

NEW HOPE AND CURE FOR GLAUCOMA TREATMENT

Although the tools for glaucoma care have become more sophisticated and advanced over the past two decades, the goal of cure is still beyond our reach, despite advanced technology and world-wide research. One of the problems lies, of course, that as with other medical problems where transplants have successfully restored an organ, the optic nerve, part of the brain, does not fall into this category. Nevertheless, the ophthalmological community has been hard at work assembling a medical tool kit that promises effective and less invasive care. As well, the pharmaceutical companies are constantly evaluating different substances in an effort to provide medications with greater efficacy and fewer side effects. Dr. Gustavo De Moraes, Research Associate Professor at New York University Medical Center and senior researcher at The New York Eye and Ear Infirmary and the research fellow Dr. Camilla Netto, on June 15 introduced some of the current research for glaucoma treatment. Dr. De Moraes has authored over seventy-five research papers and authored/co-authored seven book chapters.

The therapy today among practitioners consists of a number of strategies with focus, of course, on lowering the intraocular pressure with medication, laser, and incisional surgery, but also in protecting the optic nerve from the ravages of toxic compounds.

The pharmaceutical community continues to develop improved medications. There are a few in the pipeline that are now in trial and if these succeed in lowering the pressure sufficiently with a minimal of side effects, they will be introduced to the market. In the past few years we have witnessed a wider range of both laser treatments and incisional surgeries especially with minute-sized stents. Fortunately, these surgeries are minimally invasive, and, therefore, possess fewer side effects leading to quicker recovery periods. Newer forms of therapy using different sites in the eye offer better control, and, of course, the research on stem cell vision replacement continues unabated. Nanotechnology offers new release methods inside the eye for medication.

Among the new medications to lower the intraocular pressure, one of the recent studied is nitric oxide (NO) and other compounds that act synergistically with NO to keep the intraocular pressure low and stable . There is ongoing lab research on this substance that indicates it successfully increases the outflow of the aqueous humor (fluid inside the eye) to the drainage system. We don't have anything commercially available yet. Although the researchers have been able to demonstrate in animal models that outflow is increased, the study has not yet moved into human trials.

The star of the less invasive operations appears to be the iStent.



This infinitesimal unit creates a second pathway for the aqueous humor to seep from inside the eye to the outflow vessels thus lowering pressure. Studies indicate pressure lowering of about eight points after a year of follow up. This device is now available and may one day be an alternative to initial treatment of glaucoma.

Finally an alternative therapy for nerve protection is being seriously examined. The botanicals ginkgo biloba and Resveratrol are being studied. Ginkgo biloba, long used as a natural extract to increase blood flow is being examined by the researchers to increase blood flow and protect the optic nerve from the detrimental effects of oxidative stress. There is evidence that insufficient blood flow to the tiny vessels in the eye may be depriving the optic nerve of nutrients and leading to death of neurons in the eye (retinal ganglion cells). This is especially true of low- or normal-tension glaucoma, but may very well apply to other forms of open-angle glaucoma (OAG). Research currently underway reveals that loss of vision in normal-tension glaucoma in particular is due to both intraocular pressure and low blood flow. Although ginkgo biloba has been studied for its effects on memory and possibly slowing down Alzheimer's with varying results, its effects may be promising in the treatment of glaucoma according to Dr. De Moraes as numerous studies in animal models and humans have

demonstrated its protective effect. Blood flow is improved, especially the microcirculation in small capillaries, such as those in the optic nerve. As well ginkgo fights free radical damage and platelet aggregation (platelet clumping), and can, therefore, help increase the flow and slow the progression of the disease and visual field damage.

Resveratrol is being investigated in many labs for its effects on oxidative stress. As we age we become more susceptible to oxidative stress for we release oxygen that is injurious to the cell causing apoptosis (death of cells). Numerous studies have shown that anti-oxidative medications can slow down oxidative stress. There are currently hundreds of studies (in animals and humans) funded with millions of dollars and which have shown the benefits of Resveratrol in chronic diseases such as cancer, Alzheimer's, and glaucoma .

RISK FACTORS;

There are a group of people who have consistent low blood pressure. While this condition may be the envy of those people taking medication for high pressure, it can be detrimental to glaucoma patients. The researchers have been able to identify a relationship between glaucoma progression and some risk factors. During the nighttime hours, low blood pressure may worsen the glaucoma as it deprives the optic nerve of needed nutrients.

Maintaining the ideal blood pressure for people with normal-tension glaucoma may present a problem. Since the cardiologist is concerned with a low blood pressure to prevent strokes and heart disease, a contrary concern for ophthalmologists is to increase blood flow

during sleep time in patients suffering vision loss from lack of nutrients delivered to the eye. It, therefore, becomes important to have your ophthalmologist and cardiologist confer on the best strategy to maintain both vision and heart health. Most important is maintaining an adequate blood flow during nighttime when blood flow slows. Blood pressure medications taken in the evening may lower the blood pressure to the point where the optic nerve is not protected.

VISION RESTORATION: And the last thing and the most difficult part of the research currently underway is to try to restore vision. Retinal cells are an extension of the brain cells. These cells cannot restore by themselves. Neurological tissue cannot heal. This is where stem cells can be used to replace neurological cells or to repair damaged cells.

In the meantime, for those people who are not 100% blind, who still retain a part of their retina with healthy cells, strategies are being investigated to activate this residual vision. It's like a workout. With electrodes and exercise, it may be possible to increase and strengthen the remaining cells to compensate the damaged area.

An experiment conducted with mice demonstrated this possibility. A blind mouse received the device and it was evident that the mouse could see. The vision is not perfect but it is better than no vision. For other eye diseases such as retinitis pigmentosa, several

patients have achieved some vision using electrodes. It's not as perfect as it was but much better than not seeing.

Stem cells. As you are no doubt aware, stem cells are pluri-potential – that means they can develop into any kind of cell. One of the problems in outflow of fluid is clogging of the trabecular meshwork. Replacing damaged cells with stem cells in the trabecular meshwork may well increase the outflow and thus lower the pressure.

Within several years it may be possible to harvest stem cells from one's own blood cells. This method appears to be superior to harvesting stem cells from the skin, liver or other tissues.

This, of course, is the ultimate goal for those who have lost a major portion of their sight. Researchers are trying to develop and differentiate the stem cells into retina cells to restore the sight lost due to glaucoma but this research still needs several years before results are clearly defined. Animal research indicates progress, but it is difficult to overcome the protocols established by the Food and Drug Administration (FDA). The problem remains of providing the FDA with sufficient documentation to satisfy the requirements of safety and effectiveness and move onto to clinical trials in human beings. Then, of course, funding, most likely from National Institutes of Health (NIH) will be necessary to conduct wide-ranging clinical trials

Nanotechnology: At this stage of the art the nanotechnology research has focused on providing a device that can be inserted into the eye loaded with medication that will release the medication over a period of months. This technology will eliminate the need for daily instillation of eye drops and provide the exact amount of medication needed to maintain a steady eye pressure and minimize one of the main challenges in glaucoma: adherence. The steady supply of medication will act against pressure spikes, known to be damaging to the cells. Devices already exist to treat macular degeneration and minimally invasive surgery. Delivery of medications to the right target with precise concentration will soon be commercially available and help improve pressure lowering and minimize the side-effects.

Transorbital alternating current stimulation is a potential method to restore sight. This technology is not yet available in the United States, but it does exist in Germany. This technique consists of placing electrodes on the forehead and skin around the eye (orbits) that transmit electric impulses which may “boost” retinal ganglion cells and neurons in the visual pathway to re-establish function.

Artificial vision. A light sensor connected to an array of electrodes has already been introduced into the eyes of blind people allowing them to see shapes. This technology is moving apace. However, it does require

implantation of the device inside the eye and connect to the optic nerve and has been reserved to cases of severe blindness.

Electrodes are used to simulate the cells. In a display projected on the screen, it was possible to see that the blind spots responded to stimulation with electrodes by providing a wider field allowing better vision. Two kinds of electrodes are being explored: tiny small manual electrodes that are placed inside the eye during retinal surgery and those placed outside the eye. The purpose is to stimulate the cells to greater activity to compensate for their decreased function due to glaucoma.

The brain can also be stimulated because the retinal cells are connected to the brain. The area of stimulation is in the back of the head where the visual center exists in the brain. Some of you may have experienced this process in an alternative form of visual field test. With electrical stimulation, you don't have to do a thing but look at the screen. The stimulation tells the researcher what part of the brain is working. The researchers have found that the modification of this method allows the stimulation of the parts of the visual cortex which despite being "sick" are still alive and working.

The research in this area is gaining speed. It has moved from science fiction to reality. The problem is that while research in animals in the laboratory often indicates positive results, the researchers must close the gap between the research and clinical practice,

the so-called translational research. As stated previously, this can only be bridged with FDA approval of protocols developed in the laboratory, for safety measures must be met before the trials migrate to the human population

If you wish to supplement with Resveratrol, Dr. Netto suggested 300 to 500 milligrams. However, she advised caution with ginkgo biloba because of its blood thinning properties. Always remember to talk to your primary care doctor or cardiologist.

We want to thank Dr. De MoRaes for providing the material for this valuable workshop and Dr. Netto for delivering the research so effectively. The Group was able to get an inkling of the ongoing research, its goals, victories and future application. This information is indeed deeply appreciated.

Please note: The contents of this newsletter are for informational purposes only. The content is not intended to be a substitute for professional medical advice, diagnosis or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition.

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