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Anti-Aging of Our Optic Nerve-Dream or Reality?

—Impact of Macrophage Activation and Resveratol on Optic Nerve Health

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Abstract

This paper presents findings on the potential of combining Selective Laser Trabeculoplasty (SLT) with Resveratrol supplementation to treat optic nerve degeneration in glaucoma patients. Glaucoma is a multifactorial disease where IOP-lowering therapies often fail to halt progression, especially in low-tension glaucoma cases. SLT activates macrophages, promoting cleaning of the trabecular meshwork, while Resveratrol enhances mitochondrial function, reduces oxidative stress, and supports optic nerve regeneration. Our results from over 12,000 patients show that this integrative approach improves optic nerve health, particularly in patients with normal IOP.

Keywords

Glaucoma, Optic Nerve, SLT, Resveratrol, Mitochondria, Autophagy, AMPK Pathway

1. Introduction

Glaucoma is a leading cause of irreversible blindness worldwide, affecting millions of individuals. Traditional therapies primarily focus on lowering intraocular pressure (IOP) to delay disease progression. However, many glaucoma patients, especially those with normal-tension glaucoma, continue to experience optic nerve damage despite normal IOP levels. This paper introduces a regenerative medicine approach (utilization of body's own cells to activate healing processes), combining Selective Laser Trabeculoplasty (SLT) and Resveratrol supplementation, to address the underlying causes of optic nerve degeneration. SLT activates macrophages and enhance phagocytosis and autophagy to clean the trabecular meshwork. Our goal was to protect healthy and regenerate the damaged nerve fibers. Resveratrol enhances mitochondrial health, reduces oxidative stress, and promotes regeneration of damaged nerve fibers.

Estimates of 60% - 80% of glaucoma patients may not benefit from traditional IOP-lowering treatments.

Instead, the focus must shift toward understanding and addressing other underlying factors, such as vascular dysregulation, oxidative stress and metabolic waste [1].

Our presentation is not a statistical work, nor is it a prospective or retrospective study. It highlights observations from our extensive patient database, demonstrating the significant impact of regenerative medicine mechanisms on the entire body.

2. Methods

2.1. SLT Procedure

Selective Laser Trabeculoplasty (SLT) is a non-invasive laser procedure that targets pigmented cells in the trabecular meshwork. SLT reduces IOP by enhancing the drainage of aqueous humor and lowering outflow resistance. More importantly, SLT activates macrophages to clean the trabecular meshwork, improving tissue function without causing damage to surrounding structures.

Pathways of SLT in trabecular meshwork

SLT laser effect | Development of macrophages

Macrophages at work (Courtesy of R. Peschke and S. Paulig) | "Cleaned" trabecular meshwork

In our study each patient underwent two SLT sessions per eye. A Neodymium-YAG laser with a wavelength of 532 nm and spot size of 400 micron was used. Each session targeted two quadrants with between 20 and 50 pulses, energy 0.2 - 2 mJ/Pulse, specifically focusing on melanin-containing cells in the trabecular meshwork.

2.2. Optical Coherence Tomography (OCT)

For our study we used OCT (Topcon 3D OCT-2000) to measure the thickness of retinal nerve fiber layers (RNFL) before (Baseline) and after Selective Laser

Trabeculoplasty. This follow ups were repeated yearly to monitor changes in RNFL thickness.

2.3. Resveratrol Supplementation

Resveratrol is a naturally occurring polyphenol that has gained recognition for its neuroprotective properties, particularly in ophthalmology. Known for enhancing mitochondrial biogenesis and energy production, Resveratrol helps to regenerate retinal ganglion cells and reduce oxidative stress. Patients in this study were administered 100 mg of Resveratrol daily. This supplementation was aimed at addressing mitochondrial dysfunction, stimulating macrophage activity and promoting the overall health of the optic nerve.

Resveratrol shows significant promise in supporting neural repair and cellular rejuvenation.

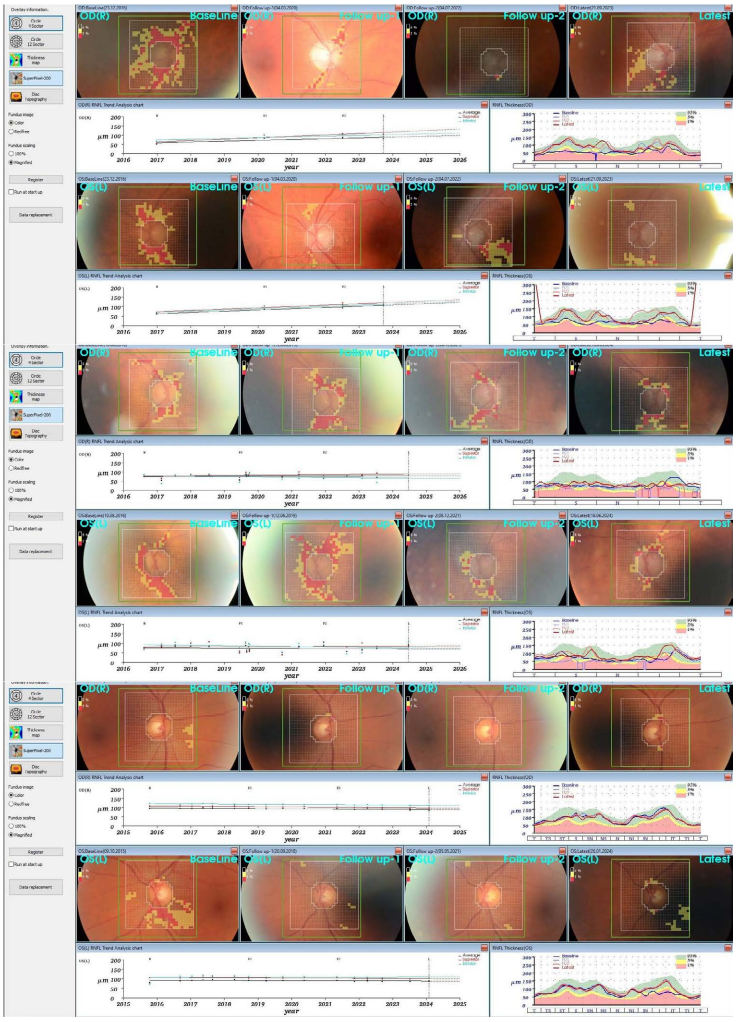
3. Results

Since 2007, we have been utilizing selective laser trabeculoplasty as part of our treatment approach and since 2012, we have incorporated Resveratrol supplementation.

Case Study 1

Case Study 2

Case Study 3



Over the years we have treated approximately 12,000 patients.

This extensive experience highlights the efficacy of SLT alongside the neuroprotective and regenerative properties of Resveratrol, offering a unique, interactive approach to patient care.

The intraocular pressure was either already well-controlled or consistently low due to the presence of low-tension glaucoma.

We observed an improvement in optic nerve fiber thickness reflectively transitioning from degeneration to regeneration of optic nerves in almost all cases.

3.1. Impact of SLT on Intraocular Pressure and Macrophage Activation

SLT effectively lowers intraocular pressure in patients by promoting the activation of macrophages, which are crucial in clearing the trabecular meshwork of cellular waste. Macrophages' ability to stimulate autophagy and remove metabolic waste contributes to better fluid outflow and lower IOP. In normal-tension glaucoma cases, where IOP is already low, SLT still promotes optic nerve regeneration by enhancing cellular cleanup.

3.2. Effect of Resveratrol on Mitochondrial Function

Resveratrol's role in improving mitochondrial function and reducing oxidative stress was evident in patients treated with this supplementation. Optical coherence tomography (OCT) scans revealed increased retinal nerve fiber layer (RNFL) thickness, indicating regeneration of the optic nerve. The neuroprotective effects of Resveratrol are linked to its ability to activate AMPK (adenosine monophosphate-activated protein kinase) and promote mitochondrial biogenesis, which is crucial in preventing further degeneration of optic nerve fibers.

4. Discussion

4.1. Macrophage Activation and Phagocytosis

SLT's activation of macrophages plays a pivotal role in cleaning metabolic waste from the trabecular meshwork. Macrophages perform autophagy by removing cellular waste and ensuring the trabecular meshwork functions efficiently. This process is vital in reducing IOP and promoting tissue health. Macrophages also facilitate optic nerve regeneration by clearing dead cells and promoting repair.

SLT targets pigment cells without causing thermal damage to adjunctive structures.

4.2. The Role of Mitochondria in Optic Nerve Health

Mitochondria play a central role in maintaining the health of retinal ganglion cells, as they generate the necessary energy for axonal function. Aging and oxidative stress lead to mitochondrial dysfunction, which is a key factor in neurodegenerative diseases like glaucoma [2].

Not only the lack of energy but unstabil delivery of oxygen damages optic nerves.

When mitochondria function poorly they trigger inflammatory responses, leading to various diseases, including neurodegenerative conditions.

Resveratrol's ability to enhance mitochondrial function, stimulate mitochondrial biogenesis and reduce oxidative stress is crucial in protecting the optic nerve. By activating AMPK, Resveratrol ensures the efficient clearance of damaged mitochondria and promotes the regeneration of optic nerve fibers.

4.3. Autophagy and Cellular Cleanup

Autophagy, the cellular process that recycles damaged organelles and proteins, is essential for maintaining optic nerve health [3]. SLT enhances autophagy by activating macrophages, which clean up the trabecular meshwork and reduce outflow resistance. Resveratrol further stimulates autophagy by activating the AMPK pathway, leading to improved cellular health and reduced oxidative stress.

4.4. AMPK and mTOR (Mammalian Target of Rapamycin) Pathways in Glaucoma Treatment

AMPK and mTOR pathways regulate cellular energy balance and are critical in controlling cell growth, repair and metabolism. AMPK is an energy sensor, activated when energy is low. There is an ability of AMPK to generate new mitochondria in aged organisms. The result is unstable oxygen delivery with hypoxia and oxidative stress with cells problems maintaining their biological activity.

So the trigger signal for AMPK is the absence of energy, leading to reduced biosynthetic pathways. Opponent mTOR is active when energy has a higher level and nutrients are available.

In glaucoma, imbalances between these pathways contribute to neurodegeneration. Resveratrol's activation of AMPK shifts the cellular environment toward energy conservation, autophagy, and repair, which is necessary for preventing optic nerve damage. The interplay between AMPK and mTOR is crucial in maintaining cellular homeostasis and preventing the progression of neurodegenerative diseases like glaucoma.

4.5. Combining SLT and Resveratrol: A Synergistic Approach

The combination of SLT and Resveratrol represents a comprehensive treatment for glaucoma by addressing both the mechanical and biological aspects of the disease. SLT lowers IOP and promotes macrophage activation, while Resveratrol enhances mitochondrial function and promotes nerve regeneration. Resveratrol mimics the effects of caloric restriction by activating similar biological pathways, associated with longevity and improved metabolic function. Like caloric restrictions, Resveratrol enhances mitochondrial function, reduces oxidative stress and promotes autophagy, all of which contributes to cellular health and longevity. This integrative approach not only halts the progression of optic nerve degeneration but also promotes the healing and regeneration of damaged tissues.

5. Conclusions

After performing over 12,000 SLT treatments and supplementing a significant percentage of patients with Resveratrol we have observed, that glaucoma is indeed a multifunctional condition.

Our findings underscore the complexity of glaucoma, highlighting that it involves a range of contributing factors beyond intraocular pressure, including neurodegenerative, vascular and cellular mechanisms.

The combination of SLT and Resveratrol offers a novel and effective approach to treating glaucoma, particularly for patients with normal-tension glaucoma. SLT activates macrophages to clear the trabecular meshwork, promoting better fluid drainage and reducing IOP. Resveratrol enhances mitochondrial function and promotes optic nerve regeneration through its antioxidant and neuroprotective properties. Together, these treatments address the underlying causes of optic nerve degeneration, providing long-term neuroprotection and improving patient outcomes.

SLT should not be limited for reducing intraocular pressure.

SLT with Resveratrol combined influences each other's effect in glaucoma treatment.

Future and further research should explore additional neuroprotective agents and lifestyle interventions that promote mitochondrial health (such as caloric restriction and exercise) and the use of autophagy enhancing agents to support optic nerve health. Ongoing work by researchers such as Professor David Sinclair Group at Harvard University may provide further insights into reversing aging processes and extending healthy lifespan.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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