

Sclera as the target tissue in progressive myopia*

Twardówka jako tkanka docelowa w postępującej krótkowzroczności

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SUMMARY

Introduction: The aim of the study was to study the eye corneal shell and connective tissue (CT) system in children with acquired and congenital progressive myopia, and to identify the informative diagnostic criteria of weakened supporting function of the sclera.

Material and methods: 155 children aged 9–17 were examined: 18 had emmetropia or hyperopia, 20 – low, 32 – moderate and 85 – high myopia. 32 children had complicated myopia (CM) due to peripheral retinal degeneration (PRD). Corneal hysteresis (CH), scleral acoustic density (SAD), X-ray vertebral topography, plantography, joint hypermobility, serum cortisol (SC), and autonomic balance were measured.

Results: Corneal hysteresis, mmHg and SAD, rel. units (mean \pm SE) were lower if myopia was higher: in low myopia, CH was 13.0 ± 0.3 , in moderate myopia, 11.9 ± 0.3 , in high myopia, 10.7 ± 0.3 ; SAD was resp. 215.9 ± 5.2 , 204.9 ± 3.7 and 192.8 ± 5.8 (#: $p < 0.05$ with regard to low myopia). The lowest CH (10.3 ± 0.4) and SAD (186.5 ± 7.3) were found in acquired CM. Congenital myopia with PRD showed CH and SAD greater than in acquired CM ($p < 0.05$). Serum cortisol (nmol/L) in hyperopia

was 335.8 ± 40.9 and dropped with higher myopia: in low myopia – 290.7 ± 58.6 , in moderate – 250.9 ± 26.4 , in high – 243.9 ± 20.5 . The lowest SC was found in acquired CM, consistent with CH and SAD. Connective tissue dysplasia progressed with higher myopia: it was found in 76.9% of children with low, 82.4% with moderate, 89.2% with high acquired myopia, and 91.7% with congenital myopia. Biomechanical defects of CT and hormonal imbalance were combined with vegetative nervous system (VNS) imbalance: in high myopia only 20.5% of children were eutonic, 61.5% – sympathotonic and 17.5% parasympathotonic.

Conclusions: School age children with progressive myopia showed biomechanical abnormalities of the corneal sclera, along with CT dysplasia, decreased SC and imbalanced VNS, more pronounced in acquired complicated myopia. Our findings contribute to the understanding of myopia pathogenesis and to the diagnostic/prognostic evaluation of myopic children, in particular when deciding whether sclera-strengthening intervention is needed.

Key words: myopia, sclera, children, connective tissue, biomechanical parameters, cortisol, autonomic system.

STRESZCZENIE

Wstęp: Celem pracy było zbadanie osłony rogówkowo-twardówkowej i systemu tkanki łącznej (CT) u dzieci z nabytą oraz wrodzoną krótkowzrocznością postępującą, a także zidentyfikowanie informacyjnych kryteriów diagnostycznych wspomagających funkcję twardówki.

Materiał i metody: Przebadano 155 dzieci w wieku 9–17 lat. 18 miało emetrię lub hiperopię, 20 miało niską krótkowzroczność, 32 średnią i 85 wysoką krótkowzroczność. 32 dzieci miało krótkowzroczność powikłaną (CM) z powodu obwodowego zwyrodnienia siatkówki. Mierzono histerezę rogówki (CH), gęstość akustyczną twardówki (SAD), topografię kręgosłupa promieniami X, plantografię, łączną hiper mobilność, poziom kortyzolu w surowicy krwi (SC) i autonomiczny balans.

Wyniki: Histereza rogówki, mmHg i SAD (jednostki względne; średnia \pm SE) były niższe w wysokiej krótkowzroczności; w niskiej krótkowzroczności CH wynosiła $13,0 \pm 0,3$, w średniej krótkowzroczności $11,9 \pm 0,3$, w wysokiej krótkowzroczności $10,7 \pm 0,3$; SAD wynosił odpowiednio $215,9 \pm 5,2$, $204,9 \pm 3,7$

i $192,8 \pm 5,8$ (#: $p < 0,05$ dotyczy niskiej krótkowzroczności). Najniższe CH ($10,3 \pm 0,4$) i SAD ($186,5 \pm 7,3$) znaleziono w nabytej CM. Wrodzona krótkowzroczność z PRD wykazywała CH i SAD większe niż nabyta CM ($p < 0,05$). Poziom kortyzolu w surowicy krwi (nmol/L) w hiperopii wynosił $335,8 \pm 40,9$ i spadał z wysokiej krótkowzroczności: w niskiej krótkowzroczności – $290,7 \pm 58,6$, w średniej – $250,9 \pm 26,4$, w wysokiej – $243,9 \pm 20,5$. Najniższe SC znaleziono w nabytej CM, złożonej z CH i SAD. Postęp dysplazji CT z wysoką krótkowzrocznością stwierdzono: u 76,9% dzieci z niską, 82,4% ze średnią, 89,2% z wysoką krótkowzrocznością nabytą i 91,7% z krótkowzrocznością wrodzoną. Biochemiczne defekty CT i hormonalne zaburzenie balansu były związane z zaburzeniami balansu w wegetatywnym układzie nerwowym: w wysokiej krótkowzroczności jedynie 20,5% dzieci było eutonicznych, 61,5% – sympatykotonicznych i 17,5% parasympatykotonicznych.

Wnioski: Uczniowie z postępującą krótkowzrocznością wykazują biochemiczne zaburzenia rogówkowo-twardówkowe wraz z dysplazją CT, spadkiem SC i zaburzeniem balansu

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wegetatywnego układu nerwowego, bardziej wyrażone w nabytej krótkowzroczności powikłanej. Nasze obserwacje przyczyniają się do zrozumienia patogenezy krótkowzroczności i diagnostyczno-prognostycznej oceny krótkowzroczności

dzieci, a zwłaszcza wówczas, gdy potrzebne jest wzmocnienie twardówki.

Słowa kluczowe: krótkowzroczność, twardówka, dzieci, tkanka łączna, parametry biochemiczne, kortyzol, system autonomiczny.

INTRODUCTION

Degenerative myopia is a significant cause of vision loss; yet there is no accepted way of controlling its causative phenotype – progressive high axial myopia [1, 2, 3]. The pathogenesis of progressive myopia is controversial; however, it is generally agreed that one important feature of severe myopia is a pathologic change in the biomechanically weakened sclera with its progressive thinning, probably due to a disturbed feedback mechanism of emmetropization and/or connective tissue (CT) metabolic disorders [4, 5].

The pathologic changes of myopic sclera include disruption of the packing of fibrils and fibres, a decrease in the average diameter of the cross section of fibrils, an increased fraction of soluble collagen, a reduction in transverse cross-linking of the scleral collagen, and a decrease in its resistance to proteolytic enzymes [6, 7, 8, 9, 10, 11, 12]. These changes result in progressive deformation of the scleral membrane and its pathologic stretching, which in turn contributes to pathologic stretching of the choroid and retina, and an irreversible decline in visual functions [6, 7].

Previous biomechanical studies showed that the stress-strain parameter values and Young's modulus of the sclera of myopic human eyes are significantly lower than those of emmetropic subjects of the same age [8]. Accordingly, several methods of surgical scleroplasty for scleral strengthening have been developed. These methods include injections of a polymeric composition, which creates a layer of foamed gel under Tenon's capsule, gradually replaced by additional CT [13], and so-called scleral reinforcement operations in which donor sclera strips or synthetic bands are placed around the back of the globe and sutured to the sclera to provide scleral support and reduce the progression of axial elongation [7, 14, 15, 16].

Numerous reports from eye surgeons who have worked during the past few decades, and our own data, testify to the fact that after such surgery myopia and the axial length of the eye remain stable for one year in 85–96% of cases, depending on the patient's age and his/her initial rate of myopia progression. In the longer perspective, however, a considerable number of patients, primarily children, manifest progression relapse (up to 60% over the period of 7 to 10 years): generally, the younger the patient, the more likely the relapse [15, 17, 18, 19, 20].

At present, a new approach is being actively developed aimed at changing the state of scleral collagen to normalize the mechanical properties of the myopic sclera and/or halt its further degradation. Basically, this approach consists in the strengthening of the three-dimensional network of collagen in the scleral tissue. One way of doing this is UV-initiated cross-linking in the presence of a photosensitizer, riboflavin [21, 22].

An even more promising nonsurgical method for strengthening scleral tissue, i.e. for improving its mechanical and enzymatic stability, is the formation of transverse cross-linking of collagen fibres with the help of bifunctional reagents, such as simple sugars, which are low-toxic compounds not requiring hard physical exposure [23, 24].

Sclera strengthening by cross-linking has not been implemented in clinical practice so far. It is clear, however, that for this approach to be effective it should be used in cases of maximally reliable individual indications. Of course, the same is true of the scleroplastic operations that have been clinically used for a long time now. These indications must rely on objectively measured parameters that reflect the state of the support facilities of the sclera.

The techniques that can now be applied to assess the biomechanical parameters of the corneoscleral capsule in the clinic include examinations achievable with an ocular response analyzer, and measurements of scleral acoustic density (SAD).

Ocular response analyzer enables measuring several new parameters: corneal compensated intraocular pressure, corneal hysteresis (CH), and the corneal resistance factor, which seems promising for studies on myopia [25]. Our own previous studies showed that CH is relevant for the biomechanical properties of both the cornea and the sclera [26].

Scleral acoustic density, the parameter proposed by *Avetisov et al.* [27], can be useful for the indirect assessment of biomechanical properties of the sclera. There are also reasons to believe that indirect information on the state of the scleral tissue can be obtained by dedicated evaluation of the general condition of the body's connective tissue, especially during myopia progression in children and adolescents.

Integrated clinical and biochemical studies reveal metabolic disorders of the body's CT system during myopia progression [28]. It has been established that myopic children and adolescents develop biomechanical disorders of the musculoskeletal system much more frequently. The disorders include flat feet, scoliosis, gastroparesis and other symptoms of CT dysplasia [28, 29]. The overwhelming majority of high congenital myopia cases are shown to reveal pathology of the musculoskeletal system. Adult myopic patients develop plural symptoms of connective tissue hyperelasticity, including joint hypermobility syndrome [30]. Our studies have shown that this syndrome is also present in adolescents who have progressive myopia [29].

These data enable us to view the sclera of the myopic eye – its connective tissue membrane – as the target tissue, since it is exactly the sclera that manifests the most conspicuous general dysplastic disorders which lead to a noticeable weakening of its support function.

Possibly, hormonal shifts (in particular, cortisol imbalance) are among the factors contributing to disorders of general CT and scleral collagen structure metabolism [31]. The first results of our study into the hormonal status of adolescents with progressing myopia corroborate this hypothesis as they reveal an imbalance of both sex (testosterone and estradiol) and glucocorticoid hormones (primarily, cortisol) [32]. Little research has been done so far on another factor, which may invoke the development of general and topical disorders of the biomechanical properties of connective tissue in children and adolescents with progressive myopia: their vegetative status. The reason for this is the known fact that the vegetative nervous system (VNS) plays a significant role in the processes of body adaptation, including CT development. There have been several individual studies that note VNS imbalance in myopic children with accommodation disorders [33, 34]. It should be stressed that dysplastic syndrome is predominantly accompanied by sympathicotonia, while healthy children develop eutonia or vagotonia more frequently [35]. In Russia VNS balance is often assessed with the help of the Kérdö vegetative index (KI), calculated from diastolic pressure and pulse frequency [36]. Over the past decades there has been an increasing awareness of the role that the autonomic nervous system plays in a diversity of diseases. Because of this, both Russian and Western authors report the use of parameters similar to KI in monitoring VNS state: like KI, they are based on the characteristics of the cardiovascular system [37, 38, 39] and recognized by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology [40]. Since sympathicotonia and parasympathicotonia differ in the intensity and the direction of metabolic processes (which mainly consist in oxidation and acid-base balance), their correlation determines the oxygen demand of the body. Hence, the parameters characterizing cardiac activity, blood circulation and oxygen transport reflect the state of VNS. Since KI is definitely associated with the presence of dysplastic syndrome, it seems reasonable to measure it in children and adolescents with progressing myopia and to see how it is connected with the local and general parameters of biomechanical CT disorders observed in this condition.

The purpose of this paper is to study the biomechanical parameters of the corneoscleral ocular shell and connective tissue system in children and adolescents with acquired and congenital progressive myopia, and to identify the informative diagnostic criteria of the weakened supporting function of the sclera.

MATERIAL AND METHODS

The study comprised 155 Caucasian children aged 9–17 (13.4 ± 2.1 years), 76% of them were 12–14 years old, examined under the same conditions in our Department of Refraction Pathology. All patients underwent auto-refraction (Huvitz MR-3100P, Korea) with cyclopentolate 1%. According to their cycloplegic refraction values 18 had emmetropia or low hyperopia

(from +0.5 to +3.5 D); 20 – low myopia (from –0.5 to –3.5 D); 32 – moderate myopia (from –3.75 to –6.25 D); 85 – high myopia (from –6.5 to –17.5 D). Among the patients with high myopia 49 had acquired myopia (mostly developed at 3–8 years) and 36 had congenital progressive myopia. Congenital myopia was diagnosed if its onset happened before the age of 3 years and in the presence of a typical eye fundus pattern (altered shape of the optic disc, its abnormal size, hyperpigmented macular area, presence of specific peripheral chorioretinal dystrophies) and slightly reduced corrected visual acuity [4, 38]. 32 children (20.6%) had myopia complicated by various forms of peripheral vitreochoreoretinal degenerations (PVCRD), including lattice degeneration, retinal white without pressure, isolated holes and breaks, hyperpigmentation. The average progression rate of all the examined myopic children was 0.89 ± 0.21 D/year.

Corneal hysteresis (ocular response analyzer, Reichert, Buffalo, NY) and SAD were considered to be local biomechanical parameters. Ocular response analyzer was also used to measure central corneal thickness. Instead of the previously used ultrasonic scanning device Ophthascan-B (Biophysic Medical) [24] we applied in our study a new ultrasound system (Voluson 730 Pro, Oceanside, CA) with a 10 to 16 MHz linear probe, which allows a more accurate measurement of SAD (Fig. 1).

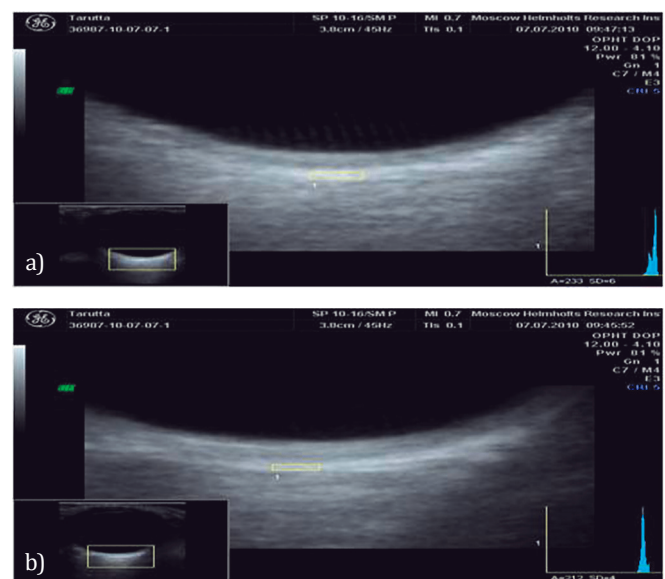


FIGURE 1. Sclera acoustic density measurement: a) emmetropic eye, b) myopic eye

To assess the general biomechanical disorders of CT the children were seen by an orthopaedic doctor who undertook an objective instrumental examination using spinal x-ray and “iStep” plantography as a valuation method of flat-footedness level. A set of criteria by C. Carter, J. Wilkinson [39], modified by P. Beighton, F.T. Horan [40], was used to detect and quantitatively measure possible symptoms of joint hypermobility, which was estimated using five parameters: 1) ability to put one’s hands flat on the floor while keeping one’s knees straight; 2) ability to bend one’s elbows backwards by more than 10°;

3) ability to bend one's knees backwards by more than 10°; 4) ability to passively flex one's thumb back on to the front of one's forearm; 5) ability to passively flex one's finger up to the back on one's hand at more than 90° (Fig. 2).

A fasting blood test for serum cortisol was taken in the morning using generally accepted practice. The normal values (not considering the refraction) vary between 138 and 635 nmol/L for children and teenagers under 16 years of age [41, 42].

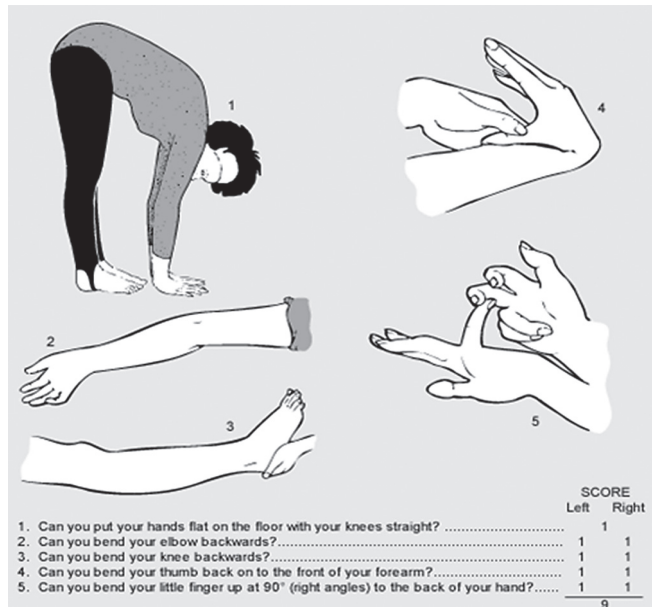


FIGURE 2. Symptoms of joint hypermobility: a set of criteria by C. Carter, J. Wilkinson [42], modified by P. Beighton, F.T. Horan [43]

To calculate the Kérdő vegetative index, diastolic pressure (d) and heart rate (p) were measured. The formula used was $KI = (1 - d/p) \times 100$. In the case of full vegetative equilibrium (eutoxia) the value of KI is close to zero. If sympathetic influences

prevail (sympathicotonia), the KI value is positive, whilst in the case of the prevalence of parasympathetic influences KI is negative. The experience shows that in middle-aged people with balanced vegetative functions the numerical values of the diastolic pressure in mmHg and of pulse rate per minute are approximately equal [32, 33].

RESULTS

As follows from the analysis of the two biomechanical parameters (CH and SAD) of eyes with progressing myopia of varying degrees, their values manifest a monotonous and statistically reliable decrease as myopic refraction grows (Table 1).

As central corneal thickness did not differ in refractive groups we can conclude that CH decrease is not connected with central corneal thickness. At the same time axial length in patients with moderate and high myopia was statistically higher than that in patients with low myopia, emmetropia or low hyperopia. This means that the decrease of CH and SAD values in moderate and high myopia are mainly caused by myopic changes in the sclera connected with eye elongation and dystrophic process developing in its connective tissue structures.

These results corroborate the idea that both parameters could appropriately be used to objectively monitor the clinical state of the myopic sclera and assess the severity of the myopic process.

In order to see whether it would also be possible to use CH and SAD as individual diagnostic and prognostic criteria we decided to analyze both parameters on groups of patients with acquired and congenital myopia specifically for complicated and uncomplicated categories (Table 2).

The comparative analysis of acquired and congenital myopia revealed differences between the parameters studied (Table 2). Congenital myopia is characterized by somewhat higher CH and SAD values than acquired myopia ($p < 0.05$). This means

TABLE 1. Axial length, central corneal thickness, corneal hysteresis and scleral acoustic density parameters in children with varying clinical refraction values

Parameter	Emmetropia and low hyperopia	Low myopia	Moderate myopia	High myopia
	mean ± st. err			
Axial length (mm)	22.1 ± 1.0	23.9 ± 0.9	25.2 ± 0.8*	27.1 ± 0.9**
Central corneal thickness (mkm)	541.0 ± 9.5	553.5 ± 6.0	556.5 ± 5.5	545.6 ± 5.9
Corneal hysteresis (mmHg)	13.5 ± 0.8	13.0 ± 0.3	11.9 ± 0.3*	10.7 ± 0.3**
Sclera acoustic density (U)	225.0 ± 1.01	215.9 ± 5.2	204.9 ± 3.7*	192.8 ± 5.8**

* the difference as compared to hyperopia is significant ($p < 0.05$)

** the difference as compared to low and moderate myopia is significant ($p < 0.05$)

TABLE 2. Corneal hysteresis and scleral acoustic density parameters in children with high acquired and congenital myopia developing with or without complications

Parameter	High acquired myopia		High congenital myopia	
	uncomplicated	complicated	uncomplicated	complicated
mean ± st. err				
Corneal hysteresis (mm Hg)	10.9 ± 0.5	10.3 ± 0.4	11.9 ± 0.3*	11.3 ± 0.5*
Sclera acoustic density (U)	201.6 ± 4.8	186.2 ± 7.3**	207.2 ± 2.7	193.7 ± 6.6**

* the difference as compared to the respective parameter of acquired myopia is significant ($p < 0.05$)

** the difference as compared to the respective parameter of uncomplicated myopia is significant ($p < 0.05$)

TABLE 3. Serum cortisol level (nmol/L) of children with various clinical refractions

Emmetropia and hyperopia	Acquired myopia					High congenital myopia		
	low	moderate	high			all	uncomplicated	complicated
			all	uncomplicated	complicated			
mean ± st. err								
335.8 ±40.9	290.7 ±58.6	250.9 ±26.4*	243.9 ±20.5*	247.6 ±30.1*	236.3 ±29.3*	339.4 ±33.2**	413.7 ±48.8**	287.4 ±38.6***

* the difference as compared to hyperopia is significant ($p < 0.05$)** the difference as compared to the respective parameter of the acquired myopia is significant ($p < 0.05$)*** the difference as compared to the uncomplicated congenital myopia is significant ($p < 0.05$)

TABLE 4. Kérdő Index for children with various clinical refractions

Emmetropia and hyperopia	Acquired myopia					High congenital myopia		
	low	moderate	high			all	uncomplicated	complicated
			all	uncomplicated	complicated			
mean ± st. err								
1.0 ±1.3	0.7 ±0.5	6.9 ±1.8*	5.2 ±3.6	11.2 ±3.2*	-3.4 ±6.2**	6.5 ±1.7*	3.0 ±1.8**	8.4 ±2.4***

* the difference as compared to hyperopia and low myopia is significant ($p < 0.05$)** the difference as compared to the uncomplicated acquired high myopia is significant ($p < 0.05$)*** the difference as compared to the uncomplicated congenital high myopia is significant ($p < 0.05$)

that the concrete form of myopia should be taken into account when an individual patient is examined for the clinical condition of his/her sclera.

It is well known that the glucocorticoid hormone cortisol is an active regulator of CT metabolism. Our studies demonstrate that there is a relative (as compared to hyperopia) decrease in the serum cortisol (SC) level in adolescents with progressive myopia and biomechanical disorders of the sclera (Table 3), but this level usually remains within the normal range (138–635 nmol/L), as was determined previously for this age group with refraction errors disregarded.

We found that in acquired myopia SC level is lower than in congenital myopia ($p < 0.05$). In complicated myopia, SC level is lower as compared to uncomplicated myopia both in acquired and congenital cases (Table 3). The lowest SC level, similar to CH and SAD values, is found in acquired complicated myopia.

We suppose that SC imbalance may be evidence of general biomechanical CT disorders in children with progressive myopia.

According to our data, CT dysplasia frequency progressed with the increase of refraction power. Such disorders were found in 33.3% of hyperopic children and adolescents. In subjects with low myopia they were found over two times as often – in 76.9% of cases. In moderate and high myopia the percentage was still higher – respectively, 82.4% and 89.2%, while in the group of our patients with high congenital myopia the disorders reached a record 91.7% of cases.

In complicated acquired and congenital myopia the prevalence of musculoskeletal disorders was no higher than in uncomplicated myopia (respectively, 77.8% and 88.3%). In both acquired and congenital myopia the most frequent types of disorders were static deformations of the spine (scoliosis or kyphosis, 45%) and the foot (flatfoot, 42%). Somewhat less frequent were dynamic deformations, primarily various symptoms of joint hypermobility (32%); in rare cases earlobe fusion and other disorders were noted. Different combinations of these

disorders were found in more than half of all cases. Since symptoms of joint hypermobility are easy to detect without any special means at an eye doctor's office, we recommend that this parameter be used for indirect evaluation of the individual CT condition and taken into account in choosing the treatment plan.

Biomechanical defects of CT and hormonal imbalance were associated with abnormalities of the VNS.

The Kérdő vegetative index (as an indicator of VNS balance) of children with moderate, high acquired uncomplicated and congenital complicated myopia was significantly higher than of those with hyperopia and low myopia (Table 4), which testifies to the fact that the VNS of these patients tends towards sympathicotonia. On the whole, the data obtained demonstrate a tendency toward KI growth with the increase of clinical refraction, which may be interpreted as evidence of a growing VNS imbalance.

The analysis of KI data obtained for the group of highly myopic children and adolescents showed that in acquired myopia the shift of KI to the negative domain (vagotonia) mainly concerns the complicated myopia cases. The difference of the mean KI values between the groups of uncomplicated and complicated acquired high myopia proved to be statistically significant, so it can be interpreted as a sign of an unfavourable course of the myopic process; more precisely, a shift towards vagotonia may be viewed as an unfavourable prognostic criterion of PVC RD development in high myopia.

According to the obtained KI values, in moderate myopia 23.1% of cases could be classed under eutonia, 69% belong to sympathicotonia, and 7.9% of cases correspond to vagotonia (all of them had PVC RD). The high myopia group included 20.5% cases of eutonia; in other cases either sympathicotonia (61.5%) or vagotonia (17.5%) were found. It is noteworthy that vagotonic cases mainly correspond to complicated myopia: while uncomplicated myopia showed the prevalence of parasympathetic influences in 11.1% of patients, PVC RD raised this figure to 23%

(which is twice as high). The maximum percentage of patients with vagotonia (57%) belonged to the group of high complicated acquired myopia; in contrast, the share of such patients in complicated congenital myopia was only 7.1%. In congenital myopia, eutonia occurred more often than in acquired myopia (27.3% and 11.8% respectively), unlike vagotonia, which was less frequent (13.6% and 23.5%, respectively).

DISCUSSION

The analysis of the data obtained enables us to make theoretical conclusions concerning the pathogenesis of progressive and complicated myopia. At the same time, we can offer practical recommendations for using certain parameters as diagnostic criteria when selecting the plan of patient management, including sclera strengthening interventions. Our studies showed that in children and adolescents with acquired progressive myopia, especially if it happens to be complicated, local biomechanical disorders (reduced CH and SAD values of the sclera, mostly in high complicated acquired myopia) are combined with general manifestations of CT dysplasia, relatively reduced cortisol level, and VHS imbalance. In future, these results may prove useful for the development of new systemic medications for the prevention of myopia progression, which could contribute to the regulation of disordered CT metabolism, hormonal shifts, and VHS imbalance.

In clinical practice, CH and SAD of the sclera can be used to assess the state of its supporting function. Reduced CH testifies to disordered biomechanical properties of the corneoscleral shell and to a progressive character of the myopic process: this may be an indication for sclera-strengthening intervention. If reduced CH is accompanied by SAD reduction, this can be viewed as a risk factor of PVC RD development or an aggravation of pathological myopic changes already present in the eye fundus: this is important, in particular, for planning the times and the scale of laser coagulation.

Congenital myopia, which should be viewed as a specific clinical form of the condition [28], is characterized by a number of distinctive features, both at the corneoscleral and the systemic levels. We established that these features include higher values of CH and SAD as compared to high acquired myopia, a less marked hormonal imbalance, and a lower variation of Kérdő index values, all of which testify to a relatively lesser activity of the process of sclera remodelling occurring during congenital myopia progression. The complicated form of high congenital myopia gives a significantly higher average KI value than the uncomplicated form; however, it mainly moves to the positive domain, which is evidence of the sympathicotonic character of VNS balance. This is different from acquired complicated myopia, where vagotonic shifts prevail.

The above characteristic features of congenital myopia may be used as additional criteria in differentiating this form from early acquired myopia. Even in cases when the form of myopia has been diagnosed precisely, these features should be used

when determining the treatment, and for prognosticating the course of the myopic process.

So far, we do not have enough facts to corroborate the hypothesis that imbalanced VNS (and KI shift) is one of the causes of weakening of myopic eye sclera. Yet, since scleral damage fits well within the general context of connective tissue dysplasia manifestations in progressive myopia, this parameter, which is definitely associated with the child's health and the state of his/her musculoskeletal system [35], may be considered, alongside other symptoms, a systematic diagnostic criterion of the weakness of the connective tissue eye shell.

Indeed, KI values generally stay within the normal range typical for eutonia in low hyperopia and low myopia. Contrariwise, this index increases in moderate myopia, demonstrating a reliable deviation from the norm into the domain of positive values, i.e. the shift of VHS balance toward sympathicotonia. With higher degrees of myopia, however, individual KI values demonstrate a very wide variation, significantly deviating towards the domain of positive or negative values. In cases of high complicated acquired myopia VNS tends towards parasymphicotonia due to the negative value of KI.

Still, KI growth, if observed dynamically, may be considered a risk factor of its unfavourable course that threatens progression or complication. Since the KI may be determined without any special conditions or devices, except one for measuring arterial blood pressure and heart rate [36], KI dynamics may be used to control the course of myopia and the effect of treatment.

Signs of joint hypermobility can also be detected with no special arrangements in an eye doctor's office [42, 43]. This parameter can be used to indirectly assess the state of individual CT and taken into account when elaborating the treatment plan, in particular when deciding whether sclera-strengthening intervention is required.

It must be mentioned that in order to ascertain the need to clinically intervene with scleral strengthening we need to track the proposed parameters over some time period. However, we had to first make sure that the suggested parameters were sufficiently linked with the myopic process and showed a significant difference in the groups with the normal and myopic refractions of diverse degrees (i.e. to perform a cross-sectional study). The results obtained in this paper show that further study is necessary.

CONCLUSIONS

Children and adolescents with progressive myopia showed biomechanical abnormalities of the corneosclera (decrease of CH and SAD) along with CT dysplasia, relatively decreased SC level, and imbalanced VNS. These disorders are more pronounced in complicated myopia, especially its acquired form. Our findings contribute to the understanding of myopia pathogenesis, as well as to diagnostic and prognostic evaluation of young myopic subjects, in particular when deciding whether sclera-strengthening intervention is required.

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