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Research Progress of Ovarian Tissue Cryopreservation and Transplantation

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Abstract: ***Age, disease and anti-tumor treatment may cause the decline or even loss of female fertility. Embryo cryopreservation, oocyte cryopreservation and ovarian tissue cryopreservation are commonly used at present. Cryopreservation and transplantation of ovarian tissue has become a fertility preservation method with medical indications in clinic, which is helpful for patients to successfully complete fertility through this technology. This paper reviews the international research progress on ovarian cryopreservation and transplantation in recent years. Despite the rapid development of ovarian tissue cryopreservation and transplantation technology, it still faces challenges such as how to reduce the loss of follicular reserve and thus prolong the effectiveness of ovarian tissue transplantation. More basic and clinical research is needed to promote the progress and development of ovarian tissue cryopreservation and transplantation technology.***

Keywords: Ovarian tissue cryopreservation; Ovarian tissue transplantation; Follicle loss.

1. INTRODUCTION

With the continuous development of cancer prevention and treatment technology, the occurrence of malignant tumors has a younger trend, and the survival rate of patients with malignant tumors before childbearing age has been greatly improved. As an important branch of assisted reproductive technology, ovarian cryopreservation technology provides new fertility hope for many female patients who suffer from reproductive capacity damage due to cancer and other diseases [1]. The occurrence of cancer not only poses a serious threat to the health of patients, but also may lead to the decline of ovarian function and premature aging, affecting fertility [2]. Especially in women receiving cancer treatment such as chemotherapy or radiotherapy, the ovaries are often directly hit by toxic substances, resulting in a decrease in ovarian reserve and early ovarian failure [3]. In this case, women may face a greater fertility crisis, leading to the risk of infertility.

The decline of ovarian function is closely related to premature ovarian failure. Premature ovarian failure not only affects women 's endocrine function, but also leads to a significant reduction in the number and quality of eggs, which seriously affects fertility [4]. Therefore, ovarian cryopreservation has become an important choice for patients with infertility caused by diseases such as tumors and corpse injuries. By cryopreservation of ovarian tissue before treatment, patients can undergo ovarian transplantation or in vitro maturation of follicles at an appropriate time in the future, thereby preserving fertility [5]. The wide application of this technology has helped many women realize their reproductive dreams and given them the opportunity to regain hope.

The advantage of ovarian cryopreservation is that it provides a wider range of choices and flexibility for patients with low fertility. With the continuous progress of fertility technology, more application forms may appear in the future, such as in vitro reproductive technology. Through the study of frozen ovarian tissue or follicles, scientists are expected to achieve in vitro maturation and reproduction of follicles, greatly improving women 's reproductive opportunities [6]-[7]. The continuous development of this field will surely bring gospel to many women who are facing fertility difficulties and add new hope and choice to their lives.

2. HISTORY AND PRESENT SITUATION OF OVARIAN TISSUE CRYOPRESERVATION AND TRANSPLANTATION

2.1 History of Ovarian Tissue Cryopreservation and Transplantation

The study of ovarian tissue cryopreservation and transplantation originated in the early 20th century. The earliest ovarian tissue cryopreservation experiments can be traced back to the 1960 s [8]. Early studies mainly focused on animal models such as rats, and scientists hope to preserve their reproductive function by cryopreservation of

ovarian tissue [9]. In the 1980 s, with the continuous development of freezing technology, ovarian tissue cryopreservation was gradually applied to clinical practice [10]-[12]. In 1999, the world 's first successful case of ovarian tissue transplantation was reported in Israel. The patient successfully conceived and gave birth after transplantation, marking the development of this technology has entered a new stage [13].

After entering the 21st century, the research on ovarian tissue cryopreservation and transplantation technology has become more and more active. The scientific research team has made new explorations in cryopreservation methods, transplantation strategies and subsequent fertility outcomes. Many countries have gradually used ovarian tissue cryopreservation as a fertility protection measure for patients with cancer, early ovarian failure and other reproductive crises [14]-[15]. Especially with the advancement of cancer treatment technology and the change of patients ' fertility concept, the clinical application of ovarian tissue cryopreservation and transplantation is gradually increasing. At this stage, many hospitals have established a technical platform for ovarian tissue cryopreservation and transplantation, which has promoted the further development of this field.

2.2 The Operation and Current Problems of Frozen Ovarian Tissue and Transplantation

The operation of ovarian tissue cryopreservation and transplantation is relatively complex, involving multiple links. In the process of cryopreservation, it is first necessary to perform surgical sampling of ovarian tissue before chemotherapy or radiotherapy. Then, the removed ovarian tissue needs to be sliced and a protective agent is added to reduce the possible ice crystal damage during cryopreservation. After that, the ovarian tissue was stored in liquid nitrogen after programmed cooling to maintain its activity. When transplanting, it is necessary to thaw first, and then evaluate the survival status of the tissue. After that, the doctor will transplant the ovarian tissue back to the patient by means of instrument implantation or direct suture.

Although ovarian tissue cryopreservation and transplantation have made some progress in technology, there are still many problems in practice [16]. The first problem is the survival rate of ovarian tissue during cryopreservation and thawing. Although the freezing technology has been continuously improved, there is still a risk of inactivation of some ovarian tissue cells. Secondly, in the functional evaluation after transplantation, how to effectively monitor the functional recovery and fertility improvement of ovarian tissue after transplantation has not yet formed a unified standard. In addition, the pregnancy outcome after ovarian tissue transplantation still needs a wider range of studies to confirm. The possible complications, the recovery of ovarian function, and the instability of hormone levels in some patients after transplantation need to be solved urgently [17]-[18].

2.3 Orthotopic and Ectopic Transplantation of Ovarian Tissue

Ovarian tissue transplantation can be divided into orthotopic transplantation and ectopic transplantation. Orthotopic transplantation refers to the direct implantation of frozen ovarian tissue into the position of the patient 's original ovary. This method has a significant effect on restoring the patient 's ovarian function [19]. In some cases, the patient 's ovarian tissue may be seriously damaged due to disease or treatment. Orthotopic transplantation can help promote the recovery of ovarian physiological function, thereby achieving normal hormone secretion and fertility.

Ectopic transplantation is to transplant ovarian tissue to other parts of the body, such as the abdominal wall, uterus or vagina [20]-[21]. The advantage of this approach is that there is no need to repair the patient 's original ovarian environment, which may protect the function of ovarian tissue in a different physiological environment. At the same time, ectopic transplantation also provides an opportunity for some patients who cannot undergo in situ surgery to survive. Studies have shown that the number of successful cases of ectopic transplantation has gradually increased, and in some cases, patients can still get pregnant after ectopic transplantation.

In general, ovarian tissue cryopreservation and transplantation technology continues to develop, and future research will focus more on improving the efficiency of cryopreservation and thawing, improving the speed of ovarian function recovery after transplantation, and evaluating fertility outcomes. With the advancement of science and technology, ovarian tissue cryopreservation and transplantation are expected to bring hope and choice to more women facing fertility difficulties.

3. EFFECTIVENESS OF OVARIAN TISSUE CRYOPRESERVATION AND TRANSPLANTATION

3.1 Fertility Success Rate after Ovarian Tissue Cryopreservation and Retransplantation

Ovarian tissue cryopreservation and transplantation technology has gained attention in the field of reproductive medicine in recent years, especially for female patients facing fertility loss due to cancer or other diseases. According to statistics, after ovarian tissue transplantation, the patient 's fertility success rate gradually increased after a series of clinical studies. It is reported that about 95 % of patients ' endocrine function returned to normal after ovarian tissue cryopreservation and retransplantation. The pregnancy rate can be as high as 50 %, and the live birth rate is about 40 % [22]. At present, the reported successful pregnancy rate is increasing, and the proportion of women who are able to give birth to healthy babies is relatively high [23]. In some prospective studies, the number of cases in which ovarian tissue transplantation as a fertility aid can achieve live births has been increasing, showing the clinical effectiveness of this technique [24].

3.2 Endocrine Level of Patients

After ovarian tissue transplantation, the patient 's endocrine level is usually effectively restored. After transplantation, the recipient 's estrogen, progesterone and other sex hormone levels will gradually return to near normal range. Studies have shown that the functional recovery of ovarian tissue significantly increased the secretion of estrogen and progesterone, thereby improving the endocrine status of patients [25]. This not only affects fertility, but also has a positive impact on bone health, cardiovascular system and women 's overall quality of life.

3.3 Comparison of Different Fertility Preservation Methods and Live Birth Rate

Nowadays, many different fertility preservation methods have evolved, including egg cryopreservation, embryo cryopreservation and ovarian tissue cryopreservation. Compared with the cryopreservation of eggs and embryos, ovarian tissue cryopreservation has some unique advantages [26]. Ovarian tissue cryopreservation can preserve multiple follicles at the same time and can further develop in the body, especially for unmarried women and patients who are about to receive radiotherapy or chemotherapy. In general, after ovarian tissue cryopreservation, the increase in live birth rate is partly due to the ability to combine multiple fertility methods, thereby improving fertility flexibility and meeting the individual needs of different patients.

Based on the above information, ovarian tissue cryopreservation and transplantation technology has shown significant effectiveness in improving women 's fertility success rate and restoring endocrine function. Although the technology is still in the stage of continuous development, its success rate and live birth rate are gradually increasing. With the advancement of related technologies and research, ovarian tissue cryopreservation and transplantation is expected to become an important choice for more women to achieve their reproductive aspirations. This brings new hope to the female group with fertility needs, and also points out the direction for the future development of reproductive medicine.

4. CHALLENGES OF OVARIAN TISSUE CRYOPRESERVATION AND TRANSPLANTATION

4.1 The Challenge of Follicular Loss and Reduction of Follicular Reserve Loss in Ovarian Tissue Cryopreservation

One of the biggest challenges of ovarian tissue cryopreservation and transplantation is the loss of follicles. In the process of freezing and thawing, the survival rate and functional recovery rate of follicles are affected by many factors, including the freezing rate, the choice of cryoprotectants and the maturity of thawing technology [27]. Clinical studies have shown that the number of frozen follicles often has a significant loss, and may even lead to insufficient ovarian function after final transplantation [28]. Therefore, how to reduce the loss of follicular reserve is an urgent problem to be solved in current technology.

Therefore, some strategies can be taken to optimize the cryopreservation process of ovarian tissue [29]. First of all, the research and application of new cryoprotectants, especially those efficient solutions that can better maintain the stability of the internal and external environment of follicular cells, can reduce cell damage. Secondly, the use of step-by-step cooling technology rather than one-time cooling helps to reduce the damage of ice crystal formation to cells. Furthermore, improved thawing techniques, especially rapid thawing methods, can more effectively maintain the activity of follicles. In addition, the selection of more mature follicles in the preparation of frozen

ovarian tissue can improve the success rate from the source and reduce the loss of follicles.

4.2 Treatment and Molecular Mechanism Changes of Primordial Follicles after Ovarian Tissue Cryopreservation and Transplantation

After ovarian tissue transplantation, how to effectively treat primordial follicles to improve the endocrine level of patients is the key to further improve the effectiveness of this technology. Studies have shown that primordial follicles after ovarian tissue transplantation can achieve in vitro maturation through certain stimulation methods, thereby enhancing their physiological functions and restoring normal secretion of endocrine hormones [30]. This can be achieved by applying hormone promoters, local microenvironment optimization, and related biomaterials to promote follicular development.

In the molecular level mechanism after transplantation, the regeneration of ovarian tissue involves a variety of complex biological processes such as hormone signal transduction pathway, apoptosis and proliferation [31]. The results show that after ovarian tissue transplantation, changes in the internal microenvironment of the ovary activate a series of transcription factors and growth factors to promote follicular development [32]. In addition, new experimental techniques such as single-cell RNA sequencing technology allow us to more accurately describe the molecular mechanism of ovarian tissue transplantation, providing new ideas for improving endocrine levels [33].

In recent years, with the development of regenerative medicine and biomaterials technology, a variety of new technologies have emerged for ovarian tissue cryopreservation and transplantation. These technologies include 3D bioprinting, nanomaterial-based bioscaffold construction, etc. [34], which can provide a more suitable microenvironment for the regeneration and repair of ovarian tissue. In addition, the combination of tissue engineering and cell therapy can greatly improve the activity and functional recovery of frozen ovarian tissue, and bring higher fertility success rate to patients.

The combination of immunotherapy and ovarian transplantation also shows broad application prospects [35]. In the study of the immune tolerance mechanism after ovarian tissue transplantation, reducing the probability of rejection after transplantation by regulating the immune microenvironment may improve the success rate after ovarian transplantation and the endocrine level of patients.

Although ovarian tissue cryopreservation and transplantation technology has shown good prospects in helping women restore fertility, it still faces problems such as follicle loss and endocrine level recovery. These challenges are expected to be effectively solved by optimizing cryopreservation and thawing techniques, improving follicular treatment methods, in-depth study of molecular mechanisms, and application of emerging technologies. With the deepening of research and technological progress, ovarian tissue cryopreservation and transplantation is expected to become a more effective and safe fertility preservation strategy. Future research should focus on improving the activity and function of ovarian tissue, while focusing on the overall quality of life of patients, to provide more women with the hope of fertility.

5. CONCLUSION

Ovarian tissue cryopreservation and transplantation technology plays a vital role in modern reproductive medicine, especially for women who face fertility loss due to treatment needs or other reasons. By cryopreservation of ovarian tissue, patients can be transplanted in the future to restore ovarian function and achieve natural pregnancy. The development of this technology has opened up a new way for the preservation and restoration of female fertility, and has gradually become an important part of clinical practice.

Studies have shown that the success rate of ovarian tissue cryopreservation and transplantation technology is gradually improving, but it still faces challenges such as follicle loss, reserve loss and endocrine level recovery. Although the pregnancy rate after transplantation is considerable, the individual differences of different patients and the quality of ovarian tissue still have a significant impact on the results. Therefore, how to improve the survival rate of follicles, optimize the treatment process, and improve the level of endocrine recovery after transplantation has become an important research direction in this field.

Looking forward to the future, the development of ovarian tissue cryopreservation and transplantation technology will continue. With the continuous improvement of cryoprotectants and cryopreservation technology, it is

expected to achieve higher follicular survival rate in the future. The development of single cell technology will help to understand the mechanism of follicular survival, so as to develop a more effective freezing and thawing program. Using the combination of biological materials and tissue engineering, research and development of scaffolds that can simulate the natural ovarian microenvironment, promote follicular maturation and functional recovery, and provide new possibilities for ovarian tissue regeneration. Future research will focus more on personalized medicine, personalized cryopreservation, transplantation and subsequent hormone replacement therapy based on the physiological and genetic characteristics of different patients, so as to more effectively meet the needs of patients. The interdisciplinary cooperation of reproductive medicine, regenerative medicine, molecular biology and other disciplines will promote the further development of this field. Multidisciplinary integration can deepen the understanding of ovarian physiological and pathological mechanisms and help the development and application of new technologies. Strengthening clinical research and accumulating more data and cases will help to comprehensively evaluate the long-term effects of ovarian tissue cryopreservation and transplantation, and provide a basis for the standardization and normalization of this technology.

Ovarian tissue cryopreservation and transplantation technology has shown good development potential in the field of reproductive medicine. In the future, it is expected to provide safer and more efficient fertility preservation programs through technological innovation, personalized medicine and multidisciplinary cooperation to help more women realize their fertility hopes. With the deepening of scientific research, this technology will play an increasingly important role in the treatment of reproductive disorders.

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