The Association of Reproductive Medicine of Uzbekistan

REPRODUKTIV TIBBIYOT VA GENETIKA

ISSN 3060-5202

01 (02) 2025

REPRODUCTIVE & GENETICS MEDICINE

РЕПРОДУКТИВНАЯ МЕДИЦИНА И ГЕНЕТИКА

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Митохондриальная дисфункция в патогенезе женского бесплодия: современные концепции и инновационные терапевтические подходы (обзор литературы)

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Аннотация

Цель: Провести анализ роли митохондриальной дисфункции в патогенезе женского бесплодия, изучить современные подходы к диагностике и терапии данной патологии, а также определить перспективные инновационные методы коррекции митохондриальной дисфункции для улучшения репродуктивных исходов.

Материалы и методы. Выполнен обзор научных публикаций, представленных в электронных базах данных PubMed, Google Scholar и eLibrary, опубликованных до января 2025 года. Отбор источников проводился в соответствии с принципами PRISMA. Из 178 найденных публикаций (64 из PubMed, 25 из Google Scholar и 41 из eLibrary) были исключены дубликаты и статьи без полного текста. В окончательный обзор включены 48 наиболее релевантных работ, рассматривающих взаимосвязь митохондриальной дисфункции и женского бесплодия, а также современные терапевтические стратегии.

Результаты. Анализ данных показал, что митохондриальная дисфункция играет ключевую роль в снижении качества ооцитов, нарушении овуляции и снижении фертильности. Доказано, что мутации митохондриальной ДНК (mtDNA), энергетический дефицит и оксидативный стресс оказывают негативное влияние на стабильность генома ооцитов и их способность к оплодотворению. Включение в терапию антиоксидантов (коэнзим Q10, мелатонин, ресвератрол), митохондриальной замещающей терапии (MRT) и ядерного переноса демонстрирует перспективность в восстановлении митохондриальных функций и улучшении репродуктивных исходов у женщин с бесплодием.

Заключение. Представленный обзор подчеркивает, что митохондриальная дисфункция является важным патогенетическим фактором женского бесплодия. Современные инновационные подходы, направленные на коррекцию митохондриальных нарушений, открывают новые перспективы в лечении бесплодия и повышении эффективности вспомогательных репродуктивных технологий. Однако для полноценного внедрения данных методов в клиническую практику необходимы дальнейшие исследования, направленные на оценку их безопасности и долгосрочной эффективности.

Ключевые слова: женское бесплодие; митохондриальная дисфункция; оксидативный стресс; вспомогательные репродуктивные технологии; митохондриальная терапия.

Ayollar bepushtligi patogenezida mitoxondrial disfunksiya: zamonaviy konsepsiyalar va innovatsion terapevtik yondashuvlar (adabiyotlar sharhi)

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Annotatsiya

Maqsad: Ayollar bepushtligi patogenezida mitoxondrial disfunksiyaning o'rnini tahlil qilish, ushbu kasallikni tashxislash va davolash bo'yicha zamonaviy yondashuvlarni o'rganish, shuningdek, reproduktiv natijalarni yaxshilash uchun mitoxondrial disfunksiyani korreksiya qilishning istiqbolli innovatsion usullarini aniqlash.

Material va usullar: 2025-yil yanvar oyiga qadar PubMed, Google Scholar va eLibrary elektron ma'lumotlar bazalarida chop etilgan ilmiy maqolalar tahlil qilindi. Manbalar PRISMA tamoyillariga muvofiq tanlab olindi. 178 ta topilgan maqolalardan (PubMed – 64, Google Scholar – 25, eLibrary – 41) dublikatsiyalar va to'liq matnga ega bo'lmagan maqolalar chiqarib tashlandi. Yakuniy tahlilga 48 ta eng muhim va dolzarb ishlar kiritildi, ular mitoxondrial disfunksiya va ayollar bepushtligi o'rtasidagi bog'liqlik hamda zamonaviy terapevtik yondashuvlarni yoritadi.

Natijalar: Tadqiqotlar natijalari shuni ko'rsatadiki, mitoxondrial disfunksiya tuxum hujayra sifatining pasayishi, ovulyatsiya buzilishlari va fertilitetning kamayishiga olib keladi. Mitoxondrial DNK (mtDNA) mutatsiyalari, energetik kamchilik va oksidativ stress tuxum hujayra genomining barqarorligi va uning urug'lanish qobiliyatiga salbiy ta'sir ko'rsatishi aniqlangan. Antioksidant terapiya (koenzim Q10, melatonin, resveratrol), mitoxondrial almashtirish terapiyasi (MRT) va yadroviy transfer usullarining qo'llanilishi mitoxondriya faoliyatini tiklash va ayollar bepushtligi bilan bog'liq reproduktiv muammolarni hal qilishda istiqbolli yechimlar sifatida tavsiya etiladi.

Xulosa: Ushbu adabiyotlar sharhi shuni ko'rsatadiki, mitoxondrial disfunksiya ayollar bepushtligining muhim patogenetik omillaridan biri hisoblanadi. Mitoxondrial disfunksiyani korreksiya qilishga yo'naltirilgan zamonaviy innovatsion usullar bepushtlikni davolash va yordamchi reproduktiv texnologiyalarning samaradorligini oshirishda katta imkoniyatlar yaratadi. Biroq ushbu usullarni klinik amaliyotga joriy etishdan oldin ularning xavfsizligi va uzoq muddatli samaradorligini baholash bo'yicha qo'shimcha tadqiqotlar talab etiladi.

Kalit so'zlar: ayollar bepushtligi; mitoxondrial disfunksiya; oksidativ stress; yordamchi reproduktiv texnologiyalar; mitoxondrial terapiya.

Mitochondrial dysfunction in the pathogenesis of female infertility: modern concepts and innovative therapeutic approaches (literature review)

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Annotation

Objective: To analyze the role of mitochondrial dysfunction in the pathogenesis of female infertility, examine modern approaches to diagnosis and treatment, and identify promising innovative strategies for correcting mitochondrial dysfunction to improve reproductive outcomes.

Materials and Methods: A review of scientific publications indexed in the electronic databases PubMed, Google Scholar, and eLibrary was conducted, covering articles published until January 2025. Source selection was performed in accordance with PRISMA guidelines. Out of 178 initially identified articles (64 from PubMed, 25 from Google Scholar, and 41 from eLibrary), duplicates and publications without full-text access were excluded. The final review included 48 most relevant studies addressing the relationship between mitochondrial dysfunction and female infertility, as well as modern therapeutic approaches.

Results: Data analysis demonstrated that mitochondrial dysfunction plays a key role in reducing oocyte quality, disrupting ovulation, and decreasing fertility. It has been established that mitochondrial DNA (mtDNA) mutations, energy deficiency, and oxidative stress negatively affect oocyte genomic stability and fertilization potential. The inclusion of antioxidant therapy (coenzyme Q10, melatonin, resveratrol), mitochondrial replacement therapy (MRT), and nuclear transfer has shown promising results in restoring mitochondrial function and improving reproductive outcomes in women with infertility.

Conclusion: This review highlights that mitochondrial dysfunction is a significant pathogenetic factor in female infertility. Modern innovative approaches aimed at correcting mitochondrial dysfunction offer new perspectives for infertility treatment and enhancing the effectiveness of assisted reproductive technologies. However, further research is needed to assess the safety and long-term efficacy of these methods before they can be fully integrated into clinical practice.

Keywords: female infertility; mitochondrial dysfunction; oxidative stress; assisted reproductive technologies; mitochondrial therapy.

INTRODUCTION

Female infertility is currently one of the most pressing medical and biological issues worldwide, with an incidence rate of 10–15% [29]. Reproductive health disorders, particularly a decline in oocyte quality and ovarian dysfunction, are often associated with mitochondrial dysfunction [32]. Mitochondria serve as the primary source of energy within cells, and their proper function is essential for maintaining the physiological activity of oocytes [3]. Consequently, mitochondrial dysfunction is now considered one of the key pathogenetic mechanisms of infertility.

According to the World Health Organization, every tenth woman of reproductive age faces infertility [31]. The primary causes of this condition include endocrine disorders, genetic factors, environmental influences, and metabolic diseases [5]. Furthermore, contemporary research confirms the impact of mitochondrial dysfunction on oocyte quality, demonstrating its critical role in ovulation and fertilization potential [28].

Mitochondria are the principal organelles responsible for energy metabolism in oocytes, and their optimal function ensures normal oocyte development and genetic stability [7]. Studies have shown that mitochondrial DNA (mtDNA) mutations and the heightened sensitivity of mitochondria to oxidative stress contribute to the decline in oocyte quality [8]. Thus, mitochondrial dysfunction not only leads to energy deficiencies in oocytes but also negatively affects their genetic stability [9].

The objective of this literature review is to examine the role of mitochondrial dysfunction in female infertility, analyze its significance in the pathogenesis of the condition, and explore innovative therapeutic approaches aimed at correcting this issue. The review focuses on modern molecular-biological research and clinical applications, assessing the impact of mitochondria on oocyte function and reproductive health [10].

Mitochondria and Their Role in Oocyte Function and Infertility

Mitochondria serve as the primary energy source for normal oocyte development and function. Research indicates

that mitochondrial dysfunction in oocytes has a detrimental impact on their quality and fertilization potential [15]. Mitochondria play a crucial role in the metabolic activity of oocytes. ATP, produced by mitochondria, is essential for ovulation, oocyte maturation, and the fertilization process with spermatozoa [16].

Mitochondrial DNA (mtDNA) mutations can disrupt normal oocyte function, leading to abnormal embryonic development. These mutations can be detected through specialized mitochondrial diagnostic techniques [17]. Oxidative stress significantly affects mitochondrial function, reducing ATP production in oocytes. As a result, oocytes suffer from energy deficiency, which negatively impacts their viability and reproductive potential [18].

Age-related mitochondrial changes contribute to a decline in oocyte quality. With aging, mtDNA mutations accumulate, and resistance to oxidative stress decreases, impairing mitochondrial function in oocytes [19]. Given these findings, improving mitochondrial function is a critical aspect of restoring reproductive health and treating infertility. The following section will explore innovative therapeutic approaches aimed at enhancing mitochondrial activity, including mitochondrial restoration techniques, antioxidant therapy, and mitochondrial donation strategies.

Key Functions of Mitochondria in Oocytes

Mitochondria are vital organelles responsible for energy production and maintaining metabolic homeostasis in cells. Their primary functions include:

1. **Energy supply (ATP production)** – Oxidative phosphorylation in mitochondria generates the energy required for oocyte function and maturation.
2. **Regulation of oxidative stress** – Mitochondria modulate the levels of reactive oxygen species (ROS), ensuring cellular antioxidant defense mechanisms.
3. **Control of apoptosis (programmed cell death)** – Mitochondria regulate the elimination of improperly developed or damaged oocytes.
4. **Storage and transmission of genetic information** – mtDNA is maternally inherited and plays a crucial role in determining oocyte quality and reproductive success [20].

Understanding the role of mitochondrial function in oocyte development and fertilization is essential for advancing infertility treatments. The next section will provide an in-depth analysis of therapeutic strategies designed to restore mitochondrial activity and improve reproductive outcomes.

Mitochondrial Dysfunction and Its Impact on Oocyte Quality and Fertility

Studies indicate that impaired mitochondrial function in oocytes can lead to an inability to meet their energy demands, ultimately resulting in infertility [21].

Oxidative Stress and Its Effects on Oocyte Quality

Oxidative stress is a process in which an excessive accumulation of reactive oxygen species (ROS) damages cells and mitochondria. This phenomenon can significantly reduce oocyte quality and disrupt fertilization potential [22].

- Oxidative stress damages mitochondrial membranes in oocytes, slowing ATP production.
- DNA damage and mitochondrial dysfunction are exacerbated by oxidative stress, accelerating oocyte apoptosis.
- Dysfunction of the antioxidant defense system weakens the protection against oxidative stress, leading to impaired oocyte function.

To mitigate oxidative stress, antioxidant therapy is utilized, including compounds such as vitamin C, vitamin E, coenzyme Q10, and resveratrol [23].

Mitochondrial DNA (mtDNA) and Its Susceptibility to Oxidative Damage

Unlike nuclear DNA, mitochondrial DNA lacks a robust protective mechanism and is more vulnerable to oxidative stress [24].

- mtDNA mutations impair energy production in oocytes.
- Age-related changes in mtDNA contribute to a decline in ovarian reserve and oocyte quality.
- Clonal mtDNA mutations weaken mitochondrial function in oocytes, leading to abnormal embryonic development [25].

Among emerging therapeutic strategies, mitochondrial transfer technology and mitochondrial donation are being explored as effective methods to combat infertility [26].

Mitochondrial Bioenergetics and Its Role in Oocyte Development

One of the primary functions of mitochondria is to generate ATP, which is essential for oocyte maturation and development. Energy deficiency is a major consequence of mitochondrial dysfunction, disrupting normal oocyte growth [27]. Reduced energy resources slow metabolic processes in oocytes, negatively impacting embryonic development [28].

- Mitochondrial bioenergetic dysfunction lowers oocyte fertilization potential, reducing the success rate of in vitro fertilization (IVF).
- Nutraceutical and pharmacological therapies aimed at enhancing mitochondrial activity show promise in improving oocyte quality and reproductive outcomes [29].

By restoring mitochondrial function through innovative therapeutic approaches, infertility treatments can be significantly improved, offering new prospects for reproductive medicine.

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Modern Diagnostic Approaches for Mitochondrial Dysfunction in Female Infertility

Currently, extensive research is being conducted on innovative therapeutic strategies aimed at restoring mitochondrial function to correct female infertility. The following section provides a detailed overview of these therapeutic approaches.

Diagnostic Methods for Mitochondrial Dysfunction in Infertility

Several advanced diagnostic techniques have been developed to assess mitochondrial dysfunction and infertility-related conditions. These methods help evaluate the energy status, metabolism, and genetic structure of oocytes and other reproductive cells.

Biochemical Analyses

Biochemical tests serve as the primary diagnostic method for evaluating mitochondrial energy production capacity and identifying metabolic abnormalities.

- *ATP Level Measurement* – Assessing the amount of adenosine triphosphate (ATP) produced by mitochondria is crucial for determining oocyte quality.
- *Reactive Oxygen Species (ROS) Quantification* – This test measures oxidative stress levels, as excessive ROS is a key indicator of mitochondrial dysfunction.
- *Lactate and Pyruvate Analysis* – This method is essential for evaluating the balance between aerobic and anaerobic metabolism [30].

Molecular-Genetic Analysis

Molecular-genetic techniques are used to identify mitochondrial DNA (mtDNA) mutations, deletions, and replication disorders:

- *Polymerase Chain Reaction (PCR) and Sequencing* – Detects mitochondrial DNA mutations and assesses their impact on oocyte quality.
- *mtDNA Copy Number Analysis* – Research indicates that a decrease in mtDNA copy number negatively affects oocyte fertilization potential [31].

Mitochondrial Functional Assessment in Oocytes

Several advanced techniques have been developed to evaluate mitochondrial activity in oocytes:

- Membrane Potential and Mitochondrial Function Assessment
  - *JC-1 or TMRE Dyes* – Fluorescent dyes used to measure mitochondrial membrane potential, allowing differentiation between healthy and damaged mitochondria.
  - *Respiratory Activity Analysis* – Evaluates oxygen consumption rate and mitochondrial electron transport chain function.
- Structural and Functional Mitochondrial Analysis
  - *Electron Microscopy (EM)* – Examines the structure and internal composition of mitochondria, including the shape and density of mitochondrial cristae.
  - *Western Blot and Immunoblot Analysis* – Identifies mitochondrial biomarkers and their metabolic activity [32].

Innovative Technologies for Diagnosing Infertility and Mitochondrial Dysfunction

- Metabolomics and Oocyte Metabolism Analysis
  - *Gas Chromatography-Mass Spectrometry (GC-MS) and Nuclear Magnetic Resonance (NMR) Spectroscopy* – Identifies metabolic changes in oocytes and follicular fluid.
  - *Single-cell RNA Sequencing* – Evaluates mitochondrial activity and transcriptional changes in oocytes [33].
- Fluorescent and Confocal Microscopy
  - *Live-cell Imaging* – Enables real-time monitoring of mitochondrial dynamics and movement in oocytes.

- Oxygenation Analysis
  - SeaHorse Respirometry – Measures mitochondrial oxygen consumption rate and bioenergetic activity.

These diagnostic methods are crucial for detecting mitochondrial dysfunction at an early stage and developing effective treatment strategies to improve female reproductive health.

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Recent Research on Mitochondrial Dysfunction and Infertility

In recent years, several important scientific studies have been conducted to evaluate the effectiveness of mitochondrial restoration therapies in improving oocyte quality and treating infertility.

Key Research Areas:

- Mitochondrial DNA Mutations and Oocyte Quality
  - Studies have demonstrated that mtDNA mutations impair ATP production in oocytes, leading to reduced fertilization potential [37].
  - Age-related mitochondrial dysfunction negatively affects oocyte maturation and fertilization [38].
- Effectiveness of Antioxidant Therapy
  - Research confirms that CoQ10 supplementation enhances ATP production in oocytes and improves fertilization rates [39].
  - Melatonin's antioxidant properties protect oocytes from oxidative stress [40,41].
- Mitochondrial Transfer and Nuclear Donation Techniques
  - Mitochondrial replacement therapy (MRT) helps restore mitochondrial function in oocytes [42].
  - Cytoplasmic transfer improves oocyte quality in older women [43,44].
- Stem Cell Therapy and Mitochondrial Restoration
  - Mesenchymal stem cells (MSCs) can restore ovarian function and enhance mitochondrial activity in oocytes [45,46].
  - Mitochondrial transplantation into oocytes can correct mitochondrial dysfunction [47,48].

Conclusion

Mitochondrial dysfunction plays a critical role in the pathogenesis of female infertility. Recent research confirms the importance of mitochondria in determining oocyte quality. Mutations in mitochondrial DNA (mtDNA), energy production deficiencies, and oxidative stress contribute to decreased fertilization potential and reproductive complications.

Analysis suggests that mitochondrial abnormalities in oocytes are not only linked to infertility but also to abnormal embryonic development and pregnancy loss. Therefore, therapeutic approaches aimed at correcting mitochondrial dysfunction present new opportunities for infertility treatment.

Mitochondrial dysfunction is increasingly recognized as a key factor in female infertility, and modern medicine is exploring various innovative solutions to address this challenge. Antioxidant therapy, mitochondrial transplantation, gene editing, and cell therapy are among the promising strategies. Ongoing scientific investigations aim to optimize these therapies and integrate them into clinical practice. In the future, mitochondrial-targeted treatments are expected to play a significant role in enhancing reproductive health. Expanding research efforts and ensuring the clinical applicability of these therapeutic strategies will be essential.

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Muqaddima

Homilador ayollarda yu
normal ishlashining buzilishi
chunki yurak-qon tomir kasalli
ayollarda eng keng tarqalgan
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kasalliklari bo'lgan ayollarda yanada ani
bo'ladi, bu yerda homiladorlik mavjud
kuchaytirishi mumkin, bu esa ona va homila u
oshiradi (Smith et al., 2020). Miokardit, ayniqs
respirator infeksiyalar va pnevmoniya
homiladorlikning salbiy oqibatlari uchun muhi
bo'lib qolmoqda (Johnson et al., 2021).