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Review Article

Recent Advances in Management of Macular Degeneration

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Abstract

In old age quality of life further deteoriate because of macular degeneration (AMD). Bothe the types dry or wet creates vision problems however dry type is not as bad as wet. The earlier management methods for AMD were combersome, the advanced methods such as, gene therapy, artificial retina involving genetic engeneering technology, using optical or laser swiches to exite neurons (optogenetics) and advanced biological techniques such as transplanting stem cells has better scope for management of macular degeneration.

INTRODUCTION

The eye's macula is located in the center of the retina, in a way it is part of the retina at the back of the eye and is responsible for providing the sharp, central vision we need for reading, driving, and seeing fine detail. It is the functional center of the retina. It is only about 5 mm. across but is responsible for our central vision, most of our colour vision and the fine detail of what we see (Figure 1).The retina is a layer of light sensitive cells that prompt nerve impulses, which are sent to the optic nerve, then travel to the brain, where images are formed.

If there is damage near the macula, the patient could notice various visual effects such as general poor vision, distortion of images such as straight lines appearing wavy, blurry spots in one's central vision, and/or vision with images appearing and disappearing.

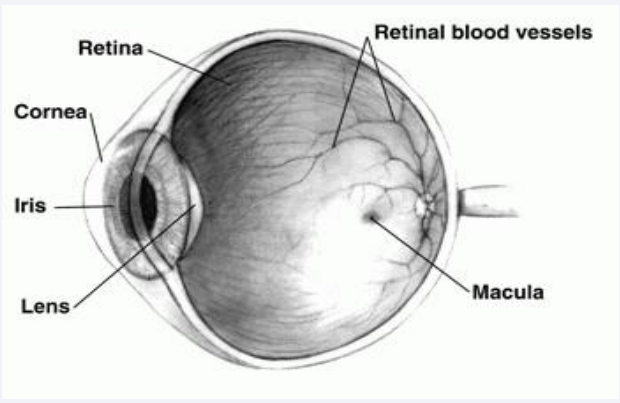

Figure 1 Position of macula.

Age-related macular degeneration (AMD), is an eye disease that affects a person's central vision that over time may get worse [1]. AMD can result in severe loss of central vision, but people rarely go blind from it and causes loss in the centre of the field of vision. In the early stages, a macular hole can cause blurred and distorted vision. Straight lines may look wavy or bowed, and may have trouble reading small print. After a while, the patient may see a small black patch or a "missing patch" in the centre of vision. Eventually, it may be the cause of severe, permanent vision loss in some people over age 60. Another form of macular degeneration, called Stargardt disease or juvenile macular degeneration, affects children and young adults [2]. Early onset macular degeneration (birth to age 7), is a genetic disease, as is middle-onset macular degeneration (age 5 to 20). People in their thirties or forties can develop a form of the disease that is also inherited. Not everyone with early AMD will develop advanced AMD, and those who develop an advanced form of the disease do not develop total blindness. However, the loss of central vision can significantly interfere with everyday activities, such as driving or reading. Besides age, certain lifestyle habits or epigenetic factors, such as, smoking, having high blood pressure or high cholesterol, obesity, eating lots of saturated fat, being light-skinned, being female, and having a light eye color are also risk factors for developing AMD. In addition to lifestyle or epigenetic factors some genes also play a role [3].

WET VS. DRY MACULAR DEGENERATION

There are two main types of age-related macular degeneration. In dry macular degeneration, the centre of the retina deteriorates. With wet macular degeneration, leaky blood vessels grow under the retina and hinders the vision. Wet macular degeneration is more serious and is the leading cause of permanent central vision

loss [4].

Dry form: People with this may have yellow deposits, called drusen, in their macula [5]. A few small drusen may not cause changes in vision. But as they get bigger and more numerous, they might dim or distort the vision, especially reading. As the condition gets worse, the light-sensitive cells in the macula get thinner and eventually die. In the atrophic form, the patient may have blind spots in the center of vision.

Blood vessels grow from underneath the wet type macula. These blood vessels leak blood and fluid into the retina. Therefore vision is distorted so that straight lines look wavy. One may also have blind spots and loss of central vision [5]. These blood vessels and their bleeding eventually form a scar, leading to permanent loss of central vision. In many patients the dry form can lead to the wet form. Wet macular degeneration accounts for approximately 10 percent of cases, but results in 90 percent of legal blindness.

MANAGEMENT OF MACULAR DEGENERATION

It is unfortunate that there's no cure for macular degeneration, though vision rehabilitation programs and low-vision devices can be used to build visual skills, develop new ways to perform daily living activities and adjust to living with age-related macular degeneration. Treatment may slow it down or keep the patient from losing too much of vision. Options are limited and patients not fully recovered.

Currently, the most common and effective clinical treatment for wet Age-related Macular Degeneration is Anti-angiogenesis drugs like anti-VEGF which is periodic intravitreal (into the eye) injection of a chemical called an "anti-VEGF." In the normal life of the human body, VEGF is a healthy molecule which supports the growth of new blood can block the creation of blood vessels and leaking from the vessels in the eye that cause wet macular degeneration. Many people who've taken these drugs have lost vision and have partially recovered.

Eye Drops

Anti-VEGF eye drops for wet AMD is another new treatment modality for AMD that is in the initial stages of clinical trial—but hasn't yet been used on humans. The treatment has been tested on animals. Once the medicated eye drops are considered safe enough for human use, clinical trials will begin. It may take more than 10 years (around the year 2030), for anti-VEGF eye drops for wet AMD to be available for consumer use [6].

Oral Tablets

An anti-VEGF pill, to be taken orally may be available to the public in the next five years (approximately 2025). The pill form of the medication will enable people with wet AMD to eliminate or reduce the frequency of anti-VEGF injections. Now in the phase II stage of clinical research trials, developers of oral medication for wet AMD are trying to work out the bugs. The medication has many side effects right now, such as nausea, leg cramps and liver changes. Once the medication can be considered safe, and dangerous side effects can be eliminated, it can be considered for consumer consumption [7].

Longer-Lasting Anti-VEGF Injections

Several new anti-VEGF medications—aimed at reducing the frequency of injections—are being developed by the drug industry. These include drugs such as Abicipar, and Sunitinab, which are estimated at around three to five years (in the year 2023 to 2025) before approval for consumer use [8].

Another new drug, Beovu has already been approved for use in the U.S. Beovu injections can last as long as three months and the innovative medication is said to be more effective at drying fluid that has accumulated in the retina due to wet AMD [9].

Laser therapy

High-energy laser light can destroy abnormal blood vessels growing in the eye.In photodynamic laser therapy. The doctor injects a light-sensitive drug -- verteporfin (Visudyne) -- into the bloodstream, and it's absorbed by the abnormal blood vessels and then the laser treatment is given. This triggers the medication to damage those newly formed blood vessels [10].

Low vision aids

These are devices that have special lenses or electronic systems to create larger images of nearby things. They help people who have vision loss from macular degeneration make the most of their remaining vision.

NEWER APPROACHES (GENETIC ENGINEERING)

Due to recent technological advancements AMD is managed better than before.

Retinal Gene Therapy

One promising new treatment, for wet AMD, involves retinal gene therapy, as an alternative to monthly eye injections. The goal of gene therapy is to employ the body to make its own anti-VEGF by inserting a harmless virus (called an adeno-associated virus/AAV), carrying the anti-VEGF gene into a person's DNA.

More specifically, RGX-314 gene therapy only requires one injection, but it must be performed via a surgical procedure. This treatment is currently getting ready to enter phase II of clinical research trials. Now that retinal gene therapy has been approved by the FDA for other retinal eye conditions (other than AMD), this type of treatment looks very promising for people with AMD. RGX-314 could potentially work to block VEGF for years after it is administered; this, in turn, would help to inhibit the development of the symptoms of wet AMD, namely, the immature blood vessels that leak blood into the retina [11].

The Port Delivery System (PDS)

The Port Delivery System (PDS), is a very small apparatus that can store anti-VEGF medication. The PDS is implanted into the eye during a surgical procedure; it functions to provide a continuous release of anti-VEFG medication into the eye. The Port Delivery System could allow people with wet AMD to avoid eye injections altogether. The procedure enables people with wet AMD to go up to two years without needing a treatment. Refilling the medication can be done via a doctor's office visit. But, the procedure to refill the medication is a bit more complex than the

anti-VEGF injections that are currently the standard treatment for wet AMD.

This innovative treatment is now in phase three clinical trials and could possibly be available for consumer use within the next three years (around the year 2023).

Optogenetics

A technique that uses a combination of light and genetic engineering to control the activity of excitable cells, such as neurons, Activity of neurons can be controlled at will by light. This has already been approved for its first clinical trials in humans [12]. The first application of optogenetics in a human disease model was in 2016 [13].

To do this, cells are genetically engineered to produce ion channels called opsins that sit in the cells' membranes and open in response to a certain wavelength of light [14]. Optogenetics is still in its early stages in human disease models. "Optogenetics" a kind of gene therapy that delivers light-sensing molecules (Opsins) into the eye [15]. Opsins generate an electrical signal when they are exposed to a particular wavelength of light. Proteins that respond to a specific type of light (for example, ChR2 only responds to blue light). As an alternative to retinal prosthesis, optogenetics can be used to restore vision by expressing optical neuromodulators such as channel rhodopsins or photochemically modified mammalian ion channels in residual retinal neurons [16].

In healthy eyes, cells called photoreceptors react to light by sending electrical signals to another type of cell, called ganglion cells. Photoreceptors in normal retinas respond to a broad spectrum of light wavelengths spanning the rainbow of visible colors [17]. The opsin that GenSight used only responds to light in the dark orange/red part of the spectrum. The special goggles take in the visual field and translate that into amber points light that could trigger the opsin in the patient's ganglion cells, and send a signal to the brain [18]. Optogenetic therapy could be used for diseases involving photoreceptor degeneration, such as retinitis pigmentosa or age-related macular degeneration. Clinical trials results obtained so far lay the groundwork for the ongoing clinical trial with the AAV2.7m8 - ChR-tdT vector for vision restoration in patients with retinitis pigmentosa [19]. The field of optogenetics has been rapidly expanding in efforts to restore visual function [20].

Although optogenetics has drawn closer to clinical utility, advances in opsin engineering, therapeutic targeting and ultimately in molecular inhibition of remodeling will play critical roles in the continued clinical advancement of optogenetic therapy [21].

Stem Cell Therapies

Stem cell therapy is gaining momentum for all types of treatment today, including many forms of cancer, as well as for dry AMD. The goal of stem cell therapy for AMD is that the new stem cells will be able to replace retinal cells that have been damaged or destroyed by symptoms of AMD.

Stem cells are often introduced into the body's blood circulation, via IV infusion. But, researchers are working on how to transplant the stem cells directly into the eyes. One strategy involves placing the stem cells into a fluid suspension that can be injected under the retina [22].

Although stem cell therapy for AMD has only been studied in small clinical trials, the experts say this treatment regime shows great promise.4 The drawback is that it may take another 10 to 15 years (around the year 2030 or 2035) for stem cell therapy to be proven effective and safe for consumers.

A small study, involving people with wet AMD, published by the New England Journal of Medicine, found that using a person's own stem cells to replace damaged retinal cells, resulted in maintaining visual acuity for one year after the procedure. The study authors wrote, "This seems to indicate the surgery helped to halt the progression of the disease."9 Although this study does not indicate that stem cell therapy is effective for dry AMD, many scientists are confident that upcoming studies on stem cell therapy for dry AMD will be promising.

4. Submacular surgery. This removes abnormal blood vessels or blood and translocates the retina.

5. Macular Degeneration Prevention A large study found that some people with dry AMD could slow the disease by taking supplements of vitamins C and E, lutein, zeaxanthin, zinc, and copper.

In conclusion, there is no single treatment that exists that does not have drawbacks. Some emerging treatments may be found to have very few side-effects, but the patient selection criteria (the criteria used to qualify as a study participant) may be very strict (such as for surgically implantable telescope lenses). Other treatments/medications can have side effects.

REFERENCES

1. Mehta S. Age-Related Macular Degeneration". Primary Care. 2015; 42: 377-391.
2. Tanna P, Strauss RW, Fujinami K. Stargardt disease: clinical features, molecular genetics, animal models and therapeutic options. British J Ophthalmol. 2017; 101: 25-30.
3. Armstrong RA, Mousavi M. Overview of Risk Factors for Age-Related Macular Degeneration (AMD). J Stem Cells. 2015; 10: 171-191.
4. Lylas G. Mogk The Difference Between Wet and Dry Age-Related Macular Degeneration.
5. Mullins RF, Russell SR, Anderson DH, Hageman GS. "Drusen associated with aging and age-related macular degeneration contain proteins common to extracellular deposits associated with atherosclerosis, elastosis, amyloidosis, and dense deposit disease". FASEB J. 200; 14: 835-846.
6. PanOptica: Anti-VEGF Eye Drop Shows Promise in Treatment of Wet.
7. Yorston D. Anti-VEGF drugs in the prevention of blindness. Community Eye Health. 2014; 27: 44-46.
8. Moisseiev E, Loewenstein A. Abicipar pegol-a novel anti-VEGF therapy with a long duration of action. Eye. 2020; 34: 605-606.
9. Robert Steinbrook. The Price of Sight-Ranibizumab, Bevacizumab, and the Treatment of Macular Degeneration. N Engl J Med. 2006; 355: 1409-1412.
10. Figueroa M, Schocket LS, DuPont J, Metelitsina TI, Grunwald JE. Effect of laser treatment for dry age related macular degeneration on

foveolar choroidal haemodynamics. Br J Ophthalmol. 2004; 88: 792-795.

11. Shannon E Boye, Sanford L Boye, Lewin AS, Hauswirth WW. A Comprehensive Review of Retinal Gene Therapy, Molecular Therapy. 2013; 21: 509-519.

12. Gupta PD. Blind can "See" through Optogenetics Technology. J Experimental and Clinical Ophthalmol. 2021; 1.

13. Boyden ES, Zhang F, Bamberg E, Nagel G, Deisseroth K. Millisecond-timescale, genetically targeted optical control of neural activity. Nat Neurosci. 2005; 8: 1263-1268.

14. Ferenczi, Emily A. Tan Xiaoqiu and Huang Christopher LH. Principles of Optogenetic Methods and Their Application to Cardiac Experimental Systems Front. Physiol. 2019; 11.

15. Yonatan Katz, Michael Sokoletsky, Ilan Lampl. In-vivo optogenetics and pharmacology in deep intracellular recordings. J Neurosci Methods. 2019; 325.

16. Simon CJ, Sahel JA, Duebel J, Herlitze S, Dalkara D. Opsins for vision restoration. Biochem Biophys Res Commun. 2020; 527: 325-330.

17. Chaurasia SS, Gupta PD. Cryptochromes: The novel circadian photoreceptors. Current Sci. 1999; 77: 632.

18. Sahel JA, Boulanger-Scemama E, Pagot C, Arleo A, Galluppi F, Martel JN, et al. Partial recovery of visual function in a blind patient after optogenetic therapy. Nat Med. 2021.

19. Gauvain G, Akolkar H, Chaffiol A, Arcizet F, Khoei MA, Desrosiers M, et al. Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Commun Biol. 2021; 4: 125.

20. Henriksen BS, Marc RE, Bernstein PS. Optogenetics for retinal disorders. J Ophthalmic Vis Res. 2014; 9: 374-382.

21. David Hutton. Optogenetic methods restore partial vision in blind patient. 2021.

22. O'Neill HC, Limnios IJ, Barnett NL. Advancing a Stem Cell Therapy for Age-Related Macular Degeneration. Curr Stem Cell Res Ther. 2020; 15: 89-97.

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