

Therapeutic Avenues in Ophthalmology- What is New?

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Abstract

Progress in ophthalmology, specifically in ocular pharmacotherapy is accompanied not only by discovering the new therapeutic agents, but also by renewed interest to old drugs, thus representing therapeutic renaissance. Advances over the past decade in drug discovery technologies have not yet led to an increase in productivity. It is a long and costly way to launch a new drug uninsured from failures, which indicates a need for cost-effective search of new directions in pharmacotherapy and generates an interest to comprehensive research of old medicines rediscovering them to underscore the new therapeutic targets, highlighting a purpose of undertaken review.

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Progress in ophthalmology, specifically in ocular pharmacotherapy is accompanied not only by discovering the new therapeutic agents, but also by renewed interest to old drugs, thus representing therapeutic renaissance. Advances over the past decade in drug discovery technologies have not yet led to an increase in productivity. It is a long and costly way to launch a new drug uninsured from failures [1], which indicates a need for cost-effective search of new directions in pharmacotherapy and generates an interest to comprehensive research of "old" medicines rediscovering them to underscore the new therapeutic targets, highlighting a priority of this strategy [2] encouraged by FDA [3].

Taken into account current economical burden worldwide, the well-known drugs are repurposed, based on the fact that any drug acts on cellular level, universally targeting different tissues and organs. Repurposing of well-known drugs is directed to discover new indications, thus expanding therapeutic horizons.

Atropine

Atropine is a well-known widely used cycloplegic and mydriatic, but recently it was revealed it's therapeutic impact in myopia demonstrated in clinical trials, despite currently undiscovered mechanism of action. Atropine now is considered as a most potent drug to control the progression of myopia in children, with strong supporting evidence from well-conducted clinical trials. Atropine targeting different intraocular structures for managing myopia will become the standard of care in most parts of the world [4]. This approach will soon become available in the United States.

Anti-vascular endothelial growth factors

From the development of therapy with anti-angiogenics or vascular endothelial growth factor inhibitors (anti-VEGF) starts a new

era in medical ophthalmology. It takes approximately 20 years before these agents come into scene. Currently, there are FDA approved: pegaptanib (Macugen, Pfizer), ranibizumab (Lucentis, Novartis), aflibercept or VEGF Trap-Eye (EYLEA, Bayer) and in common off-label use bevacizumab (Avastin, Roche) [5].

The general use of an approved medication for a new indication recognized by the medical community but not specifically indicated by a regulatory agency (FDA) is referred to as off-label use. Once the FDA approves a drug, ophthalmologists may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient.

Bevacizumab (Avastin, Roche)), represents non-selective recombinant humanized monoclonal antibody, neutralizing all isoforms of VEGF and inhibiting proliferation of endothelial cells [6]. The drug was approved by FDA only for colorectal cancer therapy, but gained a huge popularity among ophthalmologists incorporating it, as an off-label use, for therapy of several retinal diseases related to angiogenesis, such as neovascular macular degeneration, proliferative diabetic retinopathy, diabetic macular edema, retinal vein occlusion by intravitreal injections. Aforementioned is connected to significantly low cost of bevacizumab comparing ranibizumab. Recently a therapeutic horizons of bevacizumab in ophthalmology have been expanded, specifically, in pterygium and orbital vascular lesions.

Management of pterygium poses challenge taken into account a high recurrence rate. Scientific understanding of pterygium continues to develop, and recent changes have been made to how VEGF is involved in the process of fibrovascular tissue formation, which underscores the importance of anti-VEGF agents incorporation, specifically bevacizumab as a most affordable, in the treatment protocol. The general consensus is that bevacizumab offers a potential to slow down recurrences of pterygium after its surgical excision.

The latest study conducted by Atchison., *et al.* [7] explored new target for antiangiogenic therapy - orbital vascular lesions. Most benign vascular lesions of the orbit express vascular endothelial growth factor receptors (VEGFRs), therefore inhibition of angiogenesis is believed to offer effective non-surgical intervention, taken into account that they have a dislocating space-occupational effect from one hand, and from the other hand an excisional surgery represents a challenge. Researchers reported successful intravitreal anti-VEGF injection in a small series of patients with periocular epithelioid hemangioma.

Carbonic Anhydrase Inhibitors

Carbonic anhydrase inhibitors (CAI) are well-known and widely used ocular hypotensive medications in topical formulation in glaucoma, chemically structured as a sulfonamide derivatives [6]. Recently discovered new -antiedematous effect of CAI is realized by increasing the fluid hydrodynamics through retinal pigment epithelium (RPE) and pump function due to acidification of the subretinal space thus controlling and adjusting the extracellular pH gradients produced by the metabolic activity of cells and at the same time by suppression of the inflammatory process underlying the vascular and RPE leakage causing the cystoid macular edema (CME) [8].

CAI drops alone have been shown to reduce macular edema in choroideremia [9]. More recently they were included in a treatment regimen for Vogt-Koyanagi-Harada disease [10] and recommended for retinitis pigmentosa [11], syndromic retinal dystrophies such as Alström syndrome [12], and also for CME after cataract extraction [13].

Antibiotics -Tetracyclines

Tetracyclines are bacteriostatic antibiotics with a broad coverage of gram negative and gram-positive organisms [6]. Doxycycline and minocycline are commonly used in medicine semisynthetic antibiotics.

Tetracycline class with closely similar antimicrobial spectrum, and currently discovered concomitant anti-inflammatory effect, which evidenced their use for inflammatory ocular surface and eyelid disease. Specifically, these medications can at the same time not only de-

crease lid bacterial flora, but also improve meibomian gland function, reducing a cause of meibomian lipid breakdown. Accumulated evidences suggest that low-dose oral tetracyclines are effective in meibomian gland dysfunction (MGD) and blepharitis management [14,15].

Recently, it was underscored that there are potentially multiple biological bases for the protective effect of minocycline in eye diseases beyond anterior segment. The rationale for using minocycline in such retinal diseases as retinitis pigmentosa, glaucoma, retinal vein occlusion, age-related macular degeneration and diabetic retinopathy is that it has neuroprotective, anti-inflammatory and antioxidative effects [16]. Currently, there is growing evidence of the effectiveness of minocycline pharmacotherapy and hopefully soon we shall meet it as a universal ophthalmic drug. This therapeutic modality offers promising option for the retinal therapeutic landscape.

Omega- 3

Omega-3 polyunsaturated fatty acids (Omega-3-Acid Ethyl Esters) are found in oils from certain types of fish, vegetables, and other plant sources and are indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe hypertriglyceridemia [6]. Recent findings from meta-analysis based on seven randomised controlled studies indicated that omega-3 supplementation improves tear film properties [17]. While the mechanism is yet unexplained, improvements in patients with evaporative dry eye from MGD or contact lens wear have been observed following supplementation [18].

In summary, currently available findings highlight that during the next decade, pharmacotherapy in ophthalmology will experience a remarkable renaissance as well-known repurposed drugs become integrated with novel therapeutic approaches, and thus underscoring the new potential to improve the outcome of our patients.

Conclusion

Taken into account current economical burden worldwide, the well-known drugs are repurposed, based on the fact that any drug acts on cellular level, universally targeting different tissues and organs. Repurposing of well-known drugs directed to discover new indications, thus expanding therapeutic horizons is a viable approach, which can be key for “unlocking” a management of challenging eye diseases.

Bibliography

1. Tobinick EL. “The value of drug repositioning in the current pharmaceutical market”. *Drug News and Perspectives* 22.2 (2009): 119-125.
2. Ferrari R and Lüscher TF. “Reincarnated Medicines. Using Out-Dated Drugs for Novel Indications”. *European Heart Journal* 37.33 (2016): 2571-2576.
3. Huang R, *et al.* “The NCGC pharmaceutical collection: a comprehensive resource of clinically approved drugs enabling repurposing and chemical genomics”. *Science Translational Medicine* 3.80 (2011): 80ps16.
4. Tan D, *et al.* “Topical Atropine in the Control of Myopia”. *Asia-Pacific Journal of Ophthalmology (Philadelphia)* 5.6 (2016): 424-428.
5. Sassa Y and Hata Y. “Antiangiogenic drugs in the management of ocular diseases: Focus on antivascular endothelial growth factor”. *Clinical Ophthalmology* 4 (2010): 275-283.
6. www.drugs.com
7. Atchison EA, *et al.* “Expression of Vascular Endothelial Growth Factor Receptors in Benign Vascular Lesions of the Orbit”. *Ophthalmology* 123.1 (2016): 209-213.
8. Bringmann A, *et al.* “Pathomechanisms of cystoid macular edema”. *Ophthalmic Research* 36.5 (2004): 241-249.

9. Genead MA., *et al.* "Topical dorzolamide for treatment of cystoid macular edema in patients with choroideremia". *Retina* 32.4 (2012): 826-833.
10. Onishi SM., *et al.* "Topical difluprednate for the treatment of Harada's disease". *Clinical Ophthalmology* 9 (2015): 157-167.
11. Lemos Reis RF, *et al.* "Comparison of topical dorzolamide and ketorolac treatment for cystoid macular edema in retinitis pigmentosa and Usher's syndrome". *Ophthalmologica* 233.1 (2015): 43-50.
12. Larrañaga-Fragoso P, *et al.* "Topical carbonic anhydrase inhibitors in macular edema associated with Alström syndrome". *Ophthalmic Genetics* 37.4 (2016): 427-429.
13. Asahi MG., *et al.* "Strong topical steroid, NSAID, and carbonic anhydrase inhibitor cocktail for treatment of cystoid macular edema". *International Medical Case Reports Journal* 8 (2015): 305-312.
14. Thode AR and Latkany RA. "Current and emerging therapeutic strategies for the treatment of meibomian gland dysfunction (MGD)". *Drugs* 75.11 (2015): 1177-1185.
15. Doughty MJ. "On the prescribing of oral doxycycline or minocycline by UK optometrists as part of management of chronic Meibomian Gland Dysfunction (MGD)". *Contact Lens and Anterior Eye* 39.1 (2016): 2-8.
16. Stock ML., *et al.* "Antibiotics acting as neuroprotectants via mechanisms independent of their anti-infective activities". *Neuropharmacology* 73 (2013): 174-182.
17. Liu A and Ji J. "Omega-3 essential fatty acids therapy for dry eye syndrome: a meta-analysis of randomized controlled studies". *Medical Science Monitor* 20 (2014): 1583-1589.
18. Bhargava R and Kumar P. "Oral omega-3 fatty acid treatment for dry eye in contact lens wearers". *Cornea* 34.4 (2015): 413-420.

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