ARTYKUŁ PRZEGLĄDOWY REVIEW ARTICLE
DOI: 10.24292/01.OT.310322.2

Myopia differential diagnosis

Katarzyna Perz-Juszczyszyn

Department of Optometry, Sub-Faculty of Eye Disease and Optometry, Medical University in Poznan
Head: prof. Marcin Stopa, PhD, MD

HIGHLIGHTS

It is important to properly classify myopia, know its connections with complex syndromes, detect it as early as possible, correct it properly.

ABSTRACT

Due to the prevalence and the possibility of myopia progression, myopia is currently of particular interest to many specialists in both the field of optometry and ophthalmology. In the initial diagnosis of the patient, it is important to determine whether the refractive error is isolated or if it coexists with other eye disorders/diseases or general health problems. This refractive error can be divided into axial and refractive myopia. In the latter case, the change in refraction may result from too great curvature of the cornea in relation to the length of the eyeball, or an increase in the optical curvatures other than the anterior surface of the cornea, or an increase in the refractive index of at least one of the optical structures, or a shallower anterior chamber of the eye. It is also worth distinguishing myopia associated with complex syndromes.
Uncorrected myopia can significantly hinder daily functioning. It is therefore important to detect it as early as possible, correct it properly.

Key words: myopia, differentia diagnosis, axial myopia, refractive myopia

INTRODUCTION

Refractive errors are due to the biological diversity of the general population while the key factor for refractive state is the relationship between the optical power of the eye and its axial length. Moreover, there are several other factors, both external and genetic, potentially contributing to the occurrence and development of refractive errors, including concomitant ocular pathologies and systemic diseases [1–4].

Currently, among other refractive errors, myopia is raising the highest concern. Due to high incidence, over the last years eye care specialists have been searching for the most efficient strategy of slowing down myopia progression. Satisfactory effect against its progression has been observed for ortho-K lenses and 0.01% atropine [5, 6]. A technological novelty designed to correct and slow down myopia progression is the MiyoSmart spectacle lens. It has prescription power distributed all over the surface with a central treatment zone incorporating the DIMS (defocus incorporated multiple segments) technology [7].

In each case of myopia, it seems reasonable to establish whether it is as a standalone refractive error or a consequence of other ocular disorders and/or general diseases. Additionally, it should be taken into consideration that certain ocular and general diseases are related to higher incidence of myopia.

Myopia is a complex disorder, which is reflected by a wide variety of classification systems, which include refractive error, patient's age at onset, potential progression over time as well as its relations to biometric and refractive characteristics of the eye [2, 8].

In the process of differential diagnostics, it is reasonable to adopt certain criteria to classify the disorder as:

1. axial myopia
2. refractive myopia:
    a. curvature-related myopia, i.e. resulting from excessive corneal curvature as compared to axial length
    b. curvature-related myopia, i.e. being a consequence of increased refractive curvatures in the optical system (other than corneal surface curvature)
    c. myopia related to increased refractive index of at least one refractive structure of the eye
    d. anterior chamber myopia due to shallowing of the anterior chamber.

Differential diagnosis should also include the characteristics of myopia: stable, progressive or transient. It should also be mentioned that myopia may be related to complex disease syndromes [2].

AXIAL MYOPIA

Based on the Gullstrand eye model, it may be assumed that the average axial length of the eye is 24.4 mm. It should be mentioned that certain patients will show increased axal lengths as they age. Risk factors for onset and progression of axial myopia are, among others, genetic (including ethnicity), environmental (including sustained accommodative effort during near work) and retinal defocus due to undercorrected refractive error. A higher risk of myopia progression is related to earlier onset and baseline refractive error [9].

Axial lengths which exceed 26 mm and refractive errors over -6.00 D are considered cases of high myopia which affects 2% of Western Europeans and North Americans and even up to 10% of East Asians. Excessive and progressive axial elongation is termed "degenerative myopia" and may lead to degenerative changes caused by abnormal stretching of the ocular tissues, such as:

- RPE thinning with major choroidal vessels becoming noticeable
- focal areas of choroido-retinal atrophy
- changes in the optic disc and the peri-papillary region
- lattice degeneration
- lacquer cracks (within the RPE/Bruch's membrane/choriocapillaris complex)
- subretinal hemorrhages
- Fuchs spot
- posterior staphyloma
- rhegmatogenous retinal detachment
- choroidal neovascularization (CNV)
- macular schisis
- peripapillary detachment
- cataract
- glaucoma
- amblyopia
- lens subluxation [10].

Increased axial length may be secondary and induced by compression from rings implanted during certain surgical procedures used to treat retinal detachment.

Excessive eye growth is also related to congenital connective tissue disorders characterized by genetically conditioned impairments of structural protein biosynthesis and/or metabolism [11]. Therefore, the risk of myopia onset and progression affects patients with Ehlers-Danlos syndrome who exhibit excessive connective tissue tensility and a molecular defect of type III collagen synthesis. Mafran syndrome often leads to severe ocular symptoms, including high myopia resulting in complications such as lattice degeneration and retinal detachment. The syndrome is a hereditary connective tissue disease manifested as structural and functional changes of fibrillin 1, i.e. a glycoprotein essential for the formation of microfibrils. Due to a significant number of potential genetic defects of fibrillin-coding gene, Marfan syndrome is characterized by diverse clinical manifestations [12, 13].

REFRACTIVE MYOPIA

This type of myopia occurs as a result of excessive power of the optical system, as compared to the eye's axial length. The causes of this condition may vary.

Myopia resulting from excessive corneal curvature

Curvature-related myopia occurs due to excessive corneal curvature while the axial length remains at physiologically normal levels. It may constitute a variation of refractive error without any other concomitant abnormalities.

Its incidence is particularly high among preterm infants. In prematurity, the causes of myopia include a combination of steep corneal curvature and low axial length [14]. What is more, in this population cases of severe retinopathy of prematurity may lead to fibrosis retrolentalis i.e. the growth of a fibrotic masses posterior to the crystalline lens which start pushing the lens-iris diaphragm in the anterior direction. Consequently, an exacerbated myopic refractive shift will occur with potential risk of glaucoma.

Myopia caused by ciliary muscle contracture

The optical power of the eye may also increase as a consequence of ciliary muscle contracture which is usually secondary to permanent and excessive stimulation of the parasympathetic system. In such cases, underlying severe systemic pathologies are rare and the causes of accommodative effort include the following:

- excessive stimulation of accommodation, which is usually associated with prolonged near work, systemic infections, or psychogenic factors
- empty space myopia/nocturnal myopia (noticeable in certain cases) due to sustained accommodative effort in dim light or when no accommodative stimulus is present, which amounts to approx. -1.00 D
- excessive accommodative convergence which may be induce in order to maintain fusion in cases of exophoria with fusional convergence insufficiency
- spasm of the near reflex (SNR) co-occurring with a diffused reflex involving accommodative effort, convergence excess, and pupil constriction
- sympathetic paresis resulting in non-physiological dominance of the parasympathetic system at distance, e.g. in patients with Horner's syndrome and in certain cases of migraine
- brain tumors
- *Myasthenia gravis*
- myotic medication intake (carbachol, physostigmine, neostigmine, demecarium)
- fly agaric (*Amanita muscaria*) poisoning which causes the so-called mykoatropine syndrome manifested as pupil dilation, inhibition of exocrine gland secretion, impaired body temperature regulation, erethism, anxiety, hallucinations, and other psychotic symptoms [15, 16].

Myopia resulting from increased refractive index of the crystalline lens

An crucial factor for the eye's refractive state are the refractive indexes of individual structures forming its optical system which, in turn, depends on their curvatures and indexes of the optical media.

Due to the aging process, the nucleus of the crystalline lens becomes stiffer but also accumulates larger quantities of urochromatic pigment, which causes lens discoloration (initially to amber and subsequently to brown). The process influences the refractive index of the lens, causes a myopic refractive shift and increases spherical aberrations. Consequentially, certain senior patients become able to read at near without spectacle prescription. Nuclear cataract, which has a similar manifestation, may also be secondary to hypoactivity of parathyroid glands [13].

The underlying causes of altered refractive index of the crystalline lens also include systemic diseases. The most prevalent problem in the ageing population is diabetes. It is a chronic metabolic disease characterized by hyperglycemia, resulting from impaired insulin production and/or cell resistance to insulin, with characteristic long-term complications such as micro and macroangiopathy. Uncontrolled diabetes and fluctuating blood glucose levels are associated with unstable and transient refractive changes. Myopic refractive fluctuations are related to hypoglycemia which results in transitional increase in hydration of the crystalline lens and consequently causes an increment of its refractive index. The refractive changes, amounting to several diopters, may be the initial symptoms of undiagnosed diabetes. Subsequently, refraction stabilizes within approximately one week from the initiation of treatment since a normal blood glucose level is reached [17, 18].

Increased refractive index of the crystalline lens may also be observed in the following cases:

- pregnancy induced hypertension manifested as blood hypertension, proteinuria, and generalized oedema
- dysentery, with etiology including bacterial (*Shigella*) infection, which causes fever co-occuring with abdominal pain, vomiting, and bloody diarrhea
- malaria, a common contagious disease caused by *Plasmodium* infection, typically characterized by fever, anemia and headaches but also severe water and electrolyte imbalance [13, 15].

Anterior chamber myopia

In certain cases, both the axial length and the optical power of the eye, being the sum of individual contributors in the optical system, remain within normal physiological limits. However, the mutual relations between the optical structures may reduce the depth of the anterior chamber and, consequently, cause a myopic refractive shift. The above condition may occur in cases of ocular trauma with ante-

rior dislocation of the crystalline lens as well as primary congenital glaucoma (often associated with developmental disorders affecting the filtration angle), childhood glaucoma and juvenile glaucoma.

Some authors also reported cases of myopia onset induced by intake of certain medications, which was probably caused by increased curvature of the refractive surface of the lens due to ciliary body oedema. Thus, the relation between the axial length and the optical power of the eye became abnormal [15].

Some children may manifest myopia due to underlying contagious childhood diseases such as rubella, varicella, measles and pertussis. However, the etiology of refractive error in such cases remains unclear [19].

HEREDITARY MYOPIA

Certain cases of myopia may have hereditary etiology but the models of inheritance may vary. Hereditary myopia is often associated with impaired development of the ocular structures such as microphthalmia, microcornea, pupillary displacement, nyctalopia, and achromatopsia. It may be potentially related to underlying systemic diseases such as cochlear deafness or epiphysis dysplasia. Genetically hereditary myopias include:

- autosomal recessive (AR) cochlear deafness with myopia and mental impairment;
- AR dysplasia of femur head epiphysis with myopia and deafness
- autosomal dominant (AD) multifocal epiphysis dysplasia with myopia and conductive deafness
- AD microcornea with myopia and cataract
- AD microphthalmos with myopia and pupillary displacement
- AR or AD, or X-linked myopia
- X-linked nyctalopia and myopia
- AR nyctalopia with high myopia
- AR achromatopsia with myopia (*Pingelopese blindness*) [15].

DISEASE SYNDROMES RELATED TO MYOPIA

There is a long list of various disease syndromes in which myopia is an element of the clinical manifestation.

Albinism is a genetically conditioned heterogenous group of disorders affecting melanin synthesis and caused by deficiency or depletion of tyrosinase, which serves as a catalyzer in tyrosine to melanin conversion. Ocular symptoms are present only in cases of ocular albinism while oculocutaneous albinism causes ocular and skin symptoms. Tyrosinase-negative albinism is manifested by particularly poor visual acuity due to hypoplasia of the fovea, horizontal pendular nystagmus, iris transillumination caused by lack of pigmentation, pigment depletion in the fundus with visible choroidal vessels, decreased number of cross-linked fibers in the chiasm, strabismus, and refractive errors including myopia [10, 13].

Gyrate atrophy of the retina and choroid is a metabolic disease caused by mutation of the OAT gene which encodes ornithine aminotransferase, i.e. the enzyme necessary to metabolize ornithine. The mutation leads to increased levels of ornithine in plasma, urine, cerebro-spinal fluid, and aqueous humor. The clinical manifestation includes round areas of choroid atrophy which gradually become confluent and progress from the periphery towards the posterior pole. However, the foveal area remains unaffected for a relatively long time. It is associated with myopia, nyctalopia and, in the long term, a significant decrease of visual acuity to the level of legal blindness between the 4th and 6th decade of life, which is due to geographical atrophy of the retina and choroid [10].

Down's syndrome is a genetic disorder caused by the presence of a third copy of chromosome 21 and associated with several characteristic morphological features and mental retardation. Also, it is commonly associated with ocular abnormalities such as upslanting palpebral fissures, chronic blepharitis, ectropion, epicanthal folds, strabismus, nystagmus, and lens opacification (blue spots). Patients also show predispositions to keratoconus, iris hypoplasia and refractive errors, including myopia [10, 12].

Fetal alcohol syndrome (FAS) affects children who, during the fetal growth, were exposed to large doses of alcohol consumed by the mother. Several developmental disorders occur due to the toxic effect of alcohol and become noticeable in the facial morphology. These include flattened face, small head circumference, short nose with low nasal bridge, ear lobe malformations with low position of the ears, and micrognathia. The negative impact of alcohol is particularly noticeable in the nervous system leading to a significantly reduced intellectual potential in children with FAS. Moreover, common visual system abnormalities include short palpebral fissures, epicanthal folds, hypertelorism, iris coloboma, strabismus, ptosis microphthalmia, structural abnormalities of the fundus, and increased risk of myopia [20].

Marfan syndrome and Ehlers-Danlos syndrome mentioned above also show characteristic relations to myopia. However, myopia is described as a component of several less common complex disease syndromes and disease, including:

- Aberfeld syndrome
- Alport syndrome
- Bloch-Sulzberg syndrome
- Cri du Chat syndrome
- Cornelia de Lange syndrome
- Cohen syndrome
- Aland syndrome

- Kartagener syndrome
- Ito syndrome
- Kniest syndrome
- Marshall-Smith syndrome
- Noonan syndrome
- Pierre Robin syndrome.

CONCLUSION

Nowadays, myopia is a common refractive error which, if uncorrected, may lead to significant impairment of everyday functioning. Therefore, it is important to diagnose myopia as early as possible, prescribe appropriate vision correction and plan patient management based on methods which help slow down its progression A wider perspective on myopia and its potential relations with other visual system disorders and/or general diseases may be helpful in practice and contribute to a more efficient workflow thus bringing additional benefits to patients.

CORRESPONDENCE
Katarzyna Perz-Juszczyszyn
Department of Optometry, Sub-Faculty of Eye Disease and Optometry, Medical University in Poznan
60-806 Poznań, ul. Rokietnicka 5D
e-mail: kperz@ump.edu.pl

ORCID
Katarzyna Perz-Juszczyszyn – ID – https://orcid.org/0000-0001-7877-0871

References

1. Steiger A. Die Entstehung der Spharischen Refracktionen des Menschlichen Auges. Karger, Berlin 1913.
2. Benjamin WJ, Borish IM. Borish's clinical refraction. Butterworth & Heinemann, 2006.
3. Angle J, Wissmann DA. A statistical analysis of the Biological Theory of spherical error of refraction. Am J Optom Physiol Opt. 1979; 56(5): 309-14.
4. Wu PC, Huang HM, Yu HJ et al. Epidemiology of Myopia. Asia Pac J Ophthalmol (Phila). 2016; 5(6): 386-93.
5. Brennan NA, Toubouti YM, Cheng X et al. Efficacy in myopia control. Prog Retin Eye Res. 2021; 83: 100923.
6. Grzybowski A, Kanclerz P, Tsubota K et al. A review on the epidemiology of myopia in school children worldwide. BMC Ophthalmol. 2020; 20(1): 27.
7. Lam CSY, Tang WC, Tse DY et al. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol. 2020; 104(3): 363-8.
8. Grosvenor T. A review and a suggested classification system for myopia on the basis of age-related prevalence and age of onset. Am J Optom Physiol Opt. 1987; 64(7): 545-54.
9. Skuta GL, Cantor LB, Weiss JS. Optyka kliniczna (BCSC cz. 3). Elsevier Urban & Partner, Wrocław 2008.
10. Bowling B, Kanski JJ. Okulistyka kliniczna. Wydanie V. Edra Urban & Partner, Wrocław 2017.
11. Zimmermann-Górska I. Zespół Ehlersa i Danlosa. https://www.mp.pl/pacjent/reumatologia/choroby/142137,zespol-ehlersa-i-danlosa.
12. Kański JJ, Nischal KK. Okulistyka. Objawy i różnicowanie. Urban & Partner, Wrocław 2000.
13. Kokot F. Choroby wewnętrzne. PZWL, Warszawa 2000.
14. Banks MS. Infant refraction and accommodation. Int Ophthalmol Clin. 1980; 20: 205-32.
15. Roy FH. Ocular Differential Diagnosis. Lippincott Williams and Wilkins, 1997.
16. Ostrowska M. Miastenia. https://www.mp.pl/pacjent/neurologia/choroby/150964,miastenia.
17. Gwinup G, Villarreal A. Relationship of serum glucose concentration to changes in refraction. Diabetes. 1976; 25(1): 29-31.
18. Kastelan S, Gverović-Antunica A, Pelcić G et al. Refractive changes Associated with diabetes mellitus. Semin Ophthalmol. 2018; 33(7-8): 838-45.
19. Guggenheim JA, Williams C. Childhood febrile illness and the risk of myopia in UK Biobank participants. Eye. 2016; 30(4): 608-14.
20. Wozniak JR, Riley EP, Charness ME. Clinical presentation, diagnosis, and management of fetal alcohol spectrum disorder. Lancet Neurol. 2019; 18(8): 760-70.

Conflict of interest:
None.

Financial support:
None.

Ethics:
The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.