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Review

Ozone Therapy as a New Noninvasive Treatment Method in Gynecological Procedures: A Systematic Review

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Abstract: *Introduction* — Due to the specific nature of ovarian follicle reservation, the female reproductive system (FRS) is a sensitive organ. Among female pathologies, polycystic ovary syndrome (PCOS), characterized by impaired secretion of sex hormones, is the most common. Ozone therapy (OT) is a new noninvasive treatment for FRS pathologies. OT is currently an effective procedure for PCOS. The objective of this systematic review was to explain PCOS pathologies and gain a deeper understanding of the biological features of OT in the treatment of FRS pathologies, particularly PCOS.
Methods — All articles on the therapeutic role of OT for FRS, with a particular focus on PCOS, were collected without length restrictions (as of August 29, 2024). After developing MeSH-based keywords, the search strategy was defined as follows: *(('female reproduction' OR 'female reproductive system') AND ('polycystic ovary syndrome' OR 'PCOS' OR 'PCO') AND ('treatment') AND ('ozone' OR 'O_3' OR 'ozone therapy' OR 'O_3 therapy'))*. Valid PubMed, Scopus, WoS, ScienceDirect, and ISC databases were used, references were imported into EndNote X8 Citation Manager, and duplicate studies were merged. Primary screening and secondary screening were performed, and eligible articles were included in the data extraction.
Results — The initial search yielded 134 articles, and 85 duplicate studies were merged. Studies that did not meet the inclusion/exclusion criteria were excluded through primary and secondary screenings. As a result, 13 eligible articles were selected for data categorization.
Conclusion — OT serves as an adjuvant treatment method that improves oxygen metabolism, modulates the immune system, and promotes tissue repair. OT is potentially effective in suppressing inflammation, chronic pain, and infections in PCOS.

Keywords: ozone therapy, female, reproduction, pathology, polycystic ovary syndrome, PCOS, systematic review.

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Introduction

The female reproductive system (FRS) is a biological complex responsible for the production and maintenance of follicles, as well as the fertilization process and the onset of pregnancy. The ovaries play a crucial role in human reproduction by producing female sex hormones that regulate the menstrual cycle and support reproductive functions. They also provide follicles for fertilization by sperm. FRS faces various pathologies, causing a burden on the healthcare system. Ovaries with various diseases and many functional disorders, such as polycystic ovary syndrome (PCOS), are diagnosed by their anatomical and physiological features [1]. PCOS is characterized by hormonal imbalance, irregular menstrual cycles, and the presence of multiple ovarian cysts. This condition can lead to infertility, metabolic syndrome, and an increased risk of cardiovascular diseases [2]. PCOS is also affected by hyperandrogenism [3]. Therapeutic procedures for FRS pathologies encompass various approaches, including medication, surgery, and supportive care [4]. Furthermore, ovarian transplantation has been introduced as a new noninvasive therapeutic procedure for PCOS [5]. Ozone is considered a molecule with strong oxidative properties. Therefore, it has the potential to induce cellular dysfunction in various cell types. Ozone therapy (OT) has attracted attention as an alternative treatment, particularly due to its potential application in various diseases [6]. The therapeutic effect of ozone is attributes to its ability to induce controlled oxidative stress [7], stimulating the body's antioxidant defenses and improving tissue oxygenation [8].

Innovative treatments for FRS diseases are currently being proposed. OT is a new method for women's health, particularly useful in PCOS cases. Therefore, this systematic review aims to examine the scientific basis for the use of OT in the treatment of FRS diseases, with a particular focus on PCOS.

Methods

All protocols for this study were approved by Baqiyatallah University of Medical Sciences (study # IR.BMSU.AEC.1402.019). This systematic review was conducted to determine the therapeutic role of OT in FRS pathologies, with a particular focus

on the treatment of PCOS. All relevant articles discussing the therapeutic role of OT in PCOS were collected. Following the development of the research questions, MeSH-based keywords were defined, including *female reproduction*, *female reproductive system*, *PCOS*, *PCO*, *polycystic ovary syndrome*, *treatment*, *ozone*, *O3*, *ozone therapy*, and *O_3 therapy*. The search was conducted in various English-language databases such as PubMed, Scopus, WoS, ScienceDirect, and ISC. Subsequently, the Google Scholar search engine and citations of all included articles were fully screened to identify the maximum number of eligible articles. The '*OR*' and *'AND'* operators were used for within- and between-group compositions among keywords. Hence, the search strategy was defined as follows: *(('female reproduction' OR 'female reproductive system') AND ('polycystic ovary syndrome' OR 'PCOS' OR 'PCO') AND ('treatment') AND ('ozone' OR 'O_3' OR 'ozone therapy' OR 'O_3 therapy'))*. There was no time limit, all relevant articles were included in this study by August 29, 2024, and the search strategy was updated on September 20, 2024. After collecting the articles, all relevant citations were exported to EndNote X8 Citation Manager software (USA), and duplicate articles were detected and merged. Primary article screening was performed based on the title and abstract assessment of published articles. Full texts of eligible included articles were prepared for in-depth secondary screening. At all stages of primary and secondary screening, all articles presenting the role of OT in treating FRS pathologies with a focus on PCOS were fully included, while irrelevant publications (letter to the editor and non-English language studies) were excluded from the study. Two of the present review authors blindly and independently assessed the articles during screenings, while the corresponding author managed and resolved potential conflicts or disagreements between the two reviewing authors. The article sorting process was conducted based on the PRISMA 2020 flowchart (*Figure* 1). All relevant data on the included articles were collected and summarized (*Table* 1) [9].

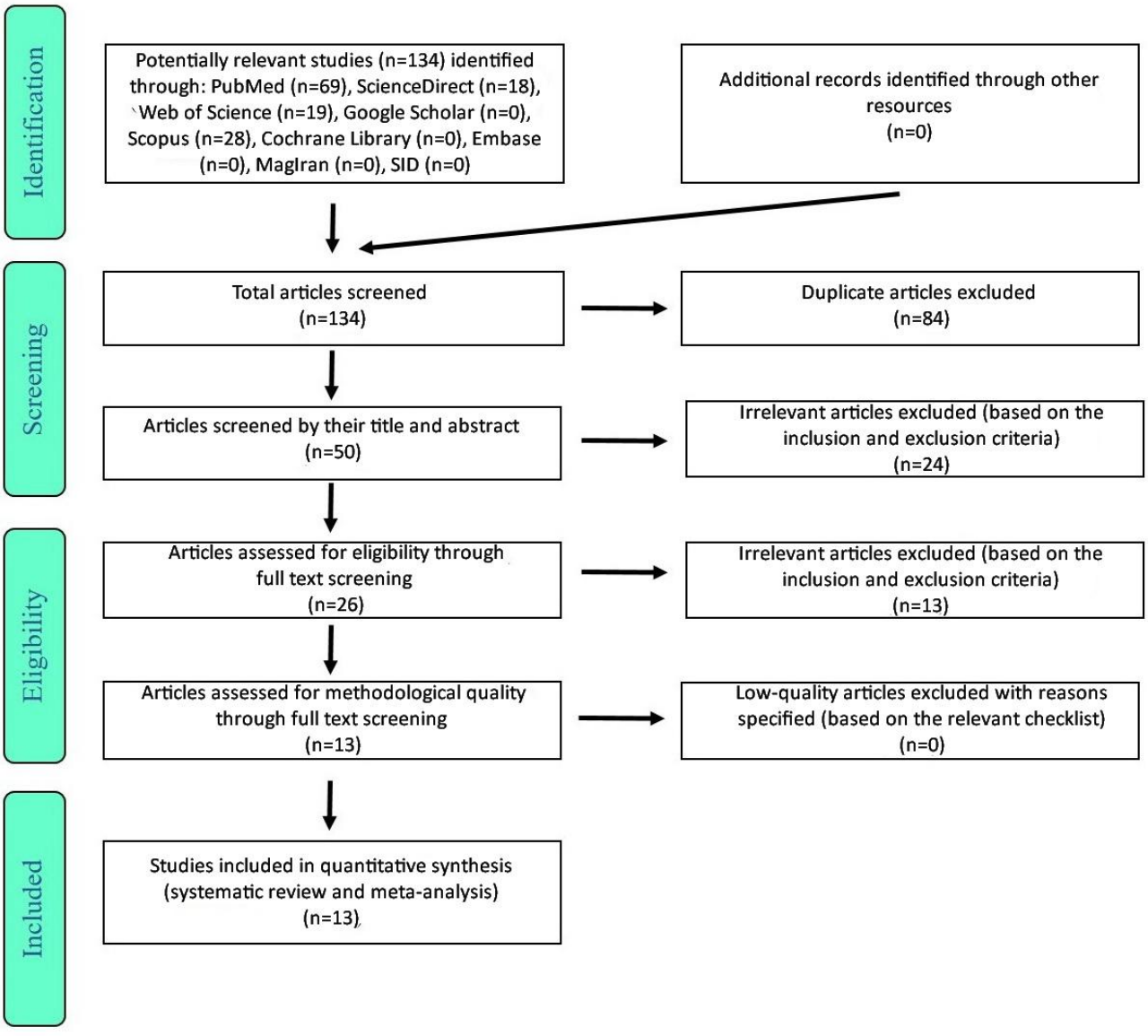

Figure 1. PRISMA 2020 flowchart for new systematic reviews, including database and citation searches.

Table 1. Data extracted from the included papers

No	First author	Year of publication	Objective of the study	Main findings	Main methodological concept	Conclusion
1	LP. Silva	2024	To evaluate the effects of ozone therapy on dogs with mammary tumors.	Ozone therapy improved oxidative profiles and quality of life in treated dogs.	A clinical study in dogs with cancer.	Ozone therapy may improve quality of life in female dogs with mammary cancer.
2	X. Wang	2024	To evaluate the effects of ozone and particulate matter on ovarian reserve in infertile women.	Exposure to ozone and fine particles negatively impacted ovarian reserve.	An epidemiological study analyzing the effects of air pollution.	Ozone exposure has been associated with decreased ovarian reserve in infertile women.
3	AR. Dias	2023	To evaluate the effects of ozone sauna and pulsed electromagnetic field (PEMF) therapy on women with reduced ovarian reserve.	Combination therapy improved the results of assisted reproductive technology cycles.	A clinical study using an ozone sauna and PEMF therapy.	Ozone therapy using an ozone sauna may improve reproductive function in women with reduced ovarian reserve.
4	AC. Ávila	2022	To evaluate the effectiveness of ozone therapy in the treatment of endometritis in mares.	Ozone therapy improved recovery and reproductive function in mares with endometritis.	An experimental study in mares receiving ozone therapy.	Ozone therapy is effective in treating endometritis in mares, improving reproductive outcomes.
5	B. Clavo	2021	To study ozone therapy for refractory pelvic pain caused by anticancer therapy.	Ozone therapy provided significant pain relief in patients with refractory pelvic pain.	A clinical study evaluating patient outcomes after therapy.	Ozone therapy requires further study as a treatment for pelvic pain syndromes.
6	B. Clavo	2020	To evaluate the long-term effects of ozone therapy on chronic pelvic pain after cancer treatment.	Long-term ozone therapy resulted in sustained pain relief and improved quality of life.	A longitudinal study in patients with chronic pain.	Ozone therapy may provide long-term benefits in the treatment of chronic pelvic pain.
7	R. Deniz	2020	To investigate the effects of ozone therapy on postoperative adhesions and ovarian function.	Ozone therapy improved ovarian function and reduced postoperative adhesions in an experimental model.	An experimental study in rats.	Ozone therapy may improve ovarian function and reduce adhesion formation after surgery.
8	Z. Merhi	2019	To study ozone therapy as an adjuvant treatment aimed to improve reproductive health in females.	Ozone therapy can improve reproductive health by addressing various factors associated with infertility.	A review of clinical studies on the use of ozone therapy.	Ozone therapy shows potential as an adjuvant treatment for female reproductive health.
9	R. Balestrero	2017	To analyze the use of oxygen-ozone therapy in the treatment of fibromyalgia.	Oxygen-ozone therapy has demonstrated potential in alleviating the symptoms of fibromyalgia.	A clinical study in patients with fibromyalgia.	Oxygen-ozone therapy may be an effective treatment option for fibromyalgia.
10	T. Constantin	2016	To study the effects of ozone therapy on postpartum endometritis in dairy cows.	Ozone therapy has been shown to improve the symptoms of endometritis and reproductive outcomes.	A pilot study in dairy cows receiving ozone therapy.	Ozone therapy may be useful in the treatment of postpartum endometritis in dairy cows.
11	MK. Aslan	2012	To evaluate the protective effect of ozone in ovarian ischemia/reperfusion injury.	Ozone application reduced ovarian tissue damage following ischemia/reperfusion.	An experimental study in rats using intraperitoneal ozone therapy.	Ozone therapy may serve as a protective measure in cases of ovarian ischemia/reperfusion injury.
12	B. Uysal	2012	To study the effect of ozone therapy on postoperative uterine adhesions.	Ozone therapy significantly reduced adhesion formation in rats after surgery.	An experimental study in rats after surgery.	Ozone therapy may reduce the formation of uterine adhesions after surgery.
13	R. Chandra-D'Mello	2001	To examine the role of ozone therapy in the treatment of female infertility.	Ozone therapy may be useful in the treatment of various conditions associated with infertility.	A review of the existing literature on the use of ozone therapy.	Ozone therapy shows promise as an adjuvant treatment for female infertility.

Results

A total of 134 potentially relevant studies were identified for data collection and extraction after searching PubMed (n=69), ScienceDirect (n=18), Web of Science (n=19), Scopus (n=28), ISC (n=0), and Google Scholar (n=0) databases. No other relevant articles were found after reference evaluation (n=0). We found and merged 85 duplicate articles during reference transfer to EndNote Citation Manager software. The remaining references (n=50) were assessed during primary screening. At this stage, irrelevant articles (n=24) were excluded based on the inclusion and exclusion criteria. In addition, after full texts of the remaining articles (n=26) were prepared for screening, a second evaluation was conducted during the second screening. As a result, 13 irrelevant articles were excluded, and only 13 eligible studies were included for data extraction (*Figure* 1), including those by L.P. Silva [10], X. Wang [11], AR. Dias [12], AC. Ávila [13], B. Clavo [14], B. Clavo [15], R. Deniz [16], Z. Merhi [17], R. Balestrero [18], T. Constantin [19], MK. Aslan [20], B. Uysal [21], and R. Chandra-D'Mello [22]. Full texts were evaluated, and the relevant data were summarized and classified as presented below.

Classification of female reproductive system pathologies

FRS is susceptible to various pathologies that significantly impact a woman's health and fertility. These pathologies can be classified based on the affected anatomical structures and four main categories of the abnormalities, as follows:

Congenital fetal anomalies. Uterine malformations are characterized by incomplete development of the uterus, leading to recurrent miscarriage. Alao, Müllerian duct agenesis, also known

as Müllerian aplasia or Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, is a developmental disorder of the uterus and some parts of the vaginal canal. These anomalies may not manifest symptoms until puberty or later, often becoming apparent during attempts to conceive [23].

Infectious diseases. Pelvic inflammatory disease (PID) can easily spread to the peritoneal cavity, causing organ adhesions. Consequently, the mobility of internal reproductive organs located within the pelvic cavity may become restricted, and fetal developmental potential is lost. Additionally, sexually transmitted infections may have a negative impact on future serious complications, such as cervical cancer [24].

Benign/malignant tumors of female reproductive system. Benign tumors include uterine fibroids or leiomyomas (noncancerous growths in the uterus that cause heavy menstrual bleeding and pelvic pain) [25], as well as ovarian cysts. While most cysts are benign and asymptomatic, larger cysts may require surgery [26]. Some malignant tumors include cervical, endometrial [27], and ovarian [28] cancer.

Hormonal disorders. These types of pathologies can potentially disrupt normal reproductive function, leading to conditions such as PCOS [29].

Common signs of female reproductive system pathologies

Early signs of FRS pathologies can manifest themselves in a variety of ways, often indicating underlying problems that require medical intervention. These signs include irregular menstrual cycles (diagnosed by unusual bleeding associated with hormonal imbalances in certain conditions such as PCOS or uterine fibroids), pelvic or abdominal pain (identified by endometriosis or ovarian cysts) [27], changes in vaginal discharge (indicating infections), dyspareunia (accompanied by PID or endometriosis) [27], infertility (a combination of conditions that affect ovulation, such as PCOS or hormonal imbalances, can contribute to infertility), and unusual menopausal symptoms before the age of 40 years (implying ovarian failure or other hormonal imbalances) [30].

Polycystic ovary syndrome and pathophysiology

PCOS is a complex endocrine disorder affecting a significant proportion of women of reproductive age, characterized by a combination of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. This pathological condition has profound implications for reproductive health, metabolic function, and psychological well-being [31]. The pathophysiology of PCOS is multifaceted and involves a complex interaction of genetic, hormonal, and environmental factors, including hyperandrogenism, insulin resistance, and anti-Müllerian hormone (AMH).

Hyperandrogenism. One of the hallmarks of PCOS is hyperandrogenism, which is characterized by elevated levels of androgens, such as testosterone, due to elevated ovarian androgen levels or adrenal influence. According to numerous published studies, this pathological phenomenon disrupts the regulation of the hypothalamic-pituitary-ovarian axis, thereby causing elevated levels of luteinizing hormone (LH). In this situation, theca cells may be prone to increased androgen production [32].

Insulin resistance. Insulin resistance is observed in cases of PCOS diagnosed as compensatory hyperinsulinemia. Hyperinsulinemia, through a positive feedback loop, accelerates ovarian androgen production [33].

Anti-Müllerian hormone. According to many published studies, serum AMH levels in women with PCOS are 2-3 times higher than in other women. Therefore, AMH is believed to play a key role in the pathogenesis of PCOS. In PCOS, the presence of multiple small follicles leads to elevated AMH levels, which can further suppress follicular maturation and contribute to anovulation [34].

Polycystic ovary syndrome treatment strategies

Treatment for PCOS is tailored to individual symptoms and associated health risks. The spectrum of PCOS ranges from significant lifestyle changes to surgery or new procedures such as OT.

Lifestyle modifications. Weight loss through diet and exercise can significantly improve insulin sensitivity and reduce androgen levels, alleviating symptoms and restoring ovulatory function [35].

Pharmacological interventions. Insulin-sensitizing drugs such as metformin are used to reduce insulin resistance and stimulate ovulation [36]. Emerging research highlights the potential of sodium-glucose cotransporter (SGLT1/2) inhibitors (such as licogliflozin) which show promise in improving insulin sensitivity and glucose tolerance in women with PCOS. These drugs can improve metabolic dysfunction, a common problem in patients with PCOS, and reduce the risk of developing type II diabetes and cardiovascular diseases associated with PCOS [37]. The use of neurokinin B antagonists can regulate LH secretion and hormonal balance [38]. Tildacerfont is being extensively studied for its ability to modulate the release of adrenocorticotropic hormone, which may help regulate adrenal androgen levels. This treatment method is particularly relevant for women with elevated adrenal androgen levels [39]. Glucagon-like peptide-1 is a hormone that regulates metabolic processes. Therefore, this drug is widely used for its potential benefit in the treatment of PCOS [40].

Ozone therapy. OT, as a novel treatment option for PCOS, is being explored as a potential adjuvant treatment option for PCOS, primarily due to its anti-inflammatory properties and ability to reduce oxidative stress [17]. OT involves administering ozone to improve the body's use of oxygen, which may help alleviate underlying issues such as chronic inflammation and hyperandrogenism. Published research suggests that ozone may improve ovarian function by stimulating follicle development and improving hormonal balance, potentially leading to more regular ovulation cycles [12]. Furthermore, OT has demonstrated efficacy in the treatment of inflammatory diseases of the reproductive tract, which may alleviate PCOS symptoms. For example, its use has been associated with a reduction in the incidence of PID and other infections.

Ozone

Ozone (O_3) is a triatomic molecule that has an angular molecular structure. The bond lengths between the oxygen atoms are approximately 1.26 Å, and the molecule exists in several resonance forms, which contributes to its stability despite being a highly reactive species. Ozone is characterized by its distinct pungent odor, which can be detected by humans at a concentration of 0.01 mol/L. Being a polar molecule, ozone is soluble in water, which allows it to react with various biomolecules in biological fluids [41], forming reactive oxygen species (ROS) in

cells [42]. These ROS can enhance physiological processes such as ATP production and activation of antioxidant enzymes. The reactivity of ozone and its ability to generate peroxides through ozonolysis make it a subject of interest for therapeutic applications, particularly in the context of bactericidal, fungicidal, and antiviral activity [43]. However, its instability at high concentrations and relatively short half-life (approximately 40 minutes at room temperature) require careful handling and use in clinical settings. Understanding the molecular properties of ozone is crucial for harnessing its therapeutic potential and reducing associated risks.

Biological properties of ozone. OT has attracted attention due to its potential biological role in various therapeutic applications, particularly due to its unique biochemical properties, such as the induction of oxidative stress in target organs [44]. This oxidative mechanism is useful in controlled therapeutic settings because it can stimulate the body's antioxidant defenses and promote healing processes. Some therapeutic applications of ozone are listed below.

Antimicrobial activity. Ozone has a broad spectrum of antimicrobial properties, effectively inactivating bacteria, viruses, and fungi. This is achieved through the oxidation of cellular components, leading to the disruption of microbial membranes and metabolic pathways [7]. These properties make OT a promising option for the treatment of infections [45].

Immunomodulation. OT can affect the immune response through multiple molecular pathways, both inhibiting and stimulating cytokine production [42]. It can increase the activity of immune cells such as macrophages and lymphocytes, thereby improving the body's ability to respond to inflammation [45].

Promoting oxygen utilization. OT can enhance oxygen delivery and utilization at the cellular level [46]. Following the formation of ROS, ozone can stimulate mitochondrial function, leading to improved ATP production and enhanced energy metabolism. This effect is beneficial in conditions where tissue hypoxia is a problem [44].

Vasodilation and improved circulation. Ozone can cause vasodilation, which can increase blood flow to affected areas [47]. Improved circulation facilitates the delivery of nutrients and oxygen while promoting the removal of metabolic waste products, thereby leading to a rapid recovery process [48].

Reduction of inflammation markers' content. NF-κB, as a key family of transcription factors, plays an important role in the response to cellular stress [42]. Thus, NF-κB can lead to the production of proinflammatory cytokines. This action helps alleviate chronic inflammatory conditions and promote tissue healing [44].

Ozone's oxidative properties as a powerful therapeutic advantage. OT is increasingly recognized for its ability to induce controlled oxidative stress, which can stimulate the adaptive response of the body's antioxidant defense systems, such as heme oxygenase-1, superoxide dismutase, and catalase [48]. This therapeutic approach utilizes ozone's properties to modulate oxidative stress in a variety of medical contexts, including diabetes treatment, chemotherapy-induced toxicity [49], neurodegenerative diseases, and PCOS [42]. Ozone acts on cell membrane fatty acids, inducing lipid peroxidation and the formation of lipid ozonation products (LOPs) [45]. These products serve as signaling molecules that further modulate cellular responses. LOPs, including 4-hydroxynonenal, act as secondary messengers by oxidizing the thiol groups of redox-sensitive proteins, thereby altering their structure and function, which activates protective signaling pathways [42]. Furthermore, LOP formation can trigger mitohormesis, activating cell survival mechanisms through pathways such as AMPK/FOXO/mTOR. Furthermore, ozone stimulates the release of nitric oxide, enhancing vasodilation and improving tissue oxygen transport. Also, OT can increase 2,3-diphosphoglycerate (2,3-DPG) levels, leading to increased oxygen release from hemoglobin, thereby further improving tissue oxygenation [44].

The role of ozone therapy in polycystic ovary syndrome. Based on published results, OT is a potential adjuvant treatment for PCOS through various mechanisms, including:

Hormonal regulation. OT restores hormonal balance by stimulating ovarian function [5]. This is particularly relevant for women with PCOS experiencing anovulation and irregular menstrual cycles [45].

Anti-inflammatory effects. Some studies characterized PCOS as accompanied by chronic inflammation. OT demonstrates anti-inflammatory properties [42] mitigating ovarian inflammation. By reducing inflammatory cytokine production, OT may improve ovarian function and overall reproductive health [48].

Insulin sensitivity improvement. OT may increase insulin sensitivity, thereby improving metabolic parameters in women with PCOS. This improvement may lead to improved hormonal regulation and ovulatory function [28].

Enhancement of ovarian blood flow. OT can improve blood circulation, which is crucial for ovarian health [47]. Improved blood flow can facilitate better delivery of nutrients and oxygen to the ovaries, potentially improving follicle development and oocyte quality [45].

Reduction of oxidative stress. OT induces controlled levels of oxidative stress in cells, which can ultimately stimulate the body's antioxidant defense. This response can reduce oxidative damage to ovarian tissue, which is often elevated in women with PCOS. By improving oxidative status, OT may help improve ovarian function and enhance fertility [44].

Potential toxicity of ozone

Ozone is a highly reactive gas. Although ozone has been proposed for various therapeutic purposes, it is also a powerful oxidant causing significant toxicity [49]. According to published studies, potential ozone toxicities include:

Respiratory toxicity. Inhalation of ozone, even at low concentrations, can cause severe irritation and fluid accumulation in the lungs, which can lead to acute lung injury [7] and chronic lung diseases such as asthma or COPD. Therefore, it is recommended to avoid ozone inhalation during therapy [48].

Cardiovascular toxicity. If ozone concentrations are too high or the volume of ozone administered exceeds 10 mL during intramuscular injection, it can locally dissolve in the interstitial fluid and generate excessive amounts of ROS. This can sometimes cause acute pain, vagal hypertonicity, and negative inotropic and chronotropic effects, potentially leading to cardiac arrest [7].

Cytotoxicity and mutagenicity. Although OT causes cellular toxicity [49], the use of reasonable ozone doses, consistent with the antioxidant activity of tissues and biological fluids, can minimize the risk of cytotoxicity and mutagenicity [48].

Other adverse effects. OT may also cause nausea, headache, and fatigue in some patients. Furthermore, the formation of air bubbles during intravenous OT can lead to air embolism and vein occlusion [49].

Discussion

OT and the use of ozone in the treatment of diseases is a protocol that is currently being developed and reviewed in animal studies. The objective of this review was to comprehensively examine OT in the treatment of FRS, especially PCOS. Our findings have shown that ozone, as an agent in charge of oxidation processes in the body, can lead to the death of damaged cells and the activation of the antioxidant defense system [7]. Therefore, the use of ozone with a certain dosage, as well as local use on the affected organ, should be considered in treatment protocols. Various studies have shown that in case of systemic application of ozone, some healthy tissues are involved as well, and there is a possibility of their damage [45]. Besides that, some published studies have shown that the use of oxidizing agents for therapeutic purposes, similar to the use of chemotherapy drugs for cancer treatment, is important and should be based on the dosage and frequency of ozone application. Also, a very few studies have been conducted on the effect of ozone on PCOS. Therefore, it is highly recommended to expand the effect of this gas on reducing the symptoms of PCOS in an animal study to provide the necessary scientific conditions for human clinical trials. In addition, there have been very few studies regarding the toxicity of this gas on the abdominal organs [48]. Therefore, it seems that the side effects of this gas, along with its therapeutic benefits, are not well known. Furthermore, the proper protocol for ozone application for ovarian stimulation should be carried out through the peritoneal cavity. Since there were few relevant animal studies presenting the therapeutic role of ozone in PCOS, it is impossible to draw a proper and reliable conclusion in this regard.

Therefore, the small number of studies with unextractable qualitative data was one of the limitations of this study. In terms of summarizing the main points of the study, it should be noted that FRS pathologies account for a significant portion of the global human disease burden. PCOS, a common disease among women, does not have a clearly defined etiology. OT has the ability to suppress the symptoms of PCOS through controlled cellular oxidation. It can induce high levels of cellular oxygen metabolism, modulate immune responses, and activate the body's antioxidant defense system. The novelty of the study can be emphasized by comparing it with previous studies and identifying any new ideas or observations. A thorough literature search is necessary to identify gaps in existing research. The introduction, discussion, and conclusion sections of the manuscript should highlight these gaps, discuss new observations, and clearly accentuate advances in knowledge to emphasize the novelty of the results.

Conclusion

OT is effective in treating many women's conditions by inducing an oxidative environment and stimulating the activity of the cellular oxidative stress system. Research has shown that this treatment protocol for PCOS requires further study and that when using ozone, the rate of administration, dose, and method of application should be considered three key factors in the therapeutic process.

Abbreviations used in the text

Female reproductive system: FRS; polycystic ovary syndrome: PCOS; ozone therapy: OT; pelvic inflammatory disease: PID; luteinizing hormone: LH; anti-Müllerian hormone: AMH; reactive oxygen species: ROS; lipid ozonation products: LOPs.

Author contributions

Conceptualization: HB and JRS. Methodology: RD. Software: RD. Validation: MI. Formal analysis: HEGGH. Investigation: AE. Resources: JRS. Data curation: HB. Writing – Original draft: RD. Writing – Review and editing: RD. Visualization: JRS. Supervision: HB.

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Availability of data and materials

The datasets used and analyzed are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that they have no conflicts of interest.

AI statement

Artificial intelligence was used to a limited extent to develop part of the article structure. It should also be noted that all sentences are original and do not contain plagiarism.

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