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Nanoparticles as a Promising Innovative Treatment Towards Infertility

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Abstract

Infertility is a disease of the reproductive system in which clinical pregnancy does not occur after twelve months or more of regular unprotected intercourse. Epidemiologically, within one year, approximately 25% of marriages do not get pregnant and suffer from this complication. Factors that mostly give rise to male infertility include testicular dysfunction, immune defence reaction, seminal tract disabilities are account for about 40 percent of cases. About 50% of infertility is related to female factors including ovulatory factor disorders, endometriosis, polycystic ovary syndrome, hyperprolactinemia, anomalies of mucus, and tubal disease. The other ten percent include unknown factors. The unique properties of nanoparticles make them a reliable tool to help married people achieve pregnancy and better prevent infertility disabilities as a clinical treatment. This paper briefly discusses the causes associated with infertility and innovative forms of treatment by the usage of nanoparticles.

Keywords: Nanoparticles, Infertility, Treatment

1 Introduction

According to the World Health Organization (WHO), infertility is a disease of the reproductive system in which clinical pregnancy does not occur after twelve months or more of regular unprotected intercourse. Epidemiologically, within one year, approximately 25% of marriages do not get pregnant and suffer from this complication. Although men are involved in about half of the causes of infertility, both men and women can cause infertility (1). Nearly 20% of infertile couples are affected by factors such as follicular rupture, ovulatory factor disorders, and mutations. Disorders of the female genitalia, including abnormal uterine cavities, pelvic adhesions, and tubal integrity, account for about 30 percent of cases. Decreased sperm motility and sperm count and their displacement in the cervical mucosa, which causes the ovum not to fertilize, account for about 10% of infertility cases. About 30 percent of infertility is due to factors related to semen quality, such as genital infection, varicocele, surgery, trauma, genetic disorders, and toxins. The other ten percent include unknown factors (2). Psychological studies have shown that infertile women are more anxious, nervous, and dependent than fertile women, and experience fears about reproduction and challenges to femininity (3). Therefore, solving infertility problems both in married life and in terms of social dimension has a significant effect on reducing mental and emotional disorders caused by infertility and increasing life expectancy. As a result, it is essential to have a promising strategy that can eliminate the problems caused by infertility.

Nanotechnology is an attractive multidisciplinary science that generally deals with the control of unique size-dependent properties in the range of one to 100 nanometers. The nanoscale of materials gives them unparalleled freedom to control and modify the behavior of matter. With intelligent material control, fundamental features such as solubility, intelligent release, circulatory protection properties, biocompatibility, and a wide range of important features can be controlled and improved. The emergence of nanoscience has revolutionized various fields of science, especially medicine (4, 5). Nanoparticles have been shown to have a wide range of applications in tissue engineering, gene delivery, drug delivery, biological labels (like fluorescent and dyes), bio-detection of pathogens, proteins tracing, tumor destruction (cancer therapy), analyze of the DNA structure, MRI as contrast agents, pharmacological studies, and purification and separation of cells and biological molecules (6). The unique properties of nanoparticles make them a reliable tool to help married people achieve pregnancy and better prevent infertility disabilities as a clinical treatment. As shown in Fig.1, the durability and enormous load-carrying capability of nanoparticles allow the attachment and selective distribution of broad cargo amounts.

2 Causes of infertility

A multicenter study conducted by the WHO successfully shows that, in 20 percent of patients, the major problem was related to men. To obtain fertility, a male needs appropriate spermatogenesis, sufficient epididymal development and sperm production, healthy sperm transportation, and effective operation of the gland along with correctly paced copulation. Factors that mostly give rise to male infertility include testicular dysfunction, immune defence reaction, seminal tract disabilities, psychopathy, early-stage cancer treatment medications like chemotherapy agents and other medications like anabolic steroids and testosterone supplementation, antifungals such as some antihypertensive and ketoconazole drugs and also hypothalamic-pituitary disorders (Figure 2) (7, 8). The latest current statistics demonstrate that 12 percent or about 7.3 million American females within the ages of 15 and 44 experience fertility disorders and even a failure to conceive or carry out childbirth.

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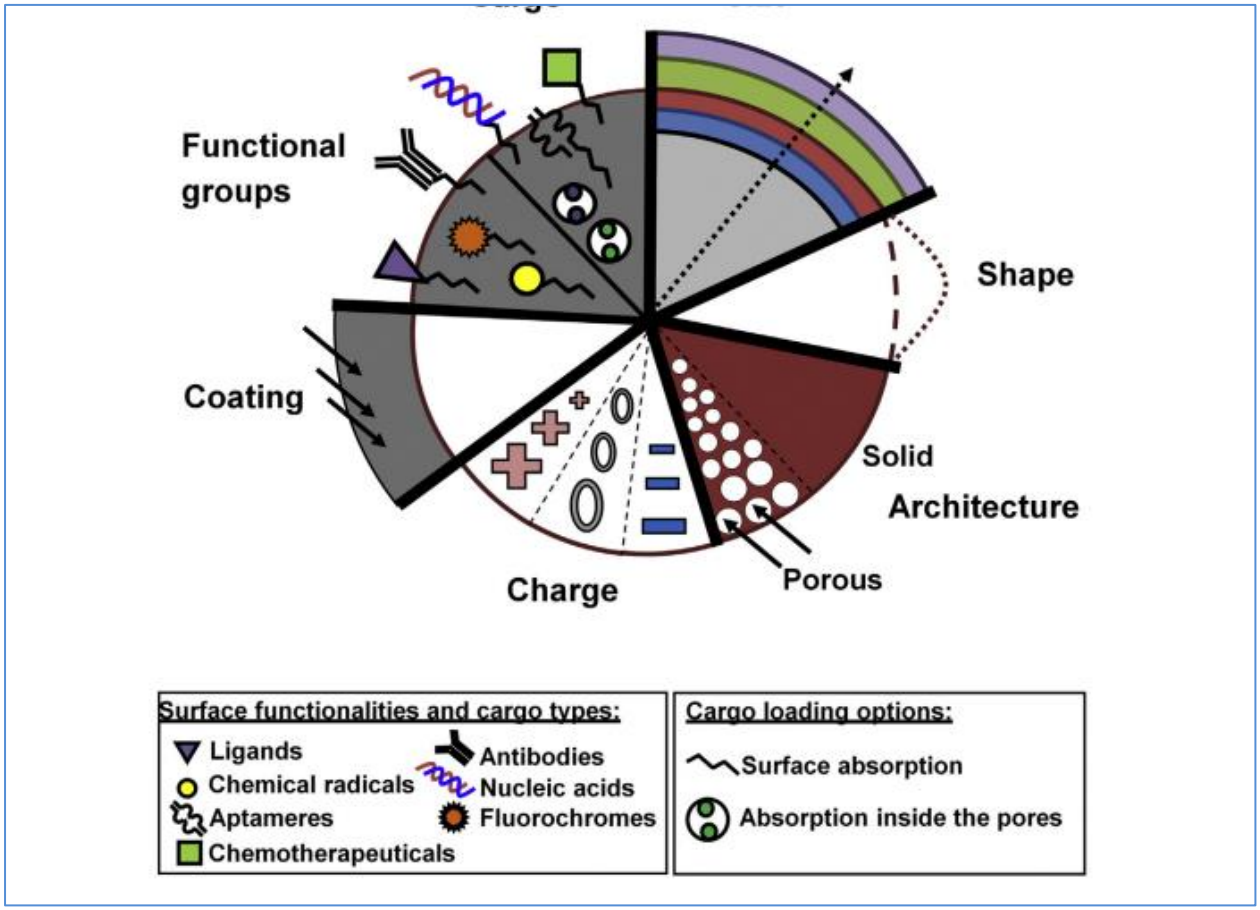

Figure 1: The durability of nanoparticles. Nanostructures are extremely flexible systems with dynamic chemical and physical characteristics

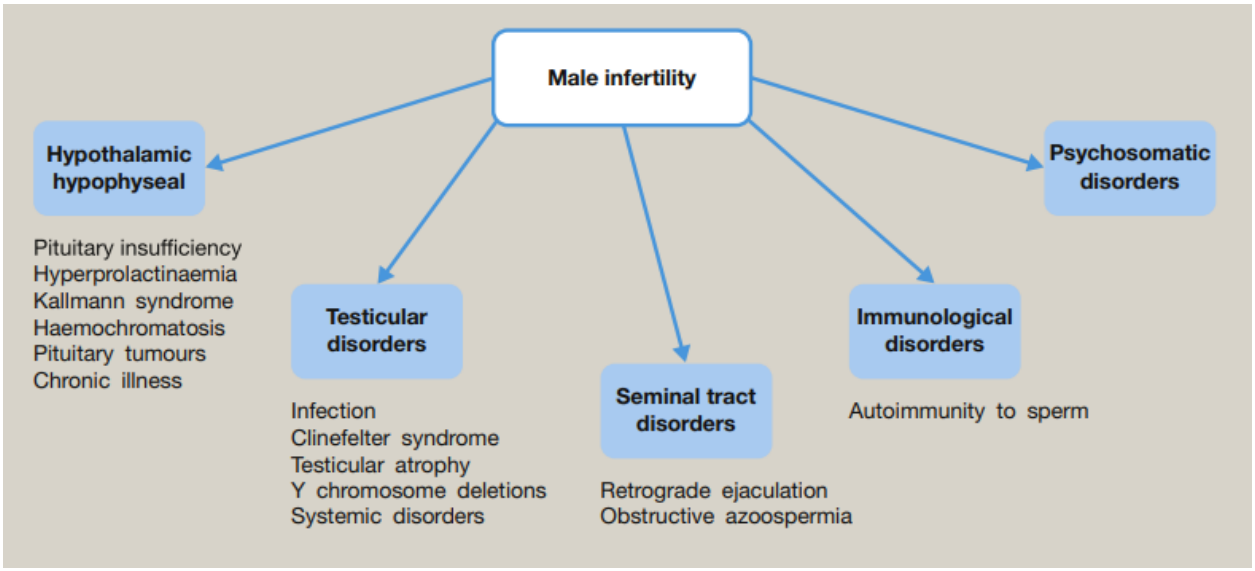

Figure 2: Male infertility factors

A variety of well-determined health behaviors have been recognized that directly cause females towards infertility, such as postponed parturition, early puberty, a background of sexual transmission of pathogenesis, and pelvic inflammation-related disorders. Relevant variables including age changes, overweight, active smoking, and the experience of ectopic pregnancy have been the most commonly correlated infertility causes in females (9). Ovulatory disturbances, endometriosis, polycystic ovary syndrome, hyperprolactinemia, anomalies of mucus, and tubal disease are also important factors in women's infertility (10).

Dysfunction	*Defective changes*
Ovarian function	Prolonged follicular phase Reduced rate of follicular growth Reduced pre-ovulatory follicle size Reduced pre-ovulatory serum oestradiol concentration Disordered and impaired LH surge Disordered early luteal phase patterns of oestradiol and progesterone Luteinized unruptured follicle
Tubal function	Alterations in normal tubo-ovarian relationships Hydrosalpinges Alterations in tubal motility by prostaglandins with accelerated tubal motility
Sperm function	Phagocitosis by macrophages
Fertilization - embryo defects	Impaired fertilization Embryo toxicity, impairs early embryo development
Endometrial defects	Luteal phase defects Endometrial antibodies Implantation defects
Early pregnancy failure	Abnormal embryos Immune reaction Auto-santibodies Cytokines (interleukin I)

Figure 3: Current infertility processes in women with endometriosis

As can be seen from Fig. 3, the correlation between infertility and endometriosis has been known for years. Also, the approximate rate of unexplained infertility has been measured to be almost 15 percent across infertile pairs who were extensively examined.

3 Treatment

Nanotechnology may improve the health of semen by reducing the percentage of antibiotics required to destroy the remnant bacteria and protect the safety of inseminated women (11). Antimicrobial impact of magnetic silver nanocomposites and further single-walled carbon nanotubes on the proliferation of infective Salmonella and Escherichia coli can enhance semen health and keep sperm unchanged (11, 12). Reactive Oxygen Species lead to irreversible destruction of surrounding healthy spermatozoa (13). Nanoparticles grafted with antioxidative enzymes as well as nanomaterials with antioxidant activity like cerium oxide may help protect against oxidative stress (14, 15). Fe3O4 magnetic nanostructures containing positive charge may be drawn to the sperm extracellular surface. Around the electromagnetic region, the Fe3O4 nanostructures are polarized to handle the movement of sperm samples. In fact, sperm acceleration intensity is a secondary function of the magnetic position distance. Subsequently, this suggested technique utilizing membrane-charged magnetic nanomaterials to track the motion of semen cells in vitro offers a straightforward remedy toward infertility. Fe3O4 magnetic nanomaterials via a positive charge will transfer sperm cells quicker because they are strongly drawn to sperm membranes. Therefore, this novel strategy to regulating the mobility of sperm cells utilizing positively surface-charged Fe_3O_4 magnetic nanomaterials offers an efficient remedy towards infertility (16).

Infertility therapy including dual drug-loaded nanomaterials greatly reduced matrix metalloproteinase operation, oxidative damage, and angiogenesis, along with the decrease in vascular volume and endometrial gland. Prevention of endometriosis-related negative consequences has often increased the amount and quality of oocytes, which has a vitally important role in pregnancy experiences. Recent findings indicate that due to the cumulative effects of poly(lactic-co-glycolic) acid nanoparticles which stacked with doxycycline and epigallocatechin gallate in quite a specific carrier, these modified nanoparticles seem to be a potential novel strategy for endometriosis therapy(17). C105Y-modified mesoporous silica nanoparticles retained their biodegradability with sperm and demonstrated a nearly fourfold rise in orientation toward zygotes, relative to unaltered MSNPs, mostly across initial phases of incubation (18). In addition, in this section, more applications of nanoparticles in infertility are mentioned, which include the following:

- Use of biocompatible magnetic nanoparticles to eliminate damage and identify spermatozoa in semen samples (19).
- Improving and increasing sperm motility and protecting the genome and cytoplasmic membrane of sperm by using cerium oxide (CeO_2) nanoparticles (20).
- Keep sperm alive due to the ability of CeO2 to retain and store oxygen, as well as act as reactive oxygen species (ROS) scavengers (20).

- Coping with oxidative degradation in sperm by the ROS scavenger power of nano-selenium (SeNPs) and improve the quality of spermatozoa (21).
- Use of heparin gold nanoparticles as a biomarker to diagnose infertility through the reaction between polyanionic heparins and polycationic protamine (protamine is the most plentiful sperm nuclear protein) (22).
- Using superparamagnetic iron oxide nanoparticles (SPION) to remove disturbed sperm to increase semen quality (23).
- increase the sperm plasma membrane efficiency through Zn nanocomplex (24).

Ethical issue

Authors are aware of, and comply with, best practice in publication ethics specifically with regard to authorship (avoidance of guest authorship), dual submission, manipulation of figures, competing interests and compliance with policies on research ethics. Authors adhere to publication requirements that submitted work is original and has not been published elsewhere in any language.

Competing interests

The authors declare that there is no conflict of interest that would prejudice the impartiality of this scientific work.

Authors' contribution

The author of this study has a complete contribution for data collection, data analyses and manuscript writing.

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