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Editorial

Presbyopia: Combating Aging

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Presbyopia is a universal natural phenomenon, characterized by physiologic decrease in the amplitude of accommodation associated with the aging process, and manifesting by decline in near vision. There is less bulging of the lens with accommodation due to a change in the crystallins of the lens that result in decrease in the elasticity of the lens fibers or hardening of the lens.

In 1791 medical Latin describes the term "presbyopia" as a "far-sightedness brought on by age", originating from Greek presbys «old man», also "elderly, aged" and -opia, from *ōps* «eye».

The incidence and prevalence of presbyopia is exponentially growing due to increased life expectancy in many parts of the world. The forecast for the year 2050 indicates that the number of persons with presbyopia will reach 1.8 billion individuals [1]. These raising numbers of persons suffered from presbyopia highlight an economic burden, representing a medico-social challenge, to meet which it is extremally important to identify a druggable target in order to successfully manage it.

Treatment options for presbyopia are currently limited to corrective lenses or invasive surgical procedures, many of which are not reversible.

Patients, who require or desire independence from corrective lenses, are looking for solutions from eyecare providers to avoid having to use reading glasses and have limited alternative choices. However, pharmacological alternatives are in development and are expected to become available in the near future. Pharmacotherapy of Presbyopia is based on the instillation of eyedrops.

What would the ideal presbyopia-correcting eyedrop look like?

It will be comfortable for patient enabling ability to see a cell phone with continuous range of vision and without compromising distance vision, will have quick onset and long duration of action, and have a good safety and tolerability profiles.

The current landscape of medical therapies for presbyopia include three different strategies [2], one of which is directed to cause a miosis producing a "pinhole effect," increasing the depth of focus by blocking unfocused, peripheral light rays and permitting only central light rays to reach the retina, the second one is intended to restore accommodation [3], and the last one - restoring lens flexibility due to lens softeners that break disulfide crosslinks [4].

Multiple efforts at pharmacological treatment of presbyopia have focused primarily on the use of such miotics as a pilocarpine in different concentrations (0.4%, 1%, 1.25%, 2%) and carbachol, very effectively constricting the pupil, but at the same time impacting on the ciliary muscle and sphincter pupilae and causing undesirable spasmus of accommodation and brow ache. Other side effects include chronic inflammation, fixed pupil, posterior synechiae, pigment dispersion, and myopic shift [5]. To avoid aforementioned effects Brimonidine was added to carbachol, the most potent cholinergic agent for pupil constriction, in combined drug "Brimochol". Addition of Brimonidine prevents pupil dilation under mesopic conditions, inhibits contraction of ciliary muscle, mitigating side effects such as headache/brow-ache and myopic shift, increases bioavailability of carbachol, leading to longer duration of action (8-12 hours), prevents redness. Clinical Trial is on the way [6] and further investigation will show acceptability of side effects and real effect of once daily dosing.

The latest results from non-randomized multicentric case-series retrospective study [7] of a patented compound containing pilocarpine and diclofenac preservative-free eye drops have shown safety and continued efficacy during 2 - 10 years follow-up, as was stated by researchers. The limitations of study include a non-randomized retrospective design.

Really unique strategy is directed to restore lens flexibility due to lens softeners that break disulfide crosslinks [4]. Lipoic acid, as an antioxidant, have shown to chemically reduce lens disulfide bonds. Lipoic acid choline ester UNR844 1.5% ophthalmic solution (formerly known as EV06) is a first in-class disease-modifying topical treatment for presbyopia evaluated in the latest prospective, randomized, double-masked, multicenter clinical trial [4] and evidenced a good safety and tolerability profiles free of impact on best-corrected distance visual acuity, pupil size, intraocular pressure with a potential to improve distance-corrected near visual acuity in twice a day dosing. Sustained effect was documented in 5 - 7 months period after discontinuation of therapy. Further efforts will be directed to increasing a bioavailability in order to change dosing to user-friendly once a day without compromising an efficacy.

Summarizing, currently available findings highlight that the most impactful promising approach in pharmacotherapy of presbyopia is directed to restore lens flexibility taking into account that presbyopia antecede a cataract, and compounds simultaneously will be effective against cataract formation thus enabling earlier noninvasive intervention and management in order to reduce number of patients with deteriorated not only near, but also a distant vision.

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