



Oxygen-based technologies in aesthetic medicine: A comparative analysis of ozone therapy and hyperbaric oxygenation (Literature Review)

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Abstract

Objective: To perform a comparative analysis of the clinical efficacy, mechanisms of action, and level of evidence of two tissue-oxygenation-modulating methods—ozone therapy and hyperbaric oxygen therapy (HBOT)—in the context of their application in aesthetic medicine.

Materials and Methods: A systematic search and analysis of scientific literature were conducted using the PubMed, Scopus, Web of Science, eLibrary, and CyberLeninka databases for the period 2018–2024. A total of 48 publications met the inclusion criteria, 81% of which were published within the last five years. Randomized controlled trials (RCTs), cohort studies, clinical case series, systematic reviews, and meta-analyses were included.

Results: Despite the shared objective of improving tissue trophism, ozone therapy and HBOT were found to differ fundamentally in their mechanisms of action. Ozone therapy, acting through pharmacological hormesis, is most effective for the local correction of acne, fine wrinkles, post-acne scars, and, in the form of ozone sclerotherapy, telangiectasias (CEAP class C1). Hyperbaric oxygen therapy, by providing physical hyperoxygenation, demonstrates the highest level of evidence in postoperative rehabilitation following plastic surgery, in the treatment of chronic wounds and complications, and also shows potential in systemic anti-aging therapy. The evidence base for HBOT is more robust, particularly in surgical practice, whereas further standardized RCTs are required for a number of ozone therapy indications.

Conclusion: Ozone therapy and hyperbaric oxygen therapy are complementary modalities within the armamentarium of aesthetic medicine. Their differentiated or combined use should be based on a clear understanding of their mechanisms of action, indication profiles, and the existing level of evidence. A promising direction is the development of personalized protocols that take into account the individual oxidative status and microcirculatory reserve of the patient.

Keywords: Ozone therapy, hyperbaric oxygen therapy, aesthetic medicine, anti-aging medicine, comparative analysis, evidence base, telangiectasias, wound healing

Introduction

Modern aesthetic medicine is characterized by dynamic development and the integration of technologies originally applied in other areas of clinical practice. Specialists focus on methods aimed not only at correcting visible age-related changes but also at systemically improving tissue trophism, microcirculation, and regenerative potential [1]. Among such physiotherapeutic approaches, ozone therapy (OT) and hyperbaric oxygen therapy (HBOT) hold a special place—methods whose fundamental basis is the regulation of oxygenation processes and redox homeostasis [2]. Despite the common goal of overcoming tissue hypoxia and stimulating reparative processes, these techniques are based on different physicochemical principles, have different points of application, and consequently, different efficacy and safety profiles and levels of scientific evidence [3]. Ozone therapy, with its pronounced local effects, has found wide application in correcting dermatological aesthetic problems, including the treatment of telangiectasias, while hyperbaric oxygen therapy has established itself as the "gold standard" in comprehensive rehabilitation after invasive procedures and in the treatment of complex wounds. The purpose of this review is a detailed comparative analysis of the mechanisms of action, areas of clinical application,

evidence base, and prospects for using ozone therapy and hyperbaric oxygen therapy in aesthetic medicine, with an emphasis on current data from evidence-based medicine.

Review Methodology

To achieve this goal, a systematic search of scientific literature was conducted in the international databases PubMed, Scopus, Web of Science, as well as in the Russian scientific libraries eLibrary and CyberLeninka for the period from 2018 to 2024. The search was performed using keywords and their combinations: "ozone therapy aesthetic medicine," "hyperbaric oxygen therapy skin rejuvenation," "ozone facial," "hyperbaric oxygen wound healing," "ozone sclerotherapy." Inclusion criteria were: randomized controlled trials (RCTs), prospective and retrospective cohort studies, clinical case series, systematic reviews, and meta-analyses published in peer-reviewed journals. Priority was given to publications from the last five years. As a result of the initial screening, over 70 publications were reviewed, from which 48 sources most fully corresponding to the objectives of the review were selected for final analysis. Of these, 39 (81%) were published between 2019 and 2024, ensuring the relevance of the presented data.

Ozone Therapy in Aesthetic Medicine: From Molecular Mechanisms to Clinical Practice

Biological Basis and Mechanisms of Action: The therapeutic effect of medical ozone (O₃) is indirect and is realized through products of its interaction with biological fluids and lipids of cell membranes [4]. The key step is the formation of reactive oxygen species (ROS) and lipid oxidation products (LOP), which at therapeutic concentrations act as signaling molecules, triggering a cascade of physiological responses [5]. This phenomenon, known as hormesis, underlies most of the aesthetically significant effects of ozone. First, activation of the antioxidant system occurs: the synthesis and activity of superoxide dismutase, glutathione peroxidase, and catalase increase, leading to a reduction in chronic oxidative stress—one of the main factors in skin aging [5]. Second, ozone stimulates microcirculation by inducing the synthesis of nitric oxide (NO), a potent vasodilator [6]. Third, dermal fibroblasts are activated, and the synthesis of type I and III collagen, elastin, and glycosaminoglycans is enhanced through the activation of transforming growth factor-beta (TGF-β) and other growth factors, as confirmed both *in vitro* and in clinical studies [7, 8]. Fourth, the inflammatory response is modulated: ozone can reduce the level of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) and increase the level of anti-inflammatory interleukins (IL-4, IL-10) [9, 10, 11]. Finally, the pronounced bactericidal, fungicidal, and virustatic effects of ozone are associated with direct damage to the membranes of microorganisms, which is particularly important in the treatment of acne and the prevention of infectious complications [12].

Modern Techniques and Clinical Indications: The aesthetic physician has several methods for administering ozone at their disposal. Local techniques include the application of ozonated olive or sunflower oil for skin care after peels and for acne, as well as the technique of meso-ozone therapy—intradermal or subcutaneous injections of an ozone-oxygen mixture into the face, neck, and décolleté area [13]. Systemic effects are achieved through major autohemotherapy with ozone or rectal insufflation of the gas mixture. The main aesthetic indications include: treatment of age-related skin changes (improvement of turgor, hydration, reduction of fine wrinkles) [14, 15]; treatment of scar deformities, including striae and post-acne scars [16]; correction of acne and seborrheic dermatitis [17]; comprehensive therapy for androgenetic alopecia [18]; rehabilitation after laser procedures and plastic surgeries to accelerate healing [19].

Ozone Sclerotherapy of Telangiectasias and Reticular Varicose Veins (C1 by CEAP): Special attention should be paid to the highly specialized technique—ozone sclerotherapy (ozone sclerotherapy), which is an effective alternative to classical sclerotherapy for the treatment of spider veins and reticular veins up to 2-3 mm in diameter [2]. The procedure involves the precise intraluminal or perivascular injection of a low-concentration ozone-oxygen mixture (usually 2-15 μg/mL) into the lumen of the target vessel [20]. The mechanism of obliteration is based on controlled oxidative stress: ozone causes damage to endothelial cells, which triggers a cascade of aseptic inflammation, platelet adhesion, vessel desolation, and subsequent replacement with connective tissue (fibrosis)

without the risk of recanalization [4, 8]. The indisputable advantages of this method over traditional sclerotherapy include: absolute hypoallergenicity (ozone is not an antigen); minimal risk of hyperpigmentation and skin ulceration in case of extravasation due to the absence of a hemolytic effect; its own antiseptic effect, excluding infectious complications; simultaneous improvement of the condition of perivascular tissues due to its positive effect on microcirculation and oxygenation [21, 2, 1]. Clinical observations and studies demonstrate high efficacy of the method (up to 85-95%) and excellent cosmetic results, especially in the correction of facial telangiectasias (couperosis) [20]. In particular, the results of our prospective study (Matveev D.V. *et al.*, 2025), dedicated to the use of an ozone-oxygen mixture for sclerobliteration of telangiectasias and reticular veins, confirm high clinical efficacy (93.7% complete vessel obliteration after 1-2 sessions) and excellent patient tolerability of the procedure, making the method promising for widespread use in outpatient aesthetic practice [22].

Evidence Base and Safety Issues: The level of evidence for the use of ozone therapy in aesthetic medicine is generally assessed as moderate (levels B-C according to the Oxford Centre for Evidence-Based Medicine scale). Most works are open-label pilot studies and clinical case series. Large, double-blind, placebo-controlled RCTs remain scarce. For instance, a 2020 systematic review and meta-analysis on the treatment of acne with ozone therapy showed statistically significant improvement; however, the authors noted the heterogeneity of the included studies and the need for more rigorous trials [23]. Russian experts emphasize the urgent need for standardization of treatment protocols (ozone concentrations, volumes, number, and frequency of procedures) to ensure reproducibility and comparability of results between centers [24]. When manipulations are performed professionally, the safety profile of ozone therapy is considered favorable. However, potential risks, mainly related to technical errors, include local pain, subcutaneous emphysema during injections, and in rare cases, gas embolism upon accidental intravascular injection of a significant volume of gas, which requires a high level of physician qualification [21]. Combined techniques, for example, ozone therapy with photodynamic therapy or platelet-rich plasma (PRP) therapy, demonstrate synergism, but their application requires further study [15, 25].

Hyperbaric Oxygenation: Fundamental Principles and Application in Aesthetic Practice

Mechanism of Action and Physiological Effects: HBOT is based on the physical Henry-Dalton law: when breathing 100% oxygen under increased atmospheric pressure (usually in the range of 1.5-3.0 ATA), there is a sharp increase in the amount of oxygen physically dissolved in the blood plasma, bypassing hemoglobin [3, 26]. This ensures oxygen delivery to tissues whose perfusion is significantly reduced due to edema, inflammation, or vascular insufficiency. Hyperoxygenation triggers a complex of responses. First, tissue hypoxia is eliminated, which is the main trigger for repair. Second, neoangiogenesis is stimulated through increased expression of vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) [27, 28]. Third, fibroblasts are directly activated, collagen synthesis and extracellular matrix formation are enhanced, as

confirmed both clinically and in experimental work [29, 30]. Fourth, HBOT modulates the inflammatory response, enhancing the bactericidal activity of neutrophils and macrophages and reducing the level of pro-inflammatory mediators [31]. An important discovery in recent years is the proof of HBOT's ability to activate endogenous stem cells and progenitor cells that migrate to areas of damage [32]. Furthermore, HBOT causes vasoconstriction without impairing tissue oxygenation, which effectively combats edema [26].

Applications and Therapeutic Protocols: HBOT sessions are conducted in specialized monoplace or multiplace hyperbaric chambers. A standard aesthetic protocol involves a pressure of 2.0-2.5 ATA, a session duration of 60-90 minutes, and a course of 10-20 daily procedures [33]. However, the use of "milder" HBOT regimens (1.3-1.5 ATA) may prove equally effective. In aesthetic medicine, several key areas of HBOT application are distinguished. The most evidence-based is rehabilitation after plastic and reconstructive surgeries (rhinoplasty, blepharoplasty, facelift, mammoplasty). Numerous studies, including RCTs and meta-analyses, demonstrate that a pre- and postoperative course of HBOT significantly reduces the incidence of complications such as wound edge necrosis and skin flap necrosis, infections, promotes faster suture healing, and reduces postoperative edema and hematomas [34, 35, 36, 37, 38]. The second indisputable indication is the treatment of complex wounds and complications: necrosis, chronic ulcers (venous, diabetic), radiation-induced skin and soft tissue injuries [39, 40, 41, 42]. In recent years, the role of HBOT in systemic anti-aging therapy has been actively studied. Pilot and randomized studies show that a course of HBOT can lead to objective improvement in skin parameters: increased dermal thickness and collagen fiber density, improved elasticity and hydration [43, 44, 45]. One of the most discussed mechanisms is the potential effect of hyperoxia on telomere length and telomerase activity, which requires further investigation [43]. HBOT is also effectively used to shorten the rehabilitation period and enhance the effectiveness of laser procedures and dermabrasion [46, 30].

Evidence Base and Safety Profile: The evidence base for HBOT, unlike ozone therapy, is one of the strongest in the field of physiotherapy, especially in the context of wound healing and postoperative management. There are a significant number of high-quality RCTs, systematic reviews, and meta-analyses. For example, the meta-analysis by Huang E.T. *et al.* (2019) convincingly demonstrated a 66% reduction in the risk of flap necrosis with the use of HBOT in reconstructive breast surgery [36]. Studies in the anti-aging field, although more preliminary, already provide statistically significant data confirmed by instrumental diagnostic methods [45, 47]. The safety of the procedure, when standard protocols are followed, is considered high. The most common side effect is middle ear barotrauma, which can be minimized by proper equalization techniques. Serious complications, such as CNS oxygen toxicity or seizures, are extremely rare [48]. General principles, indications, and prospects of HBOT are detailed in modern fundamental reviews [49, 26].

Comparative Analysis of Methods: Ozone Therapy versus Hyperbaric Oxygenation

The conducted analysis allows for a clear differentiation of the application niches of the two methods in aesthetic

medicine. By mechanism of action, HBOT is a physical method of systemic hyperoxygenation, aimed primarily at improving perfusion and oxygen delivery to ischemic tissues [3, 26]. OT is a pharmacological method, acting at the cellular and humoral level through the induction of controlled oxidative stress and activation of antioxidant and regenerative systems [4, 5]. Regarding invasiveness, HBOT is a completely non-invasive procedure, while most OT techniques involve injection (mesotherapy, sclerobliteration) or blood sampling (autohemotherapy) [13, 20, 33].

Key aesthetic indications: also differ. OT is most effective for local problems: inflammatory dermatoses (acne), initial age-related changes, small-caliber vascular pathologies (C1) [14, 17, 23, 2]. HBOT demonstrates maximum effectiveness in situations requiring systemic effects and improved trophism: rehabilitation after extensive surgical interventions, treatment of chronic wounds and necrosis, and as a component of a systemic anti-aging approach [35, 39, 36, 45]. The evidence base for HBOT is objectively stronger, especially in surgical and wound practice, as confirmed by meta-analyses [36]. Evidence for OT more often reaches the level of case series or pilot studies, and its effectiveness for a number of indications requires further validation in RCTs [23, 24]. The safety of both methods is high, provided protocols are strictly followed and staff are qualified, but the risk profiles differ: for OT—local complications and, hypothetically, embolism [21]; for HBOT—barotrauma and individual reaction to hyperoxia [48]. Combination possibilities are broad for both methods. OT is often used as an adjunct to peels, mesotherapy, PRP [19, 15]. HBOT is ideally combined with surgical and laser procedures, potentiating their results and shortening the recovery period [46, 30, 38].

Conclusion and Prospects

Thus, ozone therapy and hyperbaric oxygen therapy represent complementary, rather than competing, technologies in the arsenal of modern aesthetic medicine. Hyperbaric oxygen therapy is established as a method with a high level of evidence for solving complex problems associated with impaired tissue perfusion and healing: postoperative rehabilitation, treatment of complications and chronic wounds [39, 36]. Its role in the systemic anti-aging approach appears extremely promising but requires the accumulation of additional data from long-term studies [45, 47].

Ozone therapy, in turn, is a versatile, accessible, and effective tool for the local correction of a wide range of aesthetic skin problems—from acne and fine wrinkles to telangiectasias, where the ozone sclerotherapy technique, according to recent clinical work [22], demonstrates certain advantages over traditional sclerotherapy in terms of safety profile and efficacy. However, to transition into the category of methods with an indisputable evidence base, large multicenter randomized trials and the development of unified international protocols are required [24].

The most encouraging direction for development appears to be the creation of personalized comprehensive programs that synergistically combine both methods. For example, a pre- and postoperative course of HBOT to optimize the outcomes of plastic surgery, followed by local ozone therapy (mesotherapy, correction of residual telangiectasias) for the final improvement of skin quality and texture [19, 46, 2].

Future research should focus on identifying biomarkers that allow prediction of response to each method and on creating algorithms for the precise selection of physiotherapeutic interventions based on an assessment of the patient's individual oxidative status, microcirculatory reserve, and genetic characteristics ^[28, 1]. Such an approach will enable a transition from empirical application to scientifically grounded, personalized physiological correction, fully unlocking the potential of both ozone therapy and hyperbaric oxygen therapy in achieving aesthetic and anti-aging goals.

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