Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/33/20240423

The treatment of myopia and future development

Chenling Wu

Chongqing Depu Foreign Language School, Chongqing, 400000

wcl09192006@sina.cn

Abstract. Myopia is a relatively common disease at present, especially in the adolescent population is very high, and its prevalence increases with the passage of time, usually myopia will cause retinal detachment, glaucoma, etc., which may seriously lead to vision loss and blindness. Existing treatments include monocular lenses, contact lenses and refractive surgery, as well as the drugs atropine and pirrenzil. Studies have shown that most myopia treatments have little effect, are relatively short term, and have significant side effects. This article mainly summarizes the treatment methods of myopia, combined with the latest findings of clinical research, and put forward the possible future treatment methods.

Keywords: Therapy, Myopia, Treatment

1. Introduction

Myopia is a more common disease, ranging from 15% to 49% in adults, with little difference between men and women. Only 1.2 percent of rural children in Nepal are nearsighted, compared with 4 percent in South Africa. However, in some big cities in China, the proportion is as high as 37 percent. The proportion of the population that is nearsighted has been rising since the 1950s. A nearsighted person can see clearly at a distance (far-view point), but objects outside this range become blurry. With regular check-ups, the eye structure of most people with myopia is no different from that of non-myopia patients. It occurs in school-age children and worsens between the ages of 8 and 15 [1].

The visual image of a nearsighted person's eye is not focused on the retina, but on the front of it. When distant objects are blurred, when near objects are relatively clear. It is thought that myopia is mainly influenced by genetic and environmental factors. A study of twins shows that having a parent with high myopia can affect the child's vision, as can having a family history of the condition. In addition, the risk of myopia may be passed from parent to parent. Gene-linkage studies have identified 18 sites on 15 chromosomes that may be associated with myopia, but none of these sites have any relationship with candidate genes that cause myopia. In contrast to the single structural protein abnormalities that cause myopia, abnormalities in the control of these structural proteins may be the real cause of myopia. Environmental factors include prolonged close eye contact (such as reading, writing, use of mobile phones, tablets and computers), increased years of schooling, and lack of outdoor exercise. Of course, other studies have found that nearsightedness is related to socioeconomic status. The eye diameter is too long, the lens is too inflexible are signs of myopia, in addition to other symptoms include eye fatigue, headaches and so on.

The current hypothesis is that lack of normal visual stimulation may cause eye dysplasia. The "normal" in this hypothesis refers to the environmental stimuli that the eye has been exposed to over the

DOI: 10.54254/2753-8818/33/20240423

course of evolution, and currently people are mostly in buildings, which greatly increases the risk of myopia. If you can spend more time outdoors sports and play, then the incidence of myopia will be reduced. Some preliminary evidence suggests that outdoor activities have a protective effect on myopia, and that prolonged sunlight exposure affects the production and release of dopamine in the retina. Another closed-eye working hypothesis, also known as the "eye overuse theory," states that keeping your eyes closed for long periods of time strains the muscles inside and outside your eyes. Some studies support this hypothesis, others do not. While there is a link, cause and effect is unclear [2].

There is experimental evidence that allowing children to spend as much time outdoors as possible can prevent myopia in children, possibly because of the protective effect of natural light exposure. Wearing glasses is currently a simple and safe form of treatment, and contact lenses offer great convenience, but also carry the risk of infection. In addition, the shape of the cornea can be permanently changed by refractive surgery.

This review mainly analyzes the pathogenic factors of myopia. Through consulting a lot of data, a series of treatment methods of myopia are summarized, and the future treatment of this kind of disease is proposed and prospected.

2. The features of myopia disease

Myopia is becoming an epidemic and is a major concern in some parts of the world. The dramatic increase in the global prevalence of myopia has major implications for public health, with an increase in the incidence of high myopia and possibly pathological myopia, as well as an increase in potentially blinding eye diseases.

Refractive error is a unique condition of binocular vision inconsistencies. In order to explore the pattern of age change and its relationship with binocular refractive status, more than 150 children were divided into farsighted, nearsighted, and strabismus groups, and optimal corrected vision, refractive error, eye position, and atropine use were recorded. The results showed that refractive errors decreased in children under 6 years of age and decreased with age, and in children 3-6 years of age, the average anisometropia was higher in children with myopia and endovision than in children with farsightedness. There was no significant difference among children over 6 years old. Therefore, it is believed that the ametropia is related to age, type of refraction, amblyopia and strabismus.

3. Treatments of myopia

Standardized Currently available treatments for myopia progression include, but are not limited to, glasses, contact lenses, and medications. The evaluation of these treatments has methodological limitations and should include random assignment, concurrent control group, double-blind investigator collection of outcome data, standardized measurement, sample size, and reduction of follow-up loss to achieve accurate results.

3.1. Single vision lens

Many findings support an active reflex mechanism, in which lens induced compensatory eye growth provides strong evidence for defocus. The results suggest that ophthalmic interventions using commonly used single vision lenses (SVL) in myopic children may accelerate myopia. Nearsighted people wear contact lenses in a variety of ways, from wearing them all day, to viewing only from a distance, to contact lenses that do not require a prescription. Although pilot data suggest similar myopia progression across wearing styles, there is limited data on the relationship between myopia progression and glasses wearing styles, requiring the use of a larger sample of children and a random assignment [3].

The use of SVL to correct myopia defects is a more recommended treatment option in clinical practice. One clinical trial evaluated more than 100 myopic children around 10 years of age, about 90% of whom completed two years of SVL glasses, half of whom were randomly assigned to complete correction and half of whom were randomly assigned to correction less than 0.75 days. The 2-year progression in the fully corrected group was 0.77 days, significantly lower than the 1.0 days in the uncorrected group. The finding was unexpected and more research is needed.

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3.2. Bifocal and progressive multifocal lenses

The use of bifocal or progressive additional lenses (PAL), sometimes called nonlinear bifocal lenses, to prevent myopia yields relatively small overall therapeutic effects over 1.5 to 3 years. The largest therapeutic trial using this lens is the Myopia Correction Evaluation Trial (COMET), a multicentre, randomized, double-blind clinical trial designed to evaluate whether PAL can slow myopia progression compared to traditional SVL. 15 COMET contains 469 child nodes. The baseline myopia range for ethnic groups aged 6 to 11 years was -1.25 days to -4.50 days. The progression of myopia was measured by tropicamide astigmatic diopter. Retention rates are very high, with more than 90 percent of children completing follow-up. After 3 years, the correction of PAL group was increased compared with SVL group, and the difference was statistically significant, but not clinically significant. All the therapeutic effects occurred in the first year. Further analysis showed that for children with large adjustment lag, high myopia and short reading distance, the 3-year treatment effect was significant. These results support the role of retinal defocus in myopia progression and suggest that myopic children with large adjustment delays and myopia may benefit from wearing PAL [4].

A comet-like study was conducted in Japan. A unique feature of this study is that PAL and SVL were cross-designed to slow myopia in children. During the first half of the study, children with myopia were randomly selected to wear one type of glasses and replace the other during a 3-year follow-up. The results showed little difference between PAL and SVL at one and a half years. At the end of three years, after the children wore another type of lens, the group who wore PAL first had a lower rate of progression than the group who wore SVL first, suggesting that PAL is more effective with early intervention.

3.3. Contact lenses

Early studies using rigid permeable contact lenses (RGPs) to control myopia lacked randomization, and dropout rates were high in the contact lens group. In one study, 120 or so children were randomly assigned to wear RGP or soft contact lenses for three years. The results showed that there was significant difference in myopia progression between RGP group and soft lens group at 3 years. The slow progress of RGP lenses mainly occurs in the first year. After three years, the soft lens group had significantly higher corneal curvature steepness than the RGP group, with most of the difference occurring in the first year. The delay in myopia speed is mainly due to the flattening of the cornea, which reverses with the cessation of wearing RGP lenses, which should not be used primarily to control myopia [5].

The Pediatric Longitudinal Orthokeratology Study (LORIC) aims to determine whether wearing specially designed RGP contact lenses at night can slow axial elongation and myopia progression. The researchers compared the results of 35 children who had worn contact lenses for two years with those who had worn SVL. Since the lens causes the cornea to flatten, changes in the length of the eye axis are used as a measure of results. The results showed that the axial length of the eye increased in the internal orthokeratology group and the control group, and the difference was statistically significant.

3.4. Potion

Topical use of atropine, a non-selective muscarinic antagonist, can significantly reduce the progression of myopia. Shih et al. reported a significant slowdown in myopia progression. At one and a half years of age, children over 5 years of age were randomized to receive 0.5% atropinplus multifocal glasses, compared to SVL or multifocal glasses alone. Chua et al. reported similar results in a two-year study of 400 myopic children over the age of 5 using a different experimental paradigm. Children were randomly assigned to drug and control groups, and each child was treated with 1% atropine or carrier eye drops in one eye, once a night. Myopia at 2 years was significantly lower in the drug group than in the control group, and at the end of the study, many children in the drug group had anisometropia. Now a new clinical trial is evaluating the use of atropine at different concentrations in both eyes and measuring the progression of myopia after stopping the drug. Although atropine is used to slow the development of myopia in many countries in Asia, it is rarely used in Europe and the United States. Many clinicians consider atropine-related side effects unacceptable for long-term treatment.

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Like atropine, Pirenzepine is a muscarinic antagonist, but is less likely to produce ascariasis and monocular paralysis. Pirenzepine has been tested in two clinical trials, and in the Singapore study, children taking pirenzepine experienced a 0.47D increase in myopia over one year. Patients who used piranzapine ophthalmologic gel twice daily had an increase in myopia of 0.70 days, compared with 0.84 days in the control group. In the US study, the pirenzepine group (used once daily) saw an increase in myopia of 0.26 D over one year, while the control group saw an increase of 0.26 D.

4. Future development of myopia treatment

Gene therapy is one of the leading research directions in the field of myopia treatment, which aims to cure myopia and restore vision by intervening gene expression and regulation mechanism. Researchers in the field of myopia therapy are exploring the use of CRISPR-Cas9 technology to treat myopia. The technology allows point-to-point editing of target genes, such as those associated with axial length and diopter regulation. By precisely modifying these genes, it is possible to change the shape and regulation of the eyeball, thereby correcting myopia.

Normal genes are introduced into eye tissue to repair or enhance the function of genes associated with nearsightedness. This approach is expected to directly intervene in the pathogenesis of myopia and provide lasting therapeutic effects for patients. The frontier exploration of gene therapy provides new hope and possibility for the treatment of myopia. However, these technologies are still in laboratory studies and early clinical trials, and further research is needed to assess their safety, efficacy, and long-term effects. In addition, the ethical and legal issues associated with gene therapy need to be widely discussed and addressed [6].

Three different types of CRISPR/Cas systems have been identified. Due to its DNA interference (DNAi) properties (see RNAi), it is currently actively used in genetic engineering as a genome editing tool. Zinc finger nucleases (ZFNs) and transcription activator-like nucleases (TALENs) also utilize non-homologous end-suffixes. combined (NHEJ) mechanism. Double-strand breaks in the genome create DNA to facilitate editing. If CRISPR/Cas9 technology is to become one of the methods of gene therapy, it must achieve precise point editing. Directly enhance HDR repair to improve precise editing of the cell growth cycle mainly include cycle regulation, introduction of exogenous DNA, chemical modification of gRNA, or small molecule activation of HDR. NHEJ can repair throughout the cell growth cycle but plays a major role in the G1 phase, while HDR plays a major role in the S and G2 phases. In addition, after small molecule high-throughput scanning intervention, two small molecule preparations that can increase the ratio of HDR-β3 were screened out, and then hormone injection agonist L755507 and intracellular transporter Brefermectin A were injected.

Simultaneous editing of a single pesticide has enabled the precise editing of CRIS-PR/Cas9 technology to achieve a qualitative leap, but it is currently limited to the exchange of intracellular nucleotides and thymidine. There are also different types of genetic genes, and the replacement of only one marker is not enough to meet its requirements. In future research, the CRISPR/Cas9 system can continue to be modified to achieve precise manual replacement of bolts [7].

To increase the potential of Cas9 protein are mainly divided into the following categories: (1) Reduce or lose the endonuclease activity of Cas9 protein. Whether reduce the function of HNH or RuvC domains, or constructing CRISPRi and Fok I-DCas9 to disable the Cas9 protein endonuclease activity and retain only its nucleic acid recognition ability, and in the presence of other endonucleases Gene editing can be achieved with the help of the procedure can improve the sequence matching required for Cas9 activation. (2) Site-specific mutations were performed on the Cas9 protein to form eSpCas9 and SpCas9-HF1. This mutant weakens the non-mutated binding ability of the Cas9 protein to DNA and enhances the binding effect of the inhibitory sequence to the Cas9 protein. (3) Regulate the expression of Cas9 protein in cells.

The inducible Cas9 protein is induced by using an inducible promoter and inserting a 4-HT-dependent peptide, which reduces the exposure time of the genome to the Cas9 and sgRNA complex, which further reduces the binding probability of Cas9 to the non-deleted sequence and off- target rate decreased further. (4) Enhance the recognition ability of Cas9. Mutant D1135E has a more specific

DOI: 10.54254/2753-8818/33/20240423

recognition of standard PAMs, thereby reducing off-targets caused by recognition of non-standard PAM sequences.

By optimizing sgRNA mainly include (1) changing the length of sgRNA, truncating bases at the 5' end before the recognition sequence. (2) Increase the stability of sgRNA. For example, add all base propagation methods in gRNA. In addition, studies have shown that Cas9 orthologous enzymes have a higher ability to camouflage certain sites than SpCas9, which undoubtedly provides a new way to completely increase the amplitude. Through improvements in the CRISPR/Cas9 system, misses have been greatly reduced, but there is still a long way to go [8].

Gene editing technology is becoming more and more perfect, and Mutation hopes to use gene editing to clarify what happens to genes in the early stages of development, as well as to repair mutated genes in chromosomes and chromosomal diseases. At present, most methods of introducing Cas9 and sgRNA into fertilized eggs are through electrical conversion or intraembryonic injection, and most of them are converted into Cas9 mRNA [9]. However, most of the variants obtained by these methods suffer from mosaic phenomena. The reason for the mosaic phenomenon may be that the time from the success of sperm is limited, and it takes a long time for Cas9 mRNA to be translated into protein, which misses the opportunity of editing in single-cell fertilized eggs, while the Cas9 protein and sgRNA Half-life can definitely edit newly generated cells differently over time. Whether it is to observe the effects of genes or to avoid the occurrence of genetic diseases, it is necessary to produce a non-mosaic disappearing effect. To avoid mosaics, the Cas9 protein functions before the first copy in a cell's genome and then stops functioning. However, while this technology completely avoids the embedding phenomenon, it also has some side effects [10].

In the field of organ transplantation, this technology has been successfully used to remove porcine endogenous retroviruses in various pig organs, making pig organ transplantation possible. In the field of viral infection treatment, in vitro experiments and animal experiments have shown that packaging technology has successfully achieved the treatment of HIV, B-coronavirus and other viruses, opening a new chapter for the treatment of these diseases. CRISPR/Cas9 technology has achieved important results in many fields such as plant breeding, genetics and current therapy. CRISPR/Cas9 technology is still evolving and is expected to be useful in more fields.

5. Conclusion

At present, myopia still lacks effective treatment methods and means, so there has been a high research heat. Most research suggests that one of the simplest remedies for delaying myopia (which has not been rigorously tested in studies) may be to provide children with plenty of outdoor activities each week. Several large studies conducted in different parts of the world report that children who spend more time outdoors have lower rates of myopia than children who spend less time outdoors. But these conclusions still need clinical trials to be evaluated and serious. In this paper, the pathogenesis, prevention and treatment of myopia are summarized in detail, and it will be helpful to the future development of this field.

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