (19.62 ± 0.06 ,18.24± 0.02 pg/ml) for 12 and 14 days respectively.

Figure (6): Effect of Nickel Oxide Nanoparticles on Immunoglobulin M in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

Discussion

Effect of Nickel Oxide Nanoparticles on Luteinizing, Follicle stimulating and Testosterone Hormones in Pregnant Albino Rats for 12 and 14 days of pregnancy.

The present study showed significant (P≤0.05) increases in treated group with NIO (100mg /kg b.wt) as compared with control group for 12 and 14 days of pregnancy this change of hormones could be resulted from the hypothalamic–pituitary–gonadal (HPG) axis is the hormone system whereby the hypothalamus secretes so-called releasing hormones, which are transported via the blood to the pituitary gland. There, the releasing hormones induce the production and secretion of gonadotropins (i.e., LH and FSH), which in turn are transported by the blood to the gonads (i.e., the ovaries and testes).

Generally speaking, in females, LH and FSH stimulate the ovarian follicle that contains the maturing egg to produce estradiol. After ovulation has occurred, LH also promotes production of progesterone. Both hormones participate in a negative feedback mechanism through most of the menstrual cycle, suppressing GnRH release from the hypothalamus and LH release from the pituitary (11).

Exogenous chemicals can interfere with the normal functioning of the HPG axis, resulting in reduced fertility or even infertility in both females and males, the effects of Ni NPs on aspects of serum sex hormone levels (i.e., FSH, LH, E2 or T) in female and male rats. Increases of Ni NPs level in serum FSH and LH, with significant and

dose-dependent in females. It is probably an indication of the decreased level of serum E2 and ovarian hormone secretion following ovarian damage with Ni NPs, which increased the level of serum FSH and LH by negative feedback [12].

The change of hormone reproductive levels indicates the abnormal reproductive axis function, which correlated with male and female infertility [13]. However, the mechanisms by which NPs alter the functions of HPOA ultimately resulting in female infertility have not been investigated thoroughly [15]. Meanwhile, the amount of researches about NPs having negative effects on HPOA is relatively small. It is certain that NPs with size of 36 nm were significantly accumulated in cerebrum and cerebellum translocation via the olfactory nerve and increased with the exposure time [16]. The sizes of NPs less than 90nm could disturb the balance of GnRH, FSH and LH, such as Ni, PEG-b-PLA(17) [18].

Other study showed that gold nanoparticles reduced the level of testosterone An- other assumption is that the nanoparticles could affect the gene expression of the protein that is involved in the transport of cholesterol into the inner membrane of mitochondria and increased the synthesis of steroids. It is also possible that nanoparticles by reducing the gene expression of the mitochondrial membrane protein Star, inhibit the cholesterol transportation into the inner membrane of mitochondria, and eventually inhibit the conversion of cholesterol to pregnenolone and reduced the level of testosterone. Karpenko (2013) studied toxic effects of cerium oxide nanoparticles on sex hormones and concluded that nanoparticle reduced glandular and testosterone secretion, the gold nanoparticles reduced the level of testosterone [19].

Effect of Nickel Oxide Nanoparticles on Immunoglobulin A, G and M in Pregnant Albino Rats for 12 and 14 Days of Pregnancy.

The results of the current study as in the table () revealed that the IgA, IgG and IgM, showed significant ($P \leq 0.05$) decreases in the treated group of (12, 14) days with NIO (100mg/kg b.wt), as compared with control group. The decreases of Immunoglobulins levels in pregnant females due to that the nanoparticles can also suppress the immune system which can weaken immune response against infections and cancerous cells. These immunosuppressive properties, on the other hand, can make nanoparticles useful in preventing transplant rejection, in treating inflammatory and autoimmune diseases, and in delivering immunosuppressive drugs [20].

Nanoparticle properties are responsible for immunosuppressive effects. While some nanoparticles are used to deliver immunosuppressive drugs, others have their own immunosuppressive properties. Shen *et al.* [22] have shown that Fe_3O_4 nanoparticles weaken the antigen-specific humoral response and T cell cytokine expression in ovalbumin-challenged mice. Mitchell *et al.* [23,24] reported that multi-walled carbon nanotubes (MWCNTs) suppressed systemic humoral immunity in mice. Some nanoparticles have been shown to possess anti- inflammatory properties. CeO2 nanoparticles were reported to reduce ROS and the level of inflammatory cytokines IL-6 and TNF-α in murine macrophages [25]. After the immunization of mice with a C60 fullerene derivate conjugated to bovine thyroglobulin, they produced IgG antibodies specific to fullerenes. Other researchers were not able to detect fullerene-specific antibodies, even when they used a carrier molecule [25].

Conclusion

The hormonal results showed significant ($P \leq 0.05$) increased of treatment groups as compared with control groups. Immunological results showed significant decreases in treated groups as compared with control groups, It could be concluded that increasing concentrations of NIO- NPs and durations of exposure leads to negative effects on the pregnant albino rat.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Babylon University/College of Science, Iraq and all experiments were carried out in accordance with approved guidelines.

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