MODERN OPTIONS FOR PRESBYOPIA CORRECTION IN PATIENTS WITH COVID-19

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Abstract. *This review discusses current options of pharmacotherapy in the treatment of patients with age-related refractive disorder – presbyopia - combined with COVID-19 viral infection. Various treatment options are currently being developed to correct presbyopia, but all of them involve either eyeglass correction, or surgical intervention with application of intraocular lenses. Drug therapy in this case is preferable, since it is less cost-effective, and patients comply more readily to this type of treatment. The application of myotics for presbyopia correction, as well as the combinations of myotics and other drugs for additive treatments and side effects reduction are well documented; however, there is no sufficient data on the results of such treatment. Currently, pyrenoxine, being a component of Catalin-eye drops, has been studied in this regard. It prevents the appearance of quinoid compounds in the lens, which lead to a decreased lens elasticity and, accordingly, to the development of presbyopia. The use of Catalin-eye drops in patients with COVID-19 is especially relevant, since this virus appears to be a predictor of metabolic disorders development. It is necessary to further study Pyrenoxine as a substance that effectively reduces risks of presbyopia development.*

Keywords: *presbyopia, quinoid compounds, drug treatment, pyrenoxine, myotics.*

Mechanisms of presbyopia development. Presbyopia is a refractive error, which is defined as a violation of near vision. This condition is typical for all people over 55 and is obviously associated with aging of the body. In 2011, there were 1.272 billion cases of presbyopia worldwide [1]. In addition, the global prevalence of presbyopia is projected to increase to 1.8 billion by 2050 [2]. The potential productivity burden of uncorrected or insufficiently corrected presbyopia was estimated at $ 25.367 billion, or 0.037% of the world's gross domestic product in 2011 [1]. Presbyopia affects not only near vision, that is, at a distance of 20 to 40 cm from the eyes, but also intermediate vision, that is, at a distance of 50 to 100 cm from the eyes. Regularities of structural and functional changes in the organ vision in presbyopia remains unclear, the root cause of presbyopia is unknown, and the mechanisms leading to loss of accommodation are not defined.

Accommodation is a mechanism that allows the eyes to adjust their refractive power to focus on close objects. There are three main processes involved in accommodation. They are (1) contraction of the ciliary muscle, which in turn reduces zonular tension and leads to an increase in lens thickness, (2) constriction of the pupil, and (3) convergence of both eyes. A common cause of presbyopia is lens compaction, which restricts the accommodation of the lens.

Options of presbyopia correction. Treating and correcting presbyopia is still challenging, as there are no medications or procedures that can produce perfect vision at all distances without risk. Currently, there are several treatment options for presbyopia: optical correction, including bifocal or progressive glasses, monofocal or multifocal contact lenses, corneal or intraocular surgical procedures, and pharmacological treatment. Optical correction with eyeglasses, such as monofocal, bifocal or multifocal lenses, are common options due to an easy and non-invasive access. However, eyeglasses are perceived by many patients as uncomfortable.

Multifocal contact lenses can be an alternative to glasses, but they can cause discomfort or inconvenience in some patients, especially in those who have no experience of wearing contact lenses. Surgical options, corneal or intraocular, are of increasing inter-

est, as they are based on the most modern technologies. Corneal surgery, such as corneal monovision, corneal insertions, collagen shrinkage, or multifocal LASIK, has been one of the common methods of correcting presbyopia. They have demonstrated success in improving near vision, but there are drawbacks, such as reduced middle or far vision, reduced contrast sensitivity, dysphotopsia, or refractive regression. Due to this, some patients still need eyeglasses after the procedures.

Pharmacological treatment of presbyopia has been studied in recent years based on various drugs and different treatment regimens. Pharmacological treatment, in theory, may offer the advantage of having a condition without glasses with a lower risk of irreversible eye complications compared to surgery. In November 2021, the U.S. Food and Drug Administration approved pilocarpine hydrochloride, a 1.25% ophthalmic solution (AGN-190584), as an eye drop for the treatment of presbyopia [3]. Inducing miosis may not be an ideal solution for treating presbyopia, since miosis itself is not a physiological condition of the eye. After the approval of 1.25% ophthalmic solution pilocarpine in the United States, patients experienced the drug application with different effects. According to initial data from online sites, some patients reported that the drug improved their myopia for approximately two hours, while others did not notice any differences compared to their initial condition [4].

Finally, Tsuneyoshi Y, Higuchi A, Negishi K, Tsubota K. demonstrated that pyrenoxine is effective in treating presbyopia by slowing down the development of lens opacities and preserving its elastic properties [5].

Presbyopia and COVID-19. According to D. M. Dockery et al. (2020), data on eye damage in COVID-19 are underestimated, since emergency and hospital doctors usually do not pay attention and do not record eye symptoms that seem insignificant for the patient's general condition [6]. However, according to Kazuno Negishi, Masahiko Ayaki, stress and rapid digitalization associated with strict infection control and quarantine during a pandemic COVID-19 may be contributing factors to the development of presbyopia [7]. Long waiting times for surgery are also associated with anti-epidemic measures and restrictions that are currently related to COVID-19 pandemic [8].

M. Kovalevskaya et al. demonstrated that the level of peroxiredoxine in the lacrimal fluid of patients with cataracts is reduced [9]. Pyrenoxine-eye drops have been reported to reduce optical density in the layers of the cortical lens and under the posterior capsule in humans [10]. It has also been reported that higher lens density impairs contrast sensitivity [11]. Correlation of nuclear cataract lens density using Scheimpflug images with the lens opacity classification system and visual function and the near visual function of presbyopia is improved by increasing contrast [12]. The above facts give rise to the need for prescribing drug therapy in the form of eye drops containing pyrenoxine to elderly and senile patients who have undergone COVID-19. As stated, this fact will prevent a decrease in the elastic properties of the lens and, accordingly, presbyopia.

Catalin. The mechanism of action of Catalin (pyrenoxine)-eye drops is based on competitive inhibition of quinoid substances and pre-protection of the SH group of lens proteins from oxidation. In the study evaluating the effectiveness of cataractogenesis prevention in patients with epiretinal membrane after vitrectomy, it was demonstrated that a pyrenoxine-based drug is highly effective in preventing the development of cataracts in this group of patients [13]. Tsuneyoshi et al. have demonstrated that pyrenoxine is effective in the treatment of presbyopia by slowing down the development of opacities of the lens and preserving its elastic properties [5]. Catalin-eye drops are effective in protecting the lens from oxidative stress, especially in the early stages of cataract development [14].

Catalin-eye drops containing pyrenoxine were first registered in Japan in 1958 by Senju Pharmaceutical and are currently used in more than 20 countries around the world. The effectiveness of Catalin has been proven in both clinical and laboratory studies. J. Kociecki et al. conducted a study which included 72 patients over 40 with the initial stage of age-related cataracts and visual acuity of at least 0.5%. Of these, 35 patients received Catalin instillations, 37-placebo [15]. Results

were evaluated in 3, 6, 12, 18, and 24 months using densitometric measurements of lens transparency on an anterior segment analyzer EAS-1000 (Nidek, Japan). Catalin-eye drops in the treatment of patients with presbyopia are the most effective means that slows down the decrease in the elastic properties of the lens. The cumulative effect of the drug was observed in 18 months of treatment. Catalin-eye drops are well tolerated by patients even for long-term application. Detailed observation of patients who used Catalin manifested the intensity of opacities decreased by 3.9%, while in the control group, the intensity of opacities increased by 4.6% [15].

Conclusion. Studies of drugs that could affect age-related changes in refraction are conducted in various areas. Over the past few decades, research has focused on pharmacological strategies to prevent and decelerate progression of presbyopia using Pyrenoxine. Adequate tolerability of the drug is important for patients of all age groups, and side effects are extremely rare. High therapeutic efficacy and safety with long-term use allow recommending Catalin-eye drops for prevention of presbyopia progression. Further research on the use of pyrenoxine are required.

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СОВРЕМЕННЫЕ МЕТОДЫ ВОЗДЕЙСТВИЯ НА РАЗВИТИЕ ПРЕСБИОПИИ У ПАЦИЕНТОВ С ПЕРЕНЕСЁННЫМ COVID-19

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Аннотация. *Данный обзор освещает современные возможности фармакотерапии в лечении пациентов с возрастным нарушением рефракции - пресбиопией, развившейся на фоне перенесённого инфицирования вирусом COVID-19. Различные методы лечения разработаны в настоящее время для коррекции пресбиопии, однако все они подразумевают использование очковой коррекции, а также оперативное вмешательство с постановкой интраокулярных линз. Медикаментозная терапия в данном случае является предпочтительной, поскольку предполагает минимальное количество материальных затрат, а также комплаентность пациентов к такому виду лечения. Достоверно известно о применении миотиков для лечения пресбиопии, а также комбинаций миотиков и других препаратов для достижения аддитивных методов лечения и снижения риска развития побочных эффектов, однако данные о результатах такого лечения отсутствуют. В настоящее время исследовано вещество Пиреноксин, которое входит в состав глазных капель Каталин. Оно предотвращает появление хиноидных соединений в хрусталике, которые приводят к снижению эластичности хрусталика и, соответственно, к развитию пресбиопии. Особенно актуально применение глазных капель Каталин у пациентов с перенесенным COVID-19 как предиктором развития метаболических нарушений. Необходимо продолжить исследование Пиреноксина как вещества, эффективно снижающего риски развития пресбиопии.*

Ключевые слова: *пресбиопия, хиноидные соединения, медикаментозное лечение, пиреноксин, миотики.*