



The Antioxidant Effect of Diamond Nanoparticles on Testicular Tissue

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Dear Editor,

Today, industrial life changes have a great impact on human health. Air pollution, type of clothing, and clothing material affect men's reproductive system, impairing sperm production and leading to subfertility or infertility.

In Iran, the prevalence of infertility is 20.3%, which is higher than the global average (12% - 15%). Male factors are involved in more than 40% of infertility cases. Despite extensive research on male infertility, the etiologies are unknown in 30% - 60%, which may be due to various causes, such as environmental pollution, oxygen free radicals, and genetic and epigenetic abnormalities (1).

Evidence suggests that damage to sperm due to reactive oxygen species (ROS) is a major cause of infertility in men, leading to sperm dysfunction. A chronic or excessive increase of free radicals has a detrimental effect on the physiological function of cells and causes irreversible changes in the structure of biological macromolecules.

Damage to macromolecules in the cell includes DNA strand breakage, peroxidation of cell membrane lipids, and damage to membrane transporter proteins and intracellular enzymes (2). Spermatozoa, in particular, are prone to oxidative stress (OS) damage due to their high levels of unsaturated fatty acids and low content of antioxidant enzymes in the cytoplasm (3). In general, OS is an imbalance between the production of free radicals and the cellular antioxidant defense system in favor of free radicals, which causes oxidative damage, activation of signal pathways, and peroxidation of macromolecules in the cell. In addition, it ultimately leads to secondary effects on cell function and the progression of pathological conditions (3).

Among environmental factors, nanoparticles have a special place and can interfere with the normal function

of tissues and organs. By passing from microparticles to nanoparticles, we encounter changes in some physical properties, increasing the ratio of surface area to volume, which gradually occurs with decreasing particle size and changing the behavior of atoms on the particle surface to the behavior of internal atoms. This phenomenon affects the physical and chemical properties of the particles and allows them to act as high-performance catalysts (4).

The small size and high surface area of nanoparticles increase their chemical activity. This increase in chemical and physical activities in many nanoparticles has led to their widespread use in processes such as drug delivery, vaccination, diagnosis or treatment of a variety of diseases, tissue regeneration, immunoassay, elimination of biofluid poisoning, heat treatment of cancer cells, and dental alloys, bladder catheters, etc. (5). According to experts, nanoparticles enter the human body through the mouth and nose, penetrate body tissues, and then damage cells through ROS, changes in cytokines, and the production of free radicals (6).

The small size of nanoparticles allows the passage of cell membranes in organs such as mitochondria and allows escape from cell settlement (6). Despite the widespread use of nanoparticles and many efforts made to demonstrate the desirable properties of nanoparticles in medicine, the biological effects of these particles on cells and organs are not yet fully understood. In studies on the effect of nanoparticles on sperm-producing tubes, the results have shown that these particles in certain doses cause changes in testicular tissue, damage to germ cells, and, by inducing the OS pathway, severely reduce Leydig cells and sperm viability. They also express some genes.

Xia et al. showed that nanoparticles with high produc-

tion of ROS overcome the cell antioxidant system and increase OS and apoptosis by reducing mitochondrial function (7). Ghoshcian et al. investigated the effects of nanoparticles on the expression of BCL2 and BAX genes in the hippocampus of rats. The results showed that nanoparticles by decreasing BCL2 and increasing BAX caused instability of the mitochondrial membrane, increased the release of cytochrome c, and thus led to increased apoptosis (8).

Despite numerous and valid findings on the destructive and adverse effects of nanoparticles, some studies have shown the beneficial effects of nanoparticles. In this regard, Hamza and Diab (2020) evaluated the effects of nano-selenium on rat testicular tissue. They showed that nano-selenium had an antioxidant effect, increased enzymes superoxide dismutase and glutathione peroxidase, increased testosterone levels, and reduced malondialdehyde (9).

Kobyliak et al. investigated the antioxidant properties of cerium dioxide nanoparticles in rats. They concluded that these nanoparticles at a dose of 1 mg/kg have antioxidant properties and can treat infertility by improving sperm parameters and reducing OS (10). Afshar et al. studied the effects of simultaneous administration of iron nanoparticles and curcumin on testicular function in Wistar rats with testicular hyperthermia. They showed that iron nanoparticles have antioxidant properties and improve sperm parameters (11). Ghandehari et al. examined the antioxidant effects of silver nanoparticles on liver cancer cells (HepG2). The results showed that these nanoparticles could have a dose-dependent antioxidant effect and inhibit DPPH and ABTS free radicals and cancer cells at very low doses (IC50: 6 µg/mL) (12).

Based on our studies, treatment with diamond nanoparticles at LD50 in rats with testicular reperfusion ischemia improved cell damage and led to cell death from necrosis to apoptosis, but in normal rats, this treatment had the opposite effect and caused cellular damage and increased necrosis, indicating the dual role of nanoparticles according to cell type.

Orazizadeh et al. showed that co-administration of beta-carotene and titanium improved spermatogenesis and that beta-carotene had a strong protective effect against testicular toxicity and could be clinically beneficial (13).

In recent years, the synthesis of green nanoparticles by plants has attracted much attention and can be considered as an alternative to chemical methods for the synthesis of nanoparticles (14). Studies have shown that silver ions dramatically increase ROS production, including the radical superoxide anion, and cause OS in cells. Plants have antioxidant activity due to their secondary metabolites (such as phenol and flavonoids) and can prevent oxidative dam-

age to cells. Thus, plants have the potential to biodegrade and produce nanoparticles with antioxidant properties. Therefore, the biosynthesis of nanoparticles and antioxidants through plants as a biocompatible method is very useful and has been considered by researchers (15). Rahimi-Kalateh-Shah-Mohammad et al. showed that zinc oxide nanoparticles synthesized by a green method have antioxidant properties and are able to inhibit the growth of cancer cells (16).

In conclusion, concomitant use of coenzyme Q10 with diamond nanoparticles improves sperm parameters and reduces apoptosis, which can be attributed to the antioxidant properties and inhibition of the OS pathways of coenzyme Q10; thus, due to the dual role of nanoparticles in the reproductive system, it is recommended. In the group of infertile patients, antioxidants should be used to improve the damaged pathways.

Footnotes

Authors' Contribution: Masoumeh Masoumi wrote the proposal, carried out the project, and wrote the article. Dr. Hashemi collaborated in all stages, including proposal writing, project execution, article writing, and article submission. Dr. Salehi collaborated on the project and wrote the article. Dr. Angaji collaborated on the project and data analysis.

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