Introduction

Myopia, a serious and prevalent disorder of the eye, is a consequence of complicated interaction between genetic predisposition and environmental factors [1]. In addition to being an ametropic, a myopic (nearsightedness) the individual has disadvantages of severe complications such as retinal detachment, macular neo-vascularization, dense cataract, and glaucoma that might cause visual impairment and irreversible blindness [2]. Because of increasing prevalence of myopia across many countries, it has become an alarming challenge to vision and development of children with affects on the quality of life and an economic burden with associated cost of treatment. Therefore, studies have focused on the prevention and/or slowing down the myopia progression.

Recent data demonstrates that accommodation appears to have a minor effect on the induction and progress of myopia contrary to previous knowledge [3,4]. The non-accommodative mechanisms such as creating a myopic shift in the peripheral retina and altering corneal shape by optical interventions [3-5], and scleral collagen enhancement by pharmacological agents [3-6] have gained popularity in myopia control, and significant beneficial outcomes have been reported by many researchers. This mini-review aimed specifically at investigating the comparative effectiveness of different interventions systematically and summarizing data on the myopia control in children from recent studies.

Discussion

Previous trials suggested that progressive addition spectacle lenses, bifiocal spectacle lenses, and more outdoor activities have weak effects; peripheral defocus modifying bifocal contact lenses and orthokeratology have moderate effects; muscarinic antagonists have significant effects on myopia progression. However, all of these interventions are superior when compared to single vision spectacle lenses, rigid gas-permeable contact lenses, unifocal soft contact lenses, and placebo [3,4].

Pharmacological control

The pharmacological strategies (especially atropine) seem to show the highest efficacy in myopia control. Although earlier studies have suggested that atropine may achieve this due to its effects on lens accommodation, more recent studies have shown that the main mechanism is via non-accommodative pathway especially acting directly on receptors in the sclera [3,6,7] which slows axial elongation. Nevertheless, unavoidable side effects of atropine such as near vision blurring, photophobia, and glare and rebound after discontinuing treatment which are seen particularly in higher doses have limited its utilization. Even so, low-dose atropine and pirenzepine, a selective anti-muscarinic agent, have still been precise candidates for controlling the myopia progression with lower risk of inevitable side effects [3,4,8]. According to the study of Chia et al. [3] atropine 0.01% eye drops were more effective in myopia control with less visual side effects such as minimal pupil dilation, minimal loss of accommodation, and no near visual loss. The selective muscarinic antagonist pirenzepine was shown to inhibit experimentally induced myopia in animal studies. Qian et al. [9] reported that the mechanism of action of pirenzepine is due to both regulating the balance of matrix destruction in sclera and increasing the tyrosine hydroxylase in retina, which inhibit extension of ocular axial length.

Optical strategies

In terms of optical strategies, peripheral defocus modifying bifocal contact lenses and orthokeratology have been shown to be moderately effective management options in myopia control [4,5]. Peripheral defocus modifying bifocal contact lenses with a center...
distance-periphery reading design, which are worn during the day, alter myopia progression by forming myopic defocus in the peripheral retina that acts as a putative stimulus to slow the axial elongation [4,5,10]. Similarly, orthokeratology lenses, which are worn merely overnight flatten central cornea and reduce relative peripheral hyperopia (creating myopic defocus in the peripheral retina) that acts as a putative signal to slow the axial elongation and myopic progression [4,5,11]. However, the increasing risks of infective keratitis, the cost, and the requirement of ability to fit these lenses are the main restrictions for widespread use of these optical strategies [4,5,10,11].

Progressive addition lenses and bifocals

Progressive addition spectacle lenses and bifocal spectacle lenses have been studied in controlling the myopia, however they have controversial effects [4,8,9,12]. This might partially be explained by the lack of the natural stimulus that is required for slowing down the axial elongation. Because of their top distance-bottom near design they reduce or eliminate the accommodative effort that was previously shown to be ineffective in myopia control.

Outdoor activities

Outdoor activities have been proposed to reduce the risk of myopia progression via stimulation of dopamine release that is known to be able to reduce axial elongation [13,14]. Nonetheless, current studies have indicated that the effect is not clinically meaningful and further studies are required to clarify the value of this option [4].

Future therapies

Mesenchymal stem cells (MSCs) have been extensively used in several clinical fields in order to regenerate or reconstruct the connective tissue. The reported future of MSCs make them excellent candidates for scleral thickening and improvement of biomechanics. Transplanted MSCs would differentiate into fibroblasts and produce collagen and extracellular matrix that reinforce sclera against axial elongation and myopia progression. Additionally, modifying cell signal features by gen activating or vector transduction enables specific release of bio-signal molecules like dopamine, which was shown effective for inhibition of axial elongation and myopia progression, therefore dopamine-producing MSCs will provide mechanical and chemical support to halt myopia progression [15]. The injection of engineered stem cells such as connective tissue-supportive autologous MSCs or dopamine-releasing stem cells within the sub-scleral space with a micro-needle-based, minimally invasive, safe technique is expected to be an attractive concept in the near future.

Another promising strategy is scleral collagen cross-linking performed with glycerylaldehyde, genipin, or riboflavin and ultraviolet-A. According to the study of Wollensak et al. [16]. Scleral collagen cross-linking provided very effective and steady impact on the scleral tissue, increasing the scleral biomechanical strength over a time interval of up to 8 months. They speculated that this new treatment modality without side-effects might become an option for myopia control in children. A recent animal study has confirmed the positive effect of scleral collagen cross-linking for prevention of induced axial-elongation in a rabbit model [17]. However, the effect depends on the concentration and treatment time of additive chemicals, thus future comparative human trials with large sample sizes are required to provide better-quality data.

Conclusion

According to evidence-based meta-analytic trials, anti-muscarinic agents, peripheral defocus modifying bifocal contact lenses, and orthokeratology were found to be the most effective modalities for myopia control. However, to achieve the maximum control of myopia, it is very important to select the most effective treatment for each patient depending on the life style and individual properties. Future head-to-head comparisons in addition to intervention versus control studies are also important for planning best strategies for patients.

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