REVIEW
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The possibilities of pharmacological intervention in myopia

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ABSTRACT

This paper presents and discusses the current possibilities of pharmacological intervention in myopia. A review of the latest literature regarding the pharmacological treatment of myopia has been presented.
The results of experimental research on the potential use of: atropine, oxyphenonium, pirenzepine, chlorpyrifos, apomorphine, reserpine, 6-hydroxy dopamine, dextromethorphan, MK-801, APV, bicuculline, SR95531, CACA, TPMPA, dextrophanol, levorphanol, *D*- and *L*-naloxane, *L*-NAME, formoguanamine, b-xyloside, the central and peripheral antagonist of VIP, basic fibroblast growth factor, a solution of the basic amino acid salts in the form of succinates, in the treatment of myopia have been described. The clinical use of pirenzepine,7-methylxanthine, and atropine has been discussed.
The obtained results of experimental and clinical studies give hope that a new effective pharmacological method of myopia treatment can be discovered soon.

KEY WORDS: myopia; treatment; pharmacology

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INTRODUCTION

It is believed that currently about 1/4 of adults and 1/3 of children worldwide have myopia. This type of refractive error is the most prevalent in Asian and highly developed countries. The development of myopia is related to genetic predispositions and environmental factors. Among the environmental factors, reading, writing, and computer use have the most influence [1–4].

Although myopia is such a significant social problem, no effective treatment method has so far been developed. Various treatment methods or their combinations have been proposed so far for school myopia and progressive myopia [1, 3].

Due to myopia's high social importance and considerable interest in the latest experimental and clinical results, the authors present a review of the current opinions concerning the issue.

RESULTS OF EXPERIMENTAL STUDIES

Research into experimental myopia was started by Young [5] in 1961. The researcher noticed that monkeys develop myopia if kept in a closed space. In 1975, Hubel and Wiesel from Harvard University, while researching the plasticity of the visual cortex, discovered by chance that suturing of the eyelids in young monkeys leads to an increase in the axial length of the eye. In 1981, Hubel and Wiesel were awarded the Nobel Prize for their research into the visual cortex's structure and function. A substantial enlargement of the eye after tarsorrhaphy was not related to their work. However, they immediately concluded that this finding could be of clinical value. Therefore, they conducted extensive control studies, which they later proved through clinical observations. They observed a higher prevalence of myopia in children with ptosis and corneal scars [6].

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In 1977, intensive work on the role of tarsorrhaphy or occlusion on the development of form-deprivation myopia was started. Many experiments on monkeys, cats, rabbits, guinea pigs, shrews, squirrels, chickens, and kestrels were conducted in almost 25 laboratories worldwide. The research, conducted in this field by Raviola and Wiesel from Harvard University, Laties and Stone from the University of Pennsylvania, Wallman from the City University of New York, and Schaeffel from the University of Tübingen [7, 8] deserve special mention. In 1988, Schaeffel et al. [9] discovered that experimental myopia develops due to diffusing lenses usage. In the same year, Stone et al. [10] observed that tarsorrhaphy induces metabolic changes in the retina and, therefore, initiated research to find substances inhibiting the development of experimental myopia.

SUBSTANCES INHIBITING THE PROGRESSION OF MYOPIA

Based on experimental results, researchers from around the world tried to establish which substances could be used in the treatment of myopia. Currently, the following substances have been found to inhibit the progression of experimental myopia:

- atropine, oxyphenonium — non-selective antagonists of the muscarinic receptors [11–13];
- pirenzepine — an antagonist of the muscarinic M1 receptors [14–16];
- chlorpyrifos — a substance inhibiting acetylcholinesterase [17];
- apomorphine — a non-selective agonist of the dopamine receptors [18, 19];
- reserpine — an alkaloid of rauwolfia hampering the storage of catecholamines and serotonin in both the central and peripheral nervous system [20];
- 6-hydroxydopamine — a substance inhibiting hydroxylase of tyrosine and destroying the structure of the adrenergic endings [21–23];
- dextromethorphan, MK-801, APV — antagonists of the NMDA receptors [24];
- bicuculline, SR95531 — antagonists of the GABAA receptors [25];
- CACA, TPMPA — antagonists of the GABAA-Or receptors [25];
- dextrophanol, levorphanol, *D*- and *L*-naloxane — *D*- and *L*-enantiomers acting at opioid receptors [26];
- *L*-NAME — a nitric oxide synthase inhibitor [27, 28];
- formoguanomine — a substance inhibiting the production of proline and glutamate, leading to the fall of the thickness of the choroid, degenerative changes in the photoreceptors and the pigment epithelium of the retina [29];
- b-xyloside — a proteoglycan synthesis inhibitor [30];
- central antagonist of VIP — a hybrid peptide consisting of the C-terminal of the VIP molecule linked serially to the N-terminal portion of neurotensin [31];
- peripheral antagonist of VIP — 4Cl-D-Phe6, Leu17 [31];
- basic fibroblast of growth factor — a growth factor connected with heparin [32];
- a solution of the basic amino acid salts in the form of succinates [33].

Due to the pathogenesis of experimental myopia, which in many different aspects closely resembles the pathogenetic mechanism of progressive myopia in humans, all the substances listed above can be viewed as potential medications inhibiting myopia's progression in children and adolescents.

RESULTS OF CLINICAL STUDIES

In 2004 Siatkowski et al. [34] from the University of Oklahoma examined 277 US children aged 8-12 with myopia between –0.75 to –4.0 D. These children were given topical 2% pirenzepine gel twice a day. After a year of use, the progression of myopia decreased by 51%.

The results of Siatkowski et al. [34] were reaffirmed in 2005 by Tan et al. [35] from the Singapore Eye Research Institute. They examined 353 children from Singapore, Taiwan, and Hong Kong aged 6 to 12 with myopia between –0.75 to –4.0 D. The authors observed that pirenzepine slowed the yearly progression of myopia by 44%.

In 2008, Siatkowski et al. [36] examined 84 American children aged 8–12 with myopia between –0.75 and –4.0 D. The children received topical 2% pirenzepine gel twice daily. After two years of treatment, the progression of myopia decreased by 41%.

In the same year, Trier et al. [37] from Trier Research Laboratories in Copenhagen examined 107 Danish children aged 8 to 13 with myopia above –0.75 D. The children received an oral dose of 0.4 g of 7-methylxanthine once daily. After three

years of treatment with 7-methylxanthine, they revealed a lower progression of myopia.

In 2012 Chia et al. [38] from the Singapore Eye Research Institute examined 400 children from Singapore aged between 6 and 12 years of age with myopia higher than –2.0 D. After two years of treatment with a topical 0.01% solution of atropine, they noted a decrease of 0.5 D of myopia per year.

Following these studies, a mass-scale use of atropine in myopia treatment in many countries has been observed. It has been found that a 0.01% solution of atropine decreases the development of myopia and does not induce side effects in the anterior segment [39–42]. It has also been observed that 0.02% atropine eye drops had a better effect on myopia progression than 0.01% atropine. However, both showed similar effects on pupil diameter and accommodative amplitude after 12 months of treatment [43]. Over two years, the observed efficacy of 0.05% atropine was twice as high as 0.01% atropine. It remained the optimal concentration among the studied atropine concentrations in slowing myopia progression [44].

In Poland, studies into the role of atropine in myopia's progression were initiated by Koronczewska in the 1980s. Regretfully, the author used 0.5% atropine, which led to severe side effects. Currently, research by Grzybowski is ongoing [45, 46].

Other substances used in the above-mentioned experimental studies to slow down the eye growth during myopia development up to this day have not been attempted in clinical practice.

CONCLUSION

The obtained results of experimental and clinical studies are promising enough and raise hope that a new effective pharmacological method of myopia treatment can be discovered soon.

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