Original Article

Use of Nanotechnology in Ophthalmology

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ABSTRACT

Nanotechnology is an emerging concept which soon will be an epitome in the field of science and technology. It uses molecules in the order of nanometers to penetrate and has proven its mettle in space, medicine and various avenues of science. Various aspects of treatment and diagnosis in ophthalmology are expected to benefit from this technology in the near future. Nanotechnology will not only revolutionize our approach to current therapeutic challenges, but also enable us to address currently unsolvable problems.

Keywords: Nanotechnology, Implantable materials, Nanoceria, Trigger-fish contact lens, Vitrasert, Illuvien, I-vation.

INTRODUCTION

Nanotechnology involves creation and use of materials and devices at the size scale of intracellular structures and molecules and involves systems and constructed in the order of <100 nm. [1] To put that into perspective, a human hair is 10,000 nm to 20,000 nm in diameter, an erythrocyte is 7,000 nm wide, [1,2] a DNA strand is of the order of 2 nm in diameter and most proteins of the soils around 10nm, hence, nanotechnology exists in nature. Other naturally occurring nanomotors include kinesin and actin, which are both essential for muscle movement.[3] Still for better understanding, comparing nanometer to a meter is like marble to earth. Research and the eventual application of this budding technology needs to be shared among many areas of science. In health care, the twigs of nanotechnology are being targeted at presymptomatic diagnosis and management, which ought to modify and broaden our perspective and outlook regarding various yet unsolvable medical queries. [3]

DISCUSSION

Nanotechnology aims at "comprehensive monitoring, control, construction, repair, defense and improvement of human biological systems at the molecular level". The eye is uniquely suitable as a target for nanotechnology in the form of Biopharmaceuticals (drug delivery), implantable materials (tissue regeneration scaffolds, bioresorbable materials), implantable devices (IOP monitors, glaucoma drainage valves), and diagnostic tools (genetic testing, imaging, IOP monitoring). Nanotechnology also aims at development of regenerative medicine (replacement and improvement of cells, tissues and organs), ultrahigh resolution in vivo imaging, microsensors and feedback

devices, and artificial vision."[4] With its aid, earlier and more sensitive presymptomatic diagnosis can be made and treatment of the disease can be initiated before permanent damage to the tissues and organs sets in.

The eye is a small organ and can be easily accessed due to its exposed position, and hence, is uniquely suitable as a target for nanotechnology. Potential applications of nanomedicine in ophthalmology include "procedures, such as corneal endothelial cell transplantation, single retinal ganglion cell repair, check of retinal ganglion cell viability, building of nanofibre scaffolds, such as self assembling peptides, to create a scaffold like tissue bridging structure, to provide a framework for axonal regeneration in the case of optic nerve reconnection or eye transplantation, and ocular drug delivery." Arrestive therapies with regenerative medicine in near future will target at gene related treatment modalities to inhibit intraocular neovascularization and to block retinal cell apoptosis.[5]

Nanomaterials have a high surface to volume ratio. Anterior segment uses of nanoparticles (nanoceria particles with a "diameter of 5nm", containing cerium oxide) can utilize this attribute and hence prove beneficial in reducing or eliminating reactive oxygen species, which are otherwise established as a cause of cataracts and myriad ocular diseases. The configuration of nanoceria particles having an ample surface area to volume ratio allows them to regenerate their function as scavengers of free radicals without repetitive dosing. Future application of intravitreal nanoceria particles could be used to retard progression of "macular degeneration" and diabetic retinopathy, which are emerging as one of the "leading causes of blindness in developing nations".[6,7]

"Fluctuation of IOP is a characteristic of glaucoma", and 'ability to continuously monitor IOP" would be a valuable asset in its management, for which a disposable contact lens with an embedded sensor (CLS), also known as trigger fish, has recently been developed by Matteo Leonardi and colleagues in Switzerland. It takes readings by measuring "alterations in corneal curvature" produced by "changes in IOP". A study showed that this 175nm sized sensor made of platinum-titanium strain gauge, was sensitive enough to record a meager fluctuation of 0.2mmHg.[8]

Nanotechnology is being explored as a "means of drug delivery" – not only for systemic medications, but also for ocular applications as many of the conditions affecting the eye are treatable through ocular surface or vasculature, where conventional delivery systems prove suboptimal because of factors affecting tear dynamics, corneal impermeability to many medications, and the influence of ocular surface health on drug absorption. The cornea contains both lipophilic and hydrophilic structures and typically less than 5% of the installed drug penetrates cornea. Nanomedicines offer promise as viable alternatives to conventional drops, gels or ointments to improve drug delivery to the eye. Nanoparticles can be designed to improve penetration, controlled release and drug targeting, when used in the form of liposomes, micro/nanospheres, micro-emulsions, and dendrimers.

Treatment of blinding diseases of the eye, such as proliferative retinopathy or macular degeneration, requires effective and safe delivery of drugs to posterior eye segment tissues and here lies the importance of effective drug delivery modalities to the posterior segment of the eye compared to conventional surface delivery.

"The eye is a model organ for the local delivery of therapeutics" especially when "treating vitreous inflammation and other ophthalmic pathologies". Owing to "chronicity of certain diseases", treatment

schedules include frequent visits and in turn multiple dosing, which itself can be a cause of iatrogenic infections and toxicity to the patient. "Implantable devices and particulate drug delivery systems" which are "currently being implemented and investigated to overcome these challenges", include non biodegradable polymers, containing "ganciclovir, flucinolone acetonide, triamcinolone acetonide, and ranibizumab, and biodegradable polymers containing dexamethasone, triamcinolone acetonide and ranibizumab".[9]

Vitrasert (containing ganciclovir), the 1st implantable device in the posterior chamber of the eye, was composed of a non-biodegradable polymer, and was used to treat AIDS related CMV retinitis. Complications associated with these devices include "retinal detachment, vitreous hemorrhage, epiretinal membrane formation, dissolution of the implant". [10]

PVA device containing 5-FU is being placed subconjunctivally to prevent post op scarring following glaucoma filtration surgery. Retisert tablet containing flucinolone acetonide, became the 1st FDA approved device for use in the treatment of "non-infectious posterior uveitis". Studies have also shown it to be effective in "macular oedema due to diabetes and CRVO".[10]

"Illuvien/madidur implant containing fluocinolone acetonide (190 mcg), coated with PVA", underwent "FAME Trial" and results indicated that although cataract and raised IOP were the associated complications, but despite all it was found effective in DME, and is currently waiting FDA approval for it.[10]

I-Vation, "a helical sustained-release", 0.925mcg triamcinolone acetonide containing implant "coated in titanium, PVA, and EVA", is capable of eluting drug for 2 years. Available phase 1 clinical trial results showed its "effectiveness in treating DME", measured by reduction in macular thickness on OCT and improved visual acuity. Major complications included raised IOP and cataract development.[10]

A novel "port delivery system with ranibizumab designed to release 10mg/ml" over an ample period of time is currently being investigated in neovascular age-related macular degeneration.[10]

CONCLUSION

Hence, it seems the "emergence of nanomedicines has arisen great hopes for ophthalmic pharmacotherapy, in which nanostructured medicines are expected to cross the restrictive barriers of the eye. Although such fast inauguration of ocular nanomedicines will literally convey new challenges in the regulatory and translational processes", it will also grant a "prolific platform from which many exciting, and yet unimagined, applications of biomedical nanotechnology will emerge for pharmacotherapy of the eye".[11] Despite many leaps and bounds shown by this novel technology, obstacles to the incorporation of nanotechnology still remain, such as safe manufacturing techniques and unintended biological consequences of nanomaterial use, but with a bright ray of hope that they are not insurmountable, and revolutionary treatments for ophthalmic diseases are expected to result from this burgeoning field.

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