

A review of myopia treatment methods and their research progress

Jiaxin Tian *

International School of Jinan University, Guangzhou 510632, China

* Corresponding Author Email: 1041012805@qq.com

Abstract. Myopia is a refractive error in which light is focused in front of the retina. In recent years, with the change of people's lifestyle and the widespread use of electronic products, the number of people suffering from myopia is on the rise year by year. Therefore, how to effectively prevent and treat myopia has attracted a lot of attention. At present, the common treatments for myopia mainly include five major categories, such as drug therapy, optical correction, surgery, Chinese medicine treatment and environmental behavior therapy. In this paper, we summarize the latest research advances in myopia through the above five levels in order to provide a reference basis for the development of a more comprehensive and personalized myopia treatment plan in the future.

Keywords: Myopia; optical correction; refractive error; surgical treatment; environmental behavior therapy

1. Introduction

In the relaxed state of human eye regulation, parallel light rays are focused before the retina after passing through the refractive system of the eye is called myopia [1]. According to epidemiological data, as of 2016, the number of people with myopia worldwide was about 1.406 billion, accounting for about 22.9% of the global population. In recent years, the number of people suffering from myopia has been increasing with the increased use of electronic devices. Some reports indicate that the number of people with myopia worldwide is expected to be as high as 2.5 billion in 2030 [2]. Myopia can be classified in various ways, for example, by refractive component into axial myopia and refractive myopia. According to the severity, they can be classified as mild myopia ($\leq -3.00D$), moderate myopia ($-3.25D$ to $-6.00D$) and high myopia ($> -6.00D$) [1]. The persistent progression of myopia is an important factor in the development of blindness or other serious ocular pathologies, such as retinal detachment, macular hemorrhage, subretinal neovascularization, vitreous liquefaction, and posterior vitreous detachment [3]. Therefore, early prevention and treatment of myopia is crucial to protect patients' vision. Currently, the five major categories of commonly used treatments for myopia include pharmacological treatment, optical correction, surgical treatment, Chinese medicine treatment, and environmental behavioral treatment. Therefore, this study intends to review the latest research advances in myopia by means of a systematic review, with the aim of providing a certain reference basis for the development of more comprehensive and individualized myopia treatment plans in the future.

2. Etiology of myopia

So far, the causes of myopia are complex, and the formation of myopia is also caused by a combination of multiple factors, mainly including environmental factors and genetic factors [4]. With the continuous improvement of modern production technology, the popularity of electronic products has provided many conveniences to human life. However, at the same time, the widespread use of electronic products also brings unavoidable hidden dangers to people's health, especially to their visual acuity [5].

2.1. Genetic factors

The most common features of genetically related disorders are ethnic variability and family aggregation, both of which are prevalent in myopia patients. Wu X et al [4] found that offspring of two or one parent with myopia were 2-3 times more likely to develop myopia than offspring of parents without a history of myopia, and this is evidence that myopia is familiarly aggregated. In addition, the onset of myopia in Asian populations is characterized by a lower age and faster progression compared to other ethnic groups [4].

2.2. Environmental factors

Although genetic factors have an important role in the early onset of myopia, the high prevalence of myopia today may be attributed more to environmental factors. Maciej C et al. showed that 120 minutes of outdoor exercise per day was effective in preventing the onset of myopia [6]. Sherwin et al. showed that children who read or study with an eye distance of less than 30 cm from a book have 2.5 times the prevalence of myopia than those with a distance greater than 30 cm [7]. S. Nickles et al. found that the higher the level of education, the higher the probability of developing myopia [8]. In addition to influencing factors such as time spent outdoors, eye behavior and habits, nutritional status and electronic screen use are also important factors affecting visual acuity [2].

3. Myopia treatment methods

3.1. Pharmacological treatment

Drug therapy is a treatment method that controls the progression of myopia by altering the signaling molecules associated with the retina and sclera, and thus the progression of myopia [9]. Currently, commonly used drugs related to myopia treatment include M-receptor antagonists, N-receptor antagonists, and adenosine receptor antagonists.

Atropine is the only drug approved worldwide for myopia treatment and is a non-selective M-receptor antagonist [8], and its therapeutic and delaying effects on myopia progression have been confirmed by numerous previous studies [9-11]. Early atropine was mainly used to inhibit glandular secretion and anti-shock [12], and in recent years, the results of a large number of studies have shown that atropine is effective in delaying myopia, with commonly used concentrations of 0.5% and 1% [9-11]. At the same time, the side effects associated with atropine in the treatment of myopia have raised concerns, such as decreased ocular accommodation and blurred vision [12], and these symptoms may be related to the inhibition of the iris sphincter and ciliary muscle by high doses of atropine. In recent years, some studies have found that lower concentrations of atropine are more effective and safer than conventional concentrations in the prevention and treatment of myopia [12]. The results of Yam et al. showed that lower concentrations of atropine (0.05%) were more effective than 0.025% and 0.01% concentrations in controlling the progression of myopia [10]. Guo L et al. showed that lower concentrations of atropine (0.01%) had fewer adverse effects and higher patient compliance [11].

Representative drugs among N-receptor antagonists include sondacrine and mecamlamine, both of which inhibit myopia progression mainly by expanding the vitreous cavity volume [13]. However, there are still relatively few studies related to the use of N-receptor antagonists in myopia treatment. Therefore, the effects of N receptor antagonists on myopia still need further observational studies to follow.

The representative drug of adenosine receptor antagonists for the treatment of myopia is mainly 7-methylxanthine (7-MX), whose main mechanism of action against myopia may be related to the enhancement of scleral strength and reduction of the increase of the ocular axis [14]. However, most of the studies on 7-MX intervention in myopia are only at the stage of animal experiments, and its clinical effects and safety remain to be further observed and verified.

In addition to the drugs mentioned above, substances such as dopamine receptor activators, nitric oxide, melatonin and growth factors have been used to intervene in the development and progression of myopia. However, relevant clinical studies are still scarce and need to be further explored.

3.2. Optical correction

3.2.1 Frame glasses

Optical correction is currently the most common way to slow down the progression of myopia and is mainly divided into two types: frame glasses and contact lenses. Among them, frame glasses are chosen by most people because of their easy acceptance and non-invasive nature. The common frame glasses include Single vision lenses (SVLs), Progressive addition spectacle lenses (PALs), Defocus incorporated multiple segments, (DIMS) etc. Single vision lenses for myopia are mainly based on reducing the relative hyperopia of the peripheral retina. Smith et al [15] showed that in addition to the hyperopic detachment occurring in the central concave region, the hyperopic detachment in the peripheral retina also plays an important role in the progression of myopia, which also provides theoretical support for the application of monovision in myopia treatment.

Adjustment lag is reduced after multifocal or progressive multifocal spectacle wear is the main mechanism by which both types of frames are used in delaying myopic progression. Although there are a large number of clinical studies dedicated to comparing and evaluating the effectiveness of these two methods, the final results of these studies are currently highly variable [16-17]. Therefore, more randomized controlled trials are still needed to confirm the reliability of these two approaches in the prevention and treatment of myopia.

3.2.2 Contact lenses

Contact lenses, especially keratoplasty lenses, are a common treatment and retardation for myopia and have gained wide clinical acceptance. Common contact lenses include soft contact lenses, rigid contact lenses of non-keratomileusis design, multifocal soft contact lenses, and keratoplasty lenses. Soft contact lenses do not prevent or treat myopia, although they can improve a patient's visual acuity while worn. Rigid contact lenses can prevent and control myopia by flattening the cornea [2]. Multifocal soft contact lenses, as a new type of contact lens, are playing an increasingly important role in myopia prevention and treatment, especially in children [18-20].

Currently, the most clinical studies on contact lenses for myopia prevention and treatment include keratoplasty lenses. Keratoplasty lenses, also known as Orthokeratology lenses, are rigid contact lenses whose mechanism of delaying myopia progression is mainly through physical compression in the form of changing the morphology of the cornea, thus reducing the degree of myopia in patients. Recent studies have confirmed that long-term keratoplasty lenses can slow myopia progression by altering peripheral refractive error [21]. In addition, a large number of clinical studies have confirmed the effectiveness of keratoplasty in preventing myopia, especially in improving the length of the eye axis and vitreous depth in adolescent myopic patients [22-23].

3.3. Surgical treatment

In addition to medication and refractive correction, there are still many myopic patients who have to take surgical treatment because of the inconvenience caused by severe myopia in their daily life. The three commonly used surgical methods include keratomileusis, IOL implantation with a lens and scleral reinforcement.

3.3.1 Corneal refractive surgery

The cornea has an important role in ocular refraction. Since the 1930s, keratotomy has been widely used in the treatment of myopia, and thousands of myopic patients have been cured in this way [24]. However, due to the unpredictability and high postoperative complication rate of keratotomy [25], this approach has been gradually replaced by the later invention of excimer laser surgery.

Excimer laser surgery on the cornea is divided into Photorefractive keratectomy (PRK), Laser-assisted in situ keratomileusis (LASIK), Laser-assisted sub-epithelial keratomileusis (LASEK),

Implantable contact lens (ICRS) and Small incision lenticule extraction (SMILE), etc. A study conducted by the U.S. Food and Drug Administration (FDA) showed that 29.6% of eyes with corrected distance visual acuity (CDVA) improved by more than 50 degrees three months and 40.4% of eyes with CDVA improved by more than 50 degrees one year after the procedure compared to the preoperative period [26]. These findings demonstrate the superiority of corneal laser surgery over conventional optical correction in improving visual acuity.

PRK is a commonly used form of corneal excimer laser surgery in which the main steps include laser action on the cornea to reduce corneal refractive power after epithelial tissue removal. The first successful RPK was performed in 1988 and became the first surgical procedure approved by the FDA to treat myopia. RPK and its modifications were the method of choice for low to moderate myopia in its early years and have been widely used internationally. Although RPK has the advantages of fewer flap-related complications, less risk of infection, and the ability to develop an individualized cutting plan, it also has adverse effects such as postoperative corneal irritation symptoms and high postoperative intraocular pressure [25].

LASIK and LASEK, a popular procedure since the 1990s, have gradually replaced RPK as the common method of treating moderate to high myopia. The LASIK procedure involves the creation of a corneal flap with a microkeratome or femtosecond laser and then lifting it up, using an excimer laser to cut and ablate the central exposed area of the corneal stromal bed, and finally re-covering the flap with saline irrigation. Kobashi H et al. showed high safety and efficacy at 24 months after LASIK and that LASIK demonstrated good results in the treatment of myopia up to -8.00 D and astigmatism up to 5.00 D [27]. LASEK is similar to LASIK, with the main difference being that LASEK replaces the cut corneal flap with a corneal epithelial flap, with its main operating plane under the corneal epithelium. Compared to the previous procedure, LASEK ensures a more stable corneal biomechanics, which results in a much higher long-term safety [28]. However, it has also been found that the stability of early postoperative distance visual acuity is worse with LASEK than with LASIK, with a longer recovery period [29].

Implantable contact lens (ICRS) is a relatively new refractive surgery procedure that is performed by implanting a clear ring in the peripheral cornea to reduce refractive error and achieve vision correction. Although some studies have shown that ICRS is effective in the treatment of low to moderate myopia, there are still few studies on its long-term safety and reliability, and further studies and observations are needed.

SMILE is a relatively new refractive procedure and is gradually becoming one of the mainstream myopic refractive procedures in China. Its basic principle is similar to LASIK, but in SMILE, the corneal tissue is cut out by a femtosecond laser and completely removed through a tiny incision. Khalifa et al [30] evaluated the postoperative visual outcomes of SMILE and LASIK and found that SMILE was significantly better than LASIK in terms of safety and efficacy. However, the postoperative complications of SMILE should not be ignored, such as dry eye and corneal irritation symptoms.

3.3.2 IOL implantation with lens

Corneal refractive surgery is an irreversible procedure with strict requirements for corneal thickness; therefore, some patients with high myopia, combined with other ocular complications or thin corneas do not tolerate corneal refractive surgery [31]. For these patients, phakic intraocular lenses (PIOL) is an alternative to optical correction. Depending on the location of the implant, PIOL can be divided into three types of implants: anterior, posterior, and iris-fixed implants. Specifically, in anterior type implantation, the IOL is mainly implanted in the anterior chamber angle, in iris fixation type surgery the IOL is mainly implanted in the mid-periphery of the iris, and posterior chamber PIOL is one of the mainstream ways to treat high myopia, where the IOL is mainly fixed in the ciliary sulcus or in the capsular bag. Although PIOL has the advantages of a wide range of refractive adjustment and good refractive correction, it has a high incidence of corneal complications, a high risk of infection caused by high iris root pressure, and a high rate of pupil distortion, which

makes the procedure much riskier [32]. Therefore, more adequate preoperative evaluation and postoperative follow-up are needed to reduce the incidence of complications.

3.3.3 Scleral surgery

The number of patients with pathological myopia is increasing as the axis of the eye grows at a very rapid rate. Posterior scleral reinforcement (PSR) is a surgical procedure that can effectively slow down the progression of myopia and prevent complications by reinforcing the posterior pole of the sclera to slow down the growth of the eye. The Snyder-Thompson PSR procedure has been shown to be effective and has a generally good patient prognosis [33], but it also has disadvantages such as difficult operation and large surgical incisions. The Nurmamedov NN PSR procedure is simpler and has a smaller incision area, but its long-term clinical results and prognosis need to be further improved [33].

3.4. Traditional Chinese Medicine Treatment

In recent years, in addition to the above methods, Chinese medicine treatment for myopia has also gradually received more and more attention. According to TCM, the main causes of myopia are Yang deficiency, Yin deficiency, Heart and Yang deficiency, Liver and Kidney deficiency, Qi and Blood deficiency, long-term vision injury, and congenital heredity. Its common clinical evidence types are mainly divided into liver and kidney deficiency evidence, heart and spleen deficiency evidence, and liver depression and qi stagnation evidence [34]. Currently, the commonly used TCM treatments include herbal medicine, moxibustion, acupuncture, auricular therapy and tui na therapy.

3.4.1 Chinese herbal medicine therapy

Chinese herbal therapy is the main treatment method for myopia prevention and treatment in TCM, and it has an important role in delaying and preventing myopia. Zefeng Kang et al [35] showed that a remedy consisting of chinkinko seeds, wolfberry, cuscutea seeds, schisandra seeds, and panax ginseng could delay the progression of myopia by inhibiting the expression of VEGF genes. In addition, some findings found that Chinese herbal medicine can effectively improve blood circulation in the eyes of myopic patients, which in turn improves retinal function [36], but its clinical effects still need further study and observation.

3.4.2 Acupuncture therapy

In addition to herbal medicine, acupuncture therapy is one of the main methods of myopia prevention and treatment in TCM. Acupuncture treatment related to myopia was first recorded in the Book of Acupuncture and Moxibustion A.E. [36]. The main acupuncture points related to myopia are Zanzhu, Qiniang, Yuyao, Sizhukong, Chengqi, and Taiyang. The results of a study by Zhaochun Tian [37] and others showed that the overall efficiency of acupuncture to promote recovery of visual acuity was as high as 95%, especially for the treatment of myopia in children.

3.4.3 Ear acupuncture point therapy

Ear acupuncture is one of the more popular methods for treating low myopia in children, and its main modality is the burial of medicine (i.e., Wang Bu Liu Xing Zi) at ear acupuncture points such as Shen Men, Liver, Kidney, Heart, Brain, and New Eye. The results of a study by Li Xinqin et al. showed that the total effective rate of auricular acupuncture treatment for the relief of myopia in children was as high as 88% [38].

3.4.4 Other Chinese medical methods

In addition to the above TCM treatment methods, other commonly used TCM methods are also effective in delaying the progression of myopia, such as tui na therapy, buried thread, and intradermal acupuncture, but their effectiveness and safety still need further clinical observation and research.

3.5. Environmental behavior therapy

In recent years, as the national emphasis on myopia prevention and control among adolescents has been increasing, the role of environmental behavioral therapy in myopia prevention has received more and more general attention [2], such as timely correction of poor eye habits, maintenance of proper sitting posture, and dietary modifications.

In daily life, bad eye habits mainly include excessive eye use, too close to books, and long-term use of electronic books or products. Timely correction of bad eye habits is important to prevent myopia. In addition, poor sitting posture also increases the risk of myopia, so maintaining good sitting posture can greatly reduce the probability of developing myopia. The "three ones" rule (i.e., eyes at least one foot from a book, body at least one fist from a table, and hands at least one inch from the tip of the nose) should always be kept in mind in daily life [39]. Previous studies have shown that the occurrence of myopia is closely related to the deficiency of micronutrients such as carotenoids and lutein in the body [40], therefore, ensuring a balanced diet during the growth period plays an important role in the prevention of myopia.

In addition to the above methods, appropriate participation in outdoor sports is an effective environmental behavioral therapy to prevent myopia. Outdoor exercise can prevent myopia by reducing the overuse of the eyes. Li Liang et al. demonstrated that more than one hour of outdoor exercise per day can significantly reduce the incidence of myopia [41]. In addition to appropriate outdoor exercise, ensuring adequate sleep is also a way to relieve eye strain and reduce the incidence of myopia; therefore, ensuring adequate sleep every day is an important protective factor against myopia.

4. Conclusion

With the popularity of electronic devices, the number of myopia sufferers is increasing year by year, and gradually shows a trend of younger age. Currently, the main methods of treating myopia include five major categories: medication, optical correction, surgery, Chinese medicine, and environmental behavior therapy. Each of these five methods has its own advantages and disadvantages, among which medication, such as low concentration atropine, has been widely used in the treatment of ophthalmic diseases, with the advantages of convenience and speed, and its clinical application is very promising. Optical correction is a non-invasive treatment method, which is safe and effective, but also suffers from the deficiency of poor aesthetics and convenience. Refractive surgery, a popular treatment modality at present, has been proven to be effective in a large number of clinical studies, but there are more postoperative complications associated with surgery, and further observational studies are still needed. Traditional Chinese medicine and environmental behavior therapy have been widely recognized and applied, and are effective when used in combination with other treatment methods. All of the above five treatment methods for myopia have their own advantages and disadvantages. In clinical practice, individualized treatment plans should be developed according to the patient's own characteristics and personal wishes to achieve better treatment results.

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