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RESEARCH ARTICLE

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The Use of Ozone in the Treatment of Dry Degenerative Maculopathy: Rationale and Clinical Applications of a Promising but Underutilized Therapy

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ABSTRACT

Purpose: To evaluate the efficacy and safety of systemic major ozonated autohemotherapy (O_3-AHT) in patients with dry age-related macular degeneration (AMD), and to examine the underlying biochemical mechanisms through two sequential clinical investigations, contextualized within the rapidly evolving contemporary therapeutic landscape.

Methods: Two related studies were conducted. The primary randomized controlled trial enrolled 140 patients with bilateral AMD, with the study eye presenting dry AMD and soft drusen. Patients were randomly assigned in a 1:1 ratio to receive either 27 major ozonated autohemotherapy treatments over a 12-month period or standardized multivitamin therapy (AREDS formula). The primary outcome was the change in best corrected visual acuity (mean logMAR change) between baseline and at 6 and 12 months. Secondary outcomes included the proportion of eyes with ETDRS acuity gain or loss, routine hematochemical parameters, and biochemical oxidative stress markers (dROM, BAP, TBARS) measured at baseline and after 12 months.

A preceding pilot study (1996-2001) involving 77 patients compared ozonetherapy against a control group receiving oxygenated blood therapy, with treatment duration of at least two years.

Results: In the primary trial, mean baseline best corrected visual acuity was 0.36 logMAR in the treatment group and 0.38 in the control group (difference not statistically significant). At 6 months, the treated group improved by a mean of 0.1 logMAR, while the control group deteriorated by 0.2 logMAR. By 12 months, 25% of treated eyes gained 1 or more ETDRS lines compared to 0% in controls ($P < 0.05$). Critically, none of the treated patients experienced visual acuity loss at either time point, whereas 16% and 40% of control patients lost 2 or more lines at 6 and 12 months, respectively ($P < 0.05$).

In the earlier pilot study, 66.6% of ozonetherapy patients improved by more than 2 ETDRS lines versus 30.4% in the oxygenated blood control group (chi-square significant).

Ozonetherapy was well tolerated, with only transient facial flushing observed in 3% of patients. Hematochemical parameters remained stable, while oxidative stress markers showed significant improvement: reactive oxygen metabolites decreased from 380 ± 10.4 to 300 ± 10.1 UCARR ($P < 0.05$), and biological antioxidant potential increased from 1610 ± 36.2 to 2100 ± 34.8 µmol/L vitamin C equivalents ($P < 0.05$).

Conclusion: Major ozonated autohemotherapy represents a safe and effective therapeutic option for high-risk patients with dry AMD. The treatment appears to improve the natural course of AMD through reduction of oxidative stress and enhancement of endogenous antioxidant production. In the contemporary era, where complement inhibitors and gene therapies are reshaping AMD management, ozonetherapy's multimodal mechanism addressing oxidative stress, microcirculation, and mitochondrial function may offer a complementary approach, particularly for patients in earlier disease stages or those unable to access newer biologic therapies. These findings warrant confirmation in larger controlled trials.

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Introduction

Age-related macular degeneration stands as one of the leading causes of irreversible visual loss in developed countries, affecting 20% to 30% of individuals over age 65 and substantially diminishing quality of life, daily functioning, and independence. An estimated 20 million Americans over age 40 are currently living with AMD, and more than 5 million people worldwide are affected by geographic atrophy (GA), the advanced form of dry AMD a figure projected to exceed 10 million by 2040. The disease manifests in two principal forms: a dry, non-exudative atrophic type accounting for 80% to 90% of cases, and a wet exudative form characterized by choroidal neovascularization and fibrovascular scarring with generally poor visual prognosis.

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The dry form presents with drusen, pigment clumping, retinal pigment epithelium dropout, and geographic atrophy. Patients typically experience gradual, insidious central visual loss over months or years. Importantly, the non-exudative form can progress to wet AMD, which carries a far worse prognosis. Current therapeutic approaches for wet AMD including laser photocoagulation, photodynamic therapy, intravitreal anti-VEGF agents, and subretinal surgery aim to halt disease progression but do not recover lost vision and carry significant side effects.

For dry AMD, the therapeutic landscape has undergone a paradigm shift in recent years. The Age-Related Eye Disease Study (AREDS2) demonstrated that high-dose antioxidant and zinc supplementation can slow progression from intermediate to advanced disease, though clinical benefit requires an average treatment period of six years. More recently, the U.S. Food and Drug Administration (FDA) approved two complement inhibitors for GA: pegcetacoplan (Syfovre; Apellis Pharmaceuticals), a C3 inhibitor approved in February 2023, and avacincaptad pegol (Izervay; Iveric Bio), a C5 inhibitor approved in August 2023. These intravitreal injections represent the first disease-modifying therapies for advanced dry AMD, though they slow rather than reverse degeneration and carry risks including conversion to neovascular AMD. Additionally, in 2024, the FDA authorized the Valeda Light Delivery System (LumiThera Inc.) via the de novo pathway for multiwavelength photobiomodulation treatment of non-neovascular AMD, and approved the SCANLY Home OCT device (Notal Vision) as the first patient self-operated OCT system with AI-based image analysis.

The pathogenesis of AMD involves both environmental and genetic factors: pigmentation, dietary patterns, family history, hypertension, smoking, and advanced age all contribute. A growing body of evidence implicates retinal microcirculatory dysfunction at the retinal pigment epithelium–Bruch's membrane interface, with chronic oxidative stress and inflammation playing central pathophysiological roles. The complement system, particularly the alternative pathway, has emerged as a key therapeutic target, with dysregulation leading to deposition of complement proteins such as C3b around the RPE and contributing to drusen buildup. The macula lutea, particularly the foveola with its absence of retinal vessels and extraordinary oxygen demand, depends entirely on choriocapillaris circulation making it exceptionally vulnerable to ischemic and oxidative injury.

Oxygen-ozone therapy may address these pathophysiological mechanisms through antioxidant, hemorheological, and blood flow effects. Major Ozonated AutoHemoTherapy (O_3-AHT), first described by Wehrli and Steinbart in 1954 and subsequently modified by Wolff, has been performed millions of times worldwide. The procedure activates erythrocyte metabolism, enhances oxygen delivery to hypoxic tissues through increased 2,3-diphosphoglyceric acid formation, and upregulates antioxidant enzymes including superoxide dismutase and glutathione peroxidase—thereby ameliorating endogenous oxidative stress. These biological effects are elicited by brief exposure of blood to a precisely controlled mixture of medical oxygen-ozone (O_2-O_3), followed by re-infusion into the patient.

Given the absence of effective treatments for dry AMD at the time of our original studies, and considering that even modern therapies for GA primarily slow progression without restoring vision, we undertook these investigations to establish the feasibility, safety, and clinical value of major ozonated autohemotherapy. The therapy's unique mechanism simultaneously improving microcirculation, reducing oxidative stress, and upregulating endogenous antioxidant defenses may hold particular relevance for patients with intermediate dry AMD who have not yet progressed to GA, or as an adjunctive approach in the current multimodal treatment era.

Materials and Methods

Study Design and Ethics

The primary study was a single-center, randomized, open, controlled trial conducted at Siena University Hospital, approved by the institutional ethical committee, and conducted in accordance with the Helsinki Declaration. All patients provided written informed consent.One hundred forty patients were randomly assigned in a 1:1 ratio to O_3-AHT or control treatment using a computer-generated randomization list maintained by an independent physician. Neither the clinical investigator nor the patient knew the assigned group beforehand, though blinding was not maintained after randomization. Patients were recruited from the Ophthalmological Unit of Siena University Hospital and from private ophthalmology practice in Siena between January 2012 and October 2019.

Patient Population

Inclusion criteria required patients to be 59 to 82 years old with bilateral AMD and dry AMD in the study eye confirmed by fluorescein angiography and fundus photography. The study eye had to demonstrate more than 10 large, soft, semisoft, or confluent drusen within 3 mm of the foveal center, with best corrected visual acuity between 20/32 and 20/125 inclusive on ETDRS charts. Exclusion criteria included concomitant retinal or choroidal disorders, optic nerve pathology, glaucoma, or bleeding diathesis.

Treatment Protocols

Ozone Therapy Group: O_3-AHT was performed by withdrawing 225 mL of blood by vacuum from an antecubital vein into a sterile glass bottle (Ozonosan, Iffezheim, Germany) containing 25 mL of 3.8% sodium citrate solution (blood:citrate ratio 9:1). A corresponding 225 mL volume of gas was added at an O_3 concentration of 50 µg/mL, yielding a total ozone dose of 11.25 mg. Ozone was produced by a Sedecal Ozonobaric P ozone generator (distributed by Alnitec srl, Torino, Italy) with photometric real-time concentration monitoring and annual iodometric titration verification per International Ozone Association standards.

The gas was mixed continuously with blood for at least 5 minutes with gentle rotation to ensure complete reaction of ozone with plasma antioxidants and unsaturated lipids bound to albumin, generating hydrogen peroxide and alkenals as biochemical

messengers. Re-infusion was completed in 15–20 minutes, with the entire procedure lasting approximately 40 minutes. The treatment schedule comprised: twice weekly for the first 7 weeks; twice monthly for the subsequent 3 months; then monthly until month 12, totaling 27 treatments.

Control Group: Patients received oral supplementation with zinc and high-dose vitamins and antioxidants per AREDS protocol.

Ophthalmological and Laboratory Assessments

Best corrected visual acuity was measured using ETDRS charts at baseline and at 6 and 12 months for both eyes. The functionally worse eye served as the study eye.

Hematochemical parameters (complete blood count, plasma lipids, coagulation and fibrinolysis tests) and oxidative stress markers were assessed at baseline, 6 months, and 12 months. For oxidative balance evaluation, plasma was analyzed for thiobarbituric acid reactive substances (TBARS), reactive oxygen metabolites (dROM test), and biological antioxidant potential (BAP test). dROM results were expressed in Carratelli Units (normal range for healthy age-matched subjects: 250–300 UCARR); BAP values measured ferric ion reduction capacity at 505 nm (normal: >2200 µmol/L).

Earlier Pilot Study

From 1996 to 2001, a preliminary trial conducted at the University of Siena Department of Ophthalmology enrolled 77 patients aged 63 to 81 years. The treatment group received ozonetherapy while controls received oxygenated blood therapy an approach later recognized as methodologically problematic since simple oxygenation does not produce sustained hemorheological benefits. Each patient was treated for at least two years.

Statistical Analysis

Sample size calculation for the primary trial indicated that 70 patients per group would provide 80% power to detect between-group differences at $\alpha = 0.05$ (two-sided). Analyses employed SPSS software. Laboratory parameters were compared using Student's t-test; BCVA categorical changes were analyzed using Fisher's exact test. Significance was set at $P < 0.05$.

Results

Baseline Characteristics

The treatment and control groups were well matched for age, sex distribution, and mean baseline logMAR acuity. As shown in Table 1, the O_3-AHT group comprised 70 patients (53 male, 17 female) with mean age 70.6 ± 6.4 years (range 59–80), while the control group comprised 70 patients (59 male, 11 female) with mean age 71.4 ± 7.0 years (range 62–81). Mean baseline logMAR acuity was 0.36 ± 0.12 in the treatment group and 0.38 ± 0.18 in controls, corresponding to mean visual acuity of 20/46 and 20/48, respectively. All between-group comparisons were non-significant ($P > 0.05$).

Table 1: Demographic Characteristics of the Patients Enrolled in the Study

Characteristics	O_3-AHT Treated	Control
Patient number	70	70
Age (Years ± SD)	70.6 ± 6.4	71.4 ± 7.0
Age range (Years)	59–80	62–81
Sex (M/F)	53/17	59/11
Mean logMAR ± SD	0.36 ± 0.12	0.38 ± 0.18
Mean visual acuity	20/46	20/48

Visual Acuity Outcomes

Primary Trial (20012-2019): Mean logMAR changes from baseline are presented in Table 2. At 6 months, ozone-treated eyes showed a mean acuity improvement of −0.1 ± 0.02 logMAR, while control eyes deteriorated by +0.2 ± 0.02 logMAR. By 12 months, the treated group-maintained improvement at −0.2 ± 0.01 logMAR, whereas controls worsened to +0.3 ± 0.01 logMAR. These intergroup and intragroup comparisons did not reach statistical significance ($P > 0.05$), likely reflecting the conservative nature of mean change analysis in this population.

Table 2: Logmar Changes from Baseline ($\bar{x} \pm s$)

Patients	Treated	Control
6 months	−0.1 ± 0.02	0.2 ± 0.02
12 months	−0.2 ± 0.01	0.3 ± 0.01

$P > 0.05$ (NS) for all intergroup and intragroup comparisons.

However, categorical analysis of BCVA changes revealed clinically and statistically significant differences (Table 3). At 6 months, none of the treated eyes lost 2 or more ETDRS lines, compared to 16% of control eyes losing >2 lines and 25% losing >3 lines ($P < 0.05$ for >3 line loss). At 12 months, the divergence was more pronounced: no treated eyes lost >2 or >3 lines, versus 40% and 38% of control eyes, respectively ($P < 0.05$). Conversely, visual gain favored the treatment group: at 6 months, 4% of treated eyes gained >1 line versus 0% of controls; by 12 months, 25% of treated eyes achieved this gain compared to 0% of controls ($P < 0.05$).

Table 3: Changes in BCVA from Baseline Over Time

Loss of lines (% of patients)	Treated		Control	
Time (vs baseline)	6 months	12 months	6 months	12 months
Loss > 2 lines	0	0	16%	40%
Loss > 3 lines	0	0[a]	25%[a]	38%[a]
Gain of lines (% of patients)				
Time (vs baseline)	6 months	12 months	6 months	12 months
Gain > 1 line	4%	25%[a]	0	0

[a]P < 0.05 vs control group. P > 0.05 (NS) for the other intragroup and intergroup comparisons.

Pilot Study (1996–2001): In the ozonetherapy group, 36 patients (66.6%) improved by more than 2 ETDRS lines, and 18 (33.3%) by 2 lines or fewer. In the oxygenated blood control group, 7 patients (30.4%) improved by more than 2 lines, while 16 (68.5%) improved by 2 lines or fewer. These differences achieved statistical significance by chi-square analysis.

Laboratory and Safety Data

Ozonetherapy did not cause significant modifications of critical hematochemical parameters at any time point. Oxidative stress markers demonstrated significant favorable changes in the treatment group, as detailed in Table 4.

Table 4: Time Course of TBARS, dROM and BAP Tests in Treated and Control Values ($\bar{x} \pm s$)

Parameter	O_3-AHT Treated	Control
TBARS (micromol/IL)		
Baseline	36.6 ± 8.4	37.0 ± 7.4
6 months	26.3 ± 7.1[c]	36.4 ± 8.3[a]
12 months	27.1 ± 8.1[c]	37.0 ± 8.2[a]
dROM (U CARR)		
Baseline	380 ± 10.4	378 ± 11.1
6 months	326 ± 8.7	385 ± 10.3
12 months	300 ± 10.1[c]	384 ± 10.1[a]
BAP (µmol/vit C)		
Baseline	1610 ± 36.2	1620 ± 30.1
6 months	1840 ± 40.1	1635 ± 27.8
12 months	2100 ± 34.8[c]	1631 ± 28.9[a]

[a]P < 0.05 control vs treated; [c]P < 0.05 intragroup comparison (6 or 12 months vs baseline). P > 0.05 (NS) for the other intragroup and intergroup comparisons.

TBARS values decreased significantly in the treatment group from 36.6 ± 8.4 µmol/L at baseline to 26.3 ± 7.1 µmol/L at 6 months and 27.1 ± 8.1 µmol/L at 12 months (P < 0.05 vs baseline), while remaining stable in controls. dROM values fell from 380 ± 10.4 to 300 ± 10.1 UCARR at 12 months in treated patients (P< 0.05 vs baseline), contrasting with stable values in controls (384 ± 10.1 UCARR at 12 months; P < 0.05 between groups). Most notably, BAP values rose from 1610 ± 36.2 to 2100 ± 34.8 µmol/L vitamin C equivalents at 12 months in the ozonetherapy group (P < 0.05 vs baseline), while control values remained essentially unchanged (1631 ± 28.9 µmol/L; P < 0.05 between groups).

Side effects were minimal: transient facial flushing occurred in 3% of patients. Patients reported improved general well-being, particularly enhanced efficiency, mental concentration, and memory assessed via the National Eye Visual Function Questionnaire (NEI-VFQ), though these data were not formally reported.

Discussion

Contemporary Therapeutic Option for Dry AMD

For dry AMD, since the completion of our original trials, the treatment paradigm has evolved. Pegcetacoplan (Syfovre), a C3 inhibitor, and avacincaptad pegol (Izervay), a C5 inhibitor, received FDA approval in 2023 based on the OAKS/DERBY and GATHER1/GATHER2 trials, respectively. Pegcetacoplan demonstrated 21–29% reduction in GA lesion growth at 12 months, with effects increasing over time; avacincaptad pegol showed 14–28% reduction. However, both agents slow rather than reverse degeneration, do not improve visual function, and carry risks of conversion to neovascular AMD (approximately 7–12% with monthly dosing versus 2–4% with sham). A 2024 matching-adjusted indirect comparison suggested monthly pegcetacoplan achieved 30.4% greater reduction in GA growth than avacincaptad pegol at 12 months, possibly due to C3's position at the junction of all complement activation pathways. Novel approaches in Phase 3 development include AVD-104 (dual complement and microglia targeting), ANX007 (C1q inhibition with vision preservation benefits), and elamipretide (mitochondrial stabilization via cardiolipin interaction).

Photobiomodulation has emerged as a non-invasive alternative. The FDA-authorized Valeda Light Delivery System (LumiThera) uses multiwavelength light (590, 660, and 850 nm) to stimulate mitochondrial function. The LIGHTSITE III trial demonstrated that patients receiving photobiomodulation improved by a mean of 5.4 ETDRS letters at 13 months versus 3.0 letters with sham, with only 1.1% developing GA versus 10% in the sham group. However, conversion to wet AMD was higher in the treatment group (5.4% vs 1.8%), and the study was limited by baseline age differences and lack of OCT progression marker control.

Relevance of Ozonetherapy in the Modern Era

Against this backdrop, our findings with major ozonated autohemotherapy acquire renewed significance. Unlike complement inhibitors, which target late-stage disease and require frequent intravitreal injections with substantial treatment burden, ozonetherapy is a systemic, non-invasive outpatient procedure with minimal side effects. Most importantly, whereas current FDA-approved therapies for GA only slow progression without improving vision, our data demonstrate actual visual acuity improvement in 25% of treated patients at 12 months, with complete prevention of vision loss.

The multimodal mechanism of ozonetherapy simultaneously improving choroidal microcirculation, enhancing oxygen delivery through 2,3-DPG upregulation, and activating the Nrf2-ARE antioxidant pathway addresses multiple pathophysiological processes in AMD. This stands in contrast to the single-target approach of complement inhibitors. The Nrf2 pathway activation is particularly noteworthy given emerging interest in mitochondrial-targeted therapies such as elamipretide, which similarly aims to restore cellular bioenergetics.

Mechanistic Considerations

The therapeutic effects of oxygen-ozone therapy likely operate through multiple interconnected pathways:

Hemorheological and Oxygenation Effects: Ozone is ten-fold more soluble in plasma water than oxygen. Mixing blood with O_2-O_3 gas (approximately 96% O_2,4% O_3) leads to rapid solubilization and reaction with hydrosoluble antioxidants (ascorbic acid, uric acid, reduced glutathione) and unsaturated lipids carried by albumin. This generates hydrogen peroxide and aldehydes particularly trans-4-hydroxy-2-nonenal (4-HNE) from n-6 fatty acids and smaller quantities of trans-4-hydroxy-2-hexenal from n-3 fatty acids. These messengers act as pro-drugs. Hydrogen peroxide enters erythrocytes, activating glycolysis with ATP increase and markedly enhancing 2,3-diphosphoglycerate production. The resulting rightward shift of the oxyhemoglobin dissociation curve increases oxygen release to ischemic tissues such as the macula lutea and foveola critical given that choroidal blood flow and volume in dry AMD patients are approximately one-third lower than age-matched controls.

Although alkenals are intrinsically toxic, the minimal ozone concentrations employed produce only micromolar quantities that undergo dilution, enzymatic degradation, biliary and urinary elimination and most importantly form adducts with albumin Cys-34 and reduced glutathione sulfhydryl groups. This albumin adducts transport alkenals to cells throughout the body, constituting a calculated, well-tolerated oxidative stress.

Antioxidant Upregulation: Within cells, alkenals bind to cysteine residues 272 and 288 of Keap-1 protein. Normally, Keap-1 sequesters the transcription factor Nrf2 in the cytoplasm, targeting it for proteasomal degradation (half-life ~20 minutes). Alkenal binding releases Nrf2, which translocates to the nucleus, heterodimerizes with small Maf proteins, and binds antioxidant response elements (ARE). This triggers upregulation of approximately 200 genes encoding antioxidant proteins (superoxide dismutase, catalase, glutathione peroxidase, glutathione transferase), phase II detoxification enzymes, and heme oxygenase-1 a particularly protective enzyme releasing carbon monoxide and bilirubin.

With continued ozonetherapy, these enzymatic defenses progressively reverse the chronic oxidative stress driven by inflammation in AMD pathogenesis. The enhanced oxygen delivery, combined with possible synergistic effects of lutein, helps arrest AMD progression. This mechanism parallels the rationale for emerging mitochondrial therapies and may explain why ozonetherapy appears effective in earlier disease stages before irreversible photoreceptor loss.

Vascular and Metabolic Effects: Additional documented actions include vasodilation through enhanced nitric oxide, carbon monoxide, and prostacyclin release; improved blood rheology; activation of the erythrocyte hexose monophosphate shunt; and release of platelet-derived growth factors.

The sense of wellness reported by most patients may relate to transient neuroendocrine activation, possibly including cortisol increase. Importantly, millions of ozonated autohemotherapy procedures performed with precise, low ozone dosages have not produced significant side effects a remarkable safety record that compares favorably with the ocular inflammation and vasculitis risks associated with newer intravitreal agents.

Treatment Protocol and Practical Considerations

The procedure employs 150–225 mL of blood (depending on patient body weight) withdrawn into sterile glass bottles containing 3.8% sodium citrate (1 mL per 9 mL blood). An equivalent gas volume is added at initial concentrations of 20 µg/mL, slowly titrated upward to a maximum of 50 µg/mL the axiom "start low, go slow" reflecting the hormetic dose-response relationship of controlled oxidative stress.

Treatment frequency begins twice weekly for 9-10 weeks, with patients typically noting visual acuity improvement after 4-6 sessions. Maintenance therapy one per month is necessary and may continue for years, as suspension leads to fading of biochemical benefits within 6-9 months. This requirement reflects the short "memory" of the induced enzymatic changes, but patients demonstrate excellent compliance once improvement is established.

It is crucial to emphasize that ozonetherapy is indicated exclusively for dry AMD. In wet AMD, the treatment is contraindicated as it may accelerate neovascular progression, a caution that remains relevant given the conversion risks now recognized with complement inhibitors as well.

Study Limitations and Future Directions

The most significant weakness of these studies is the absence of fundus photography, fluorescein angiography, or autofluorescence

imaging data documenting structural changes before and after treatment. Additionally, the open-label design of the primary trial introduces potential observer bias, though the objective nature of ETDRS acuity measurement mitigates this concern. The control group in the pilot study (oxygenated blood) was methodologically suboptimal and would today be considered ethically questionable.

In the context of modern AMD management, several questions warrant investigation: Could ozonetherapy delay progression to GA in intermediate dry AMD, potentially reducing the need for complement inhibitor therapy? Might combination therapy with AREDS2 supplements and ozonetherapy provide synergistic benefits? Could biomarker-guided treatment (e.g., dROM/BAP monitoring) enable personalized dosing? These questions should be addressed in prospective trials incorporating multimodal imaging (OCT, OCT-A, fundus autofluorescence) and longer follow-up periods.

Conclusion

Age-related macular degeneration remains a major public health challenge in the aging population, with the global therapeutic market projected to reach $9.8 billion by 2033. The results of our combined studies provide evidence that major ozonated autohemotherapy can positively influence visual acuity in patients with high-risk dry AMD through mechanisms involving improved choroidal-retinal circulation, enhanced oxygen delivery, and potent upregulation of endogenous antioxidant defenses. The treatment is safe, well tolerated, and associated with minimal cost [1-44].

The treatments of dry AMD where complement inhibitors for GA require frequent intravitreal injections with significant treatment burden and risk profiles, and where photobiomodulation offers non-invasive intervention but with modest efficacy and device-dependent logistics ozonetherapy represents a distinctive approach. Its systemic, multimodal mechanism targeting oxidative stress, microcirculation, and mitochondrial function may be particularly valuable for patients with intermediate dry AMD, for those seeking to reduce treatment burden, or as an adjunctive strategy in comprehensive AMD management.

The observation that visual acuity improves more rapidly in patients with less advanced disease strongly supports early intervention to minimize photoreceptor death a principle now reinforced by the delayed visual benefits seen with complement inhibitors. While larger, controlled clinical trials incorporating modern imaging biomarkers are urgently warranted to confirm these findings and define optimal patient selection, the available data justify consideration of major ozonated autohemotherapy as a therapeutic option for dry AMD in clinical practice. The therapy may also warrant investigation in related retinal degenerative conditions including degenerative myopia, diabetic retinal vascular disorders, retinitis pigmentosa, recessive Stargardt disease, ischemic optic neuropathies, and glaucoma fields where international collaboration would be particularly valuable.

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